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Event-related potentials in young children

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EVENT-RELATED POTENTIALS IN YOUNG CHILDREN

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ABSTRACT

Auditory event-related potentials (ERPs) were examined in 48 subjects between 3-, 4-, and 5-years-old (n = 16, 18, and 14, respectively). The study attempted to: (a) document the ontogeny of the N1-P2-N2-P3 complex; (b) establish a profile of auditory ERPs and apply a uniform measurement system; (c) delineate the trajectory of auditory ERPs in the Ignore condition; (d) examine the developmental "status" of the nontask P3; and (e) compare the nontask P3 with the oft-reported, task-related P3b. A nontask "oddball" paradigm was used (based on p = .3 for 2 kHz Rare and p = .7 for 500 Hz Common tones). Active sites included Fz, Cz, Pz and one EOG lead. No more than 20 Rare tones were averaged per subject.

Key findings showed that application of peak-to-peak ERP minima of 40 ms and 4 μV effectively measured N1-P2-N2-P3 in all subjects and age groups. The delineation of N1-P2-N2-P3 was most consistent in response to the 70% Common tone. All 12 Common regression slopes (for each ERP by SITE) were significant, compared to only 1 of 12 Rare slopes, $p \leq .05$. The slope for the Common/P3 at Pz was 33 ms/yr (versus 10 ms/yr for the Rare/P3). Habituation may contribute to the steeper negative slope for Common (versus Rare) ERPs. In conclusion, the Ignore condition effectively delineated emerging patterns of ERP stability and change in early childhood.

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I. INTRODUCTION

Event-related potentials (**ERPs**) are far-field reflections of patterned neural activities associated with informational transactions of the brain (Hillyard & Kutas, 1983). The most prominent ERPs consist of a series of four consecutive, polarity-reversing waves known as the N1-P2-N2-P3 complex (N1 and N2 are negative; P2 and P3, positive). The time base of the N1-P2-N2-P3 complex generally is specified from 70 (earliest occurrence of N1) up to 600 or 700 milliseconds (**ms**). As time-locked manifestations of brain activities, ERPs normally occur in preparation for or in response to discrete events (Coles, Gratton & Fabiani, 1990; Courchesne, 1987). Such events may be exogenous or endogenous with regard to the subject. **Exogenous** ERPs normally occur within 70 ms post-stimulus. They are generally regarded as insensitive to the psychological state of the subject. Thus, exogenous ERPs are considered sensory, obligatory, and stimulus-bound. In short, they are sensitive to the physical properties of the stimulus (Coles et al., 1990; Donchin, Ritter, & McCallum, 1978). In fact, exogenous ERPs are so consistent across most subjects that slight variations in their normal morphology are commonly associated with sensory or neurological dysfunction (Hillyard & Picton, 1987).

In contrast, the **endogenous** components are highly sensitive to changes in the state of the subject, task relevance, and the information processing demands related to the task (Donchin et al., 1978; Hillyard & Picton, 1987; Kramer, Sirevaag & Braune, 1987). Although endogenous ERPs may be triggered by sensory events, they are not fully characterized by the sensory qualities associated with the stimulus. More important are the instructions and task(s) assigned to the eliciting events (Donchin et al., 1978) and the intrinsic characteristics attributed to the stimulus by the subject (Rosler, 1983).

Responses to auditory stimulation are divided into three sequential categories. First, the **early latency response** occurs within 10 ms of a stimulus and is referred to as the brainstem auditory evoked potential (**BAEP**). The BAEP is thought to reflect activity of the peripheral and brainstem auditory structures. Second, the **midlatency response**, which occurs between 10 and 50 or 60 ms, is thought to reflect a combination of muscle reflex activity and neural activity. Finally, the **long latency ERPs** begin between 50 and 70 ms and last in some paradigms for a full second or longer, depending on stimulus conditions, the nature and complexity of the task, and subject age (Coles et al., 1990; Courchesne, 1990; Goodin, 1986).

Oddball Paradigm

The best-known method for obtaining ERPs, known as the "oddball" paradigm, involves the random or pseudo-random presentation of low probability **Rare** stimuli (usually $p \leq .2$) among more frequently occurring **Common** stimuli (Sutton, Braren, Zubin and John, 1965). The Rare stimulus also is called the target stimulus and the Common stimulus the nontarget stimulus. References to the Common or Rare tones will be capitalized.

Auditory ERP studies often use a 2 kHz Rare tone ($p = .2$) interspersed with a 1 kHz Common tone ($p = .8$). when no specific task is assigned, the subject sits quietly and listens to the stimulus train in a passive or nontask run referred to as the **passive** or **Ignore condition.** This study uses the latter term. When the subject is given a task to perform in relation to the stimulus train, the run is known as the **Attend condition.** Normally, the subject is instructed to signal or count silently each target stimulus detected during the Attend condition. Although the task assigned may be very simple, this "task relevance" (perceived or real) is known to augment the amplitude of P3 (Picton & Hillyard, 1974; Oken, 1989). Verification of response accuracy during the Attend condition is critical.

Interest in ERPs has lasted almost three decades following Sutton et al.'s (1965) seminal publication, "Evoked potential correlates of waveforms evoked for certain and uncertain stimuli." The most dramatic of five observed waveforms was a large positive component whose peak amplitude occurred around 300 ms. This waveform was larger for uncertain stimuli in 36 experiments involving eight subjects. In a subsequent study, Sutton, Tueting, Zubin, & John (1967) documented a variety of tasks and conditions that elicited the late positive peak that has come to be known as the P300 or P3 (this paper normally uses the latter term). Sutton et al. (1965 & 1967) concluded that the mechanism which mediates the amplitude of the P3 was capable of fine discriminations and might even be preset for release by a stimulus with no particular significance.

Amplitude fluctuations of the P3 component were thought to reflect the information content of the stimulus. The array of complex psychological factors that influenced ERPs led Sutton et al. (1967) to conclude that late positive ERPs were a function of the significance of the stimuli to the subject. In effect, P3 appeared to index an underlying relationship between a variety of complex psychological factors and their influence on ERPs.

During the following two decades, continued interest in the P3 and other ERPs yielded a wealth of findings associated with task conditions, task difficulty, stimulus probability, and subjective value of the stimulus. Detailed reviews of this literature are provided by Pritchard (1981), Hillyard and Kutas (1983), and Hillyard and Picton, (1987). The myriad of psychological variables repeatedly elicited by the P3 prompted Sutton (1979) to conclude there was no longer any question about the importance of ERPs. Thus, he urged ERP researchers to pursue more formative, theoretical approaches. Sutton cast a guiding question about ERP components: "What are their **psychological** functional roles?"

ERPs and EEGs

Long latency ERPs can be derived from the same amplifiers and filters that are used for recording electroencephalograms (**EEGs**). Both are usually derived from scalp sites based on the International 10-20 system (Jasper, 1958). The distinguishing quality of ERPs compared to traditional EEG measures is that ERP activity is time-locked to a specified event (Coles et al., 1990; Courchesne, 1987). The amplitude of most ERPs is less

than half as large as the EEG, which has a "running average" of about 50 μV. In order to increase the discrimination of the ERP signal from the background EEG, time-locked samples of EEG to repeated occurrences of a low probability event are averaged (Coles et al., 1990). A cardinal assumption of ERP research is that ongoing EEG is <u>not</u> time-locked to the repetitive ERP event. Since the EEG presumably varies randomly from event to event, it is assumed that it will average to zero.

The resulting ERP function (voltage x time) contains several peaks which are quantified according to a fairly uniform nomenclature. Most standard measurement procedures specify polarity, amplitude, latency, and scalp location (Coles et al., 1990; Goodin, 1986; Hillyard & Picton, 1987). Standard procedures measure ERP latency in **ms** and the concurrent amplitude in microvolts (μV). The time base of the N1-P2-N2-P3 complex is generally specified from 70 ms (earliest occurrence of N1) up to 600 ms or longer for the P3, depending on stimulus conditions, the nature and complexity of the task, and subject age (Coles et al., 1990; Courchesne, 1990). When averaged across subjects and trials for the same condition, the composite four-wave-complex is called a **grand average**, which graphically confirms the salience of time-lock ERP measures within the continuous record of the "running EEG."

This averaging process represents a fundamental element of design that distinguishes ERP studies from EEG research. In effect, ERPs are "buried" in the running EEG and as discrete events are not well-defined unless repeated presentations of the same stimuli occur. It is through the ongoing summation or averaging of separate trials that an individual subject's ERP profile "emerges." During data collection of each trial, the target (Rare) and nontarget (Common) stimuli are stored and averaged separately. The subsequent averaging across subjects for all Common (or Rare) trials yields the composite **grand average profile.**

The initial long latency ERP is the N1 or N100. It is often referred to as the "vertex potential" because its amplitude is normally largest at the vertex (Davis & Zerlin, 1966). As the first long latency ERP, N1 may occur as early as 50 ms. Most studies that focus on the four-wave N1-P2-N2-P3 complex, use 70 ms for the earliest occurrence of N1 (Coles et al., 1990; Courchesne, 1987). Subsequent references to ERPs subsume the "long latency" referent since this study focuses on the 70 to 700 ms ERP window.

A major advantage of ERP studies is that their non-invasive approach allows investigators to manipulate various experimental factors in cooperative subjects (Donchin & Coles, 1988). Even the emergence of information processing abilities during infancy and early childhood can be examined via ERPs. In light of the scores of studies that have looked at behavioral measures of early cognitive development, what additional information of importance can be gained by using ERPs? Cohen (1985) suggests two possibilities. First, to seek new knowledge about infant memory, perception, or cognition that can be obtained from ERP work that would be difficult or impossible to obtain from behavioral work. Second, to look at the degree of correspondence when it is possible to record behavioral and ERP data.

Most studies that have attempted to elucidate the mechanisms involved in infant information processing have relied extensively on paradigms that are based on behavioral measures (Nelson & Collins, 1991). The paired-comparison and habituation paradigms are cases in point (Bornstein, 1985; Fantz, 1961, 1963). Studies of looking time may index the degree of subject interest, and the infant's ability to initiate, maintain, and terminate a response. However, the concomitant stream of information processing is not measured. This creates a potential

confound between information processing mechanisms related to response selection and those related to response execution (Nelson & Collins, 1991). In contrast, ERPs offer two important advantages. First, they provide a running record of information processing. Second, they are not limited to onset or offset measures, nor to the duration of task-specific processing (Nelson & Collins, 1991). This study is designed to capitalize on these advantages.

The present study focuses on auditory ERPs in healthy three-, four-, and five-year-olds. The emergence of ERPs during infancy and early childhood lacks systematic documentation. Although the entire time period from birth to middle childhood is not well delineated (Courchesne, 1983), this study concentrates on 3-to-5-year-olds. To some extent Sutton's (1979) focal question about the functional role of ERPs is recast for this study: What do ERPs (especially N1-P2-N2-P3) reveal about the ontogeny of information processing systems in young children? Do emergent patterns of ERP development shed light on fundamental aspects of brain development? How stable are ERPs in young children, and how early can stability of ERP waveforms be documented?

Recording Techniques

Careful consideration must be paid to several factors related to recording ERPs, especially sampling rate, the signal-to-noise-ratio, band pass filter settings and problems related to artifact.

A standard axiom in ERP research is that if the sampling rate exceeds the highest frequency of a given signal by a factor of two, it will contain all the essential information of that signal. This is known as the Nyquist frequency, which also presupposes continuous sampling and perfect filtering. In case either assumption is not fully met, a more conservative sampling rate (3-to-5-times faster than the highest frequency of interest) is encouraged (Ray, 1990). Otherwise, frequencies above half the sampling rate will result in aliasing and appear as spurious low-frequency components not present in the original EEG signal (Regan, 1989).

The time-locked ERPs typically reflect a series of small voltage fluctuations that are embedded in the much greater background EEG. Extraction of the much smaller ERPs represents a major measurement challenge (Coles et

al., 1990) that has produced various techniques for increasing the signal-to-noise ratio. Two that are essential involve filtering and averaging.

Most endogenous ERP activity occurs at frequencies between 0.5 and 20 Hz. Filtering allows for the attenuation of noise that occurs at a different frequency from the signal. Either at the time of recording or prior to waveform analysis, activity outside of this frequency range can be attenuated by means of analog or digital filters (Coles et al., 1990; Regan, 1989). Correct selection of filter settings is vital; otherwise, ERP amplitude, latency and general waveform all may be seriously distorted. In general, ERP studies employ a low band pass (**LBP**) cut-off that does not exceed 0.5 Hz (Polich, 1993). The high band pass filter (**HBP**) usually is set $\geq$ 30 Hz.

The averaging of ERPs is based on repetition of the event associated with the ERP and concurrent computer summation of the time-locked electrical activity (Glasser & Ruchkin, 1976). Summation of time-locked ERP trials hinges on three critical assumptions: relatively constant ERP signals over trials, random distribution of noise across trials, and independence of ERP signals from the background noise. As long as these assumptions are accurate, the

signal-to-noise ratio has been shown to increase by the square root of the number of trials included in the average (Coles et al., 1990). One additional issue that must be resolved concerns electrooculographic (EOG) potentials. If EOG is time-locked to the stimulus or the subject's response, it may seriously contaminate the signal.

Artifact is extraneous electrocortical activity that can interfere with ERP recordings. The ability of modern equipment to extract a hidden signal from noise does not diminish the need to take all possible precautions to minimize nonsignal contamination of ERPs. Subject comfort and clarity of instructions (especially related to movement) are critical for every ERP recording session. Subject movement and random eye movements normally are associated with non-time-locked artifact. In contrast, stimulus-locked eye movements are a potential source of persistent artifact that may propagate a signal that can be recorded as far back as the vertex (Regan, 1989).

Measurement and Quantification of ERPs

The measurement of ERP components is problematic. Although most waveform identification and measurement follow one of two basic procedures, variations in how either approach is applied within a particular study may

hamper comparisons between studies. The most basic form of ERP identification specifies respective scalp distributions and empirically measures the polarity, maximum amplitude, and concurrent latency for each peak and trough for that site. Amplitude is normally linked to either the baseline, a prestimulus level, a voltage level (base-to-peak amplitude), or to some other peak in the waveform (peak-to-peak amplitude) (Coles et al., 1990; Hillyard & Picton, 1987; Polich, 1993). Advantages of this approach are its simplicity and reproducibility. Drawbacks include coping with overlapping components and the risk of missing important information related to distinct cerebral processes that may be embedded in overlapping ERPs.

Four ERP measurement techniques that are used by various investigators are discussed briefly. The first approach specifies the earliest acceptable occurrence for the P3, and then designates the largest positive deflection within a specified latency window as the P3. For example, Picton, Stuss, Champagne, and Nelson (1984) specified 250 to 700 ms as the window for P3. Thus, P3 is identified first, followed by preceding ERPs of interest (N2, P2, and N1).

The second approach measures each waveform in the N1-P2-N2-P3 complex in a forward direction (Goodin, 1986)

beginning with N1 (normally $\geq$ 70 ms). Then based on the latency window for each respective peak, the P3 is measured last as the largest peak within a specified (minimum and maximum) latency window.

A third approach, the subtraction technique, is primarily employed for identifying N2 and P3 in the Attend condition since N2 and P3 are both known to be enhanced by the active condition. The sum of all nontarget stimuli for each subject is subtracted from the sum of all target stimuli (Goodin, Squires, Henderson, & Starr, 1978). This "ERP difference complex" is examined within specified latency windows. The subtraction technique can be combined with either forward or backward procedures (above).

A fourth approach, principal component analysis or **PCA**, is based on multivariate statistics and is considerably more complex. PCA describes the structure of variance associated with a set of ERP waveforms and is derived from the pattern of covariance between the voltage values for each timepoint (Coles et al., 1990). Although PCA offers a set of analytic tools that can neatly dissect ERPs into various overlapping components (Hillyard & Picton, 1987), the technique has notable shortcomings. First, it does not always provide a valid representation of experimental variability (Wood & McCarthy, 1984), nor are the resultant

waveforms easy to interpret as valid physiological entities (Picton, 1992). Second, PCA is not able to discriminate between variance due to amplitude change or latency change (Regan, 1989). Thus, it should not be utilized for components whose latency is known to change as a function of experimental manipulation (Hillyard & Picton, 1987). The high likelihood of developmental and individual variability in young children makes PCA particularly problematic as an analytic tool with younger subjects.

For waveforms that are particularly difficult to measure, a comparison/extrapolation procedure may augment any of the aforementioned approaches (see Brown, Marsh, & LaRue, 1983; Tokioka, 1987 for examples of how this procedure is applied).

The P300 complex

No ERP has attracted more attention than the P300. It is a positive wave that normally has maximum amplitude over midline parietal and central regions. The P3 generally occurs between 250 and 600 ms in normal adults (Oken, 1989), although more complex or demanding tasks may produce P300 latencies as late as 900 ms or longer (Courchesne, 1987; Goodin, Squires, & Starr, 1983; Kutas, McCarthy, & Donchin, 1977; Regan, 1989).

Fundamental to P3 studies is the role played by low probability, infrequent stimuli. In most designs, the added element of task relevance (assigned to the subject in the Attend condition) accentuates P3 amplitude. The P3 can be elicited by stimuli from auditory, visual or somatosensory modalities (Oken, 1989). The P3 can even be elicited by using a set time interval within a stimulus train, so that the absence of a stimulus in that train induces the P3 (Picton & Hillyard, 1974).

Two distinct waveforms that have been associated with the P3 are of interest in this study: the ubiquitous, task-dependent **P3b**, as reported by Sutton et al. (1965); and, the earlier-occurring **P3a** (Squires, Squires & Hillyard, 1975). Three factors related to P3a are notable. First, it is evoked by occasional shifts in either the pitch or loudness of an ongoing stimulus train, even if the subject is not assigned any task in relation to the target stimulus. The absence of any pre-assigned task demonstrates that P3a is a distinct brain phenomenon from the task dependent P3b (Squires et al., 1975). Second, P3a has a more frontal-central distribution in adults. Third, P3a latencies may occur between 220 and 280 ms, which is at least 60 ms earlier than P3b (Polich, 1988). This P3a component may be analogous to the "P3" component observed

by Roth (1973) under similar conditions--inattention to unpredictable stimulus shifts. Roth reported an even shorter mean latency of 217 ms.

This raises the issue of the earliest P3a occurrence. It may not be feasible to fully resolve this issue because of a more complex problem posed by Squires, Donchin, Herning and McCarthy (1977). They observed that N2 (a negative peak at 210 ms, thus the N210 wave) reflected stimulus frequency independent of task. This was so closely linked with the occurrence of P3a in the same experimental condition (Rare stimulus detected regardless of task requirement, including an "inattentive state"), that Squires et al. (1977) speculated that N210 and the following P3a at 270 ms may be interdependent aspects of the same process. In effect, if the non-task dependent P3a is embedded in N2, it may not be possible to disentangle P3a and N2.

The fact that P3a is not observed as consistently as P3b poses another challenge: How to characterize P3a if it represents a distinct brain phenomenon from that associated with P3b? Squires et al. (1975) suggest that P3a detects any "mismatch" in an ongoing stimulus train. Thus, it may function as a sensory mechanism that registers change in background stimulus with or without an assigned task.

High information content in combination with an infrequent event consistently elicits the P3b. In adults, the task-dependent P3b has a mean latency of approximately 350 ms and only occurs when the subject actively attends to the stimulus train (Squires et al., 1975). The reported latency range for P3b varies considerably in different studies. Usually, it is evident between 280-600 ms (Courchesne, 1990; Picton, 1992). A marked decrease in amplitude and increase in latency is noted in relation to increased perceptual difficulty (Ruchkin, Sutton and Mahaffey, 1987).

The most important antecedent conditions related to P3 amplitude are stimulus probability (infrequency) and task relevance. The early work of Sutton et al. (1965, 1967) showed clearly that P3 amplitude was inversely related to the probability of task-relevant events. As stimulus probability decreased, P3 amplitude increased. Subsequent studies extended the a priori influence of event probability by showing that the sequence of preceding events and subjective probability actually control P3 amplitude (Duncan-Johnson & Donchin, 1977; Squires, Wickens, Squires, & Donchin, 1976).

Another factor that influences the amplitude of P3b is the relevance of the eliciting stimulus. Generally speaking, even infrequent events do not elicit P3b if the subject is performing a different task concomitant to the presentation of the target stimulus (Duncan-Johnson & Donchin, 1977). The P3b is elicited only if the subject **uses** the stimuli to perform a relevant task (Coles et al., 1990; Donchin, 1981). In fact the greater the processing demands for primary-task relevant events, the more P3 amplitude increases (Sirevaag, Kramer, Coles, & Donchin, 1984). Thus, processing demands appear to interact with simple forms of task relevance.

A fundamental antecedent condition for P3 latency is stimulus evaluation time. If P3 amplitude is sensitive to probability, then processes required to establish the rareness of an event must occur before P3 does (Donchin, 1979). Support for this view includes evidence that P3 latency increases as categorization becomes more difficult (Kutas, McCarthy, & Donchin, 1977). Conversely, P3 latency is affected little, if any, by response selection factors or stimulus-response compatibility (McCarthy & Donchin, 1981; Ragot, 1984). The latency of P3 apparently depends more on the completion of encoding processes (stimulus categorization or evaluation) than it does on processes related to current overt response (Coles et al., 1990).

How consistent is the latency of the P3? Using the standard "oddball paradigm," Polich (1986) showed that P3 latency was consistent over successive two-trial averages in normal young adults with fewer than 20 trials. Although P3 amplitude decreased progressively over the same two-trial averages, Polich concluded that even a few trials may yield a reliable assessment of individual component latency. Polich (1987) also showed that minor variations in task conditions slightly altered auditory P3 latency, but only at Pz when the task was to silently count each Rare tone occurrence. The non-counting finger tap or button-press responses were 12 to 22 ms shorter than the counting task for 16 college students. In a serial study of nine subjects, Sklare and Lynn (1984) found up to an 18 ms difference in P3 latency between trial 1 and 2, and up to a 12 ms difference between the average of two trials performed 15 to 30 days apart. Whether or not subtle task variations with young subjects would reveal latency shifts with younger subjects is unknown, but merits attention.

The specified P3 latency range varies considerably from one study to another. P3 latency has been reported by Brown, Marsh, and LaRue (1983) as the first positive wave to occur after 250 ms. Picton, Stuss, Champagne and Nelson (1984) identified the P3 between 250 and 700 ms. Both

Courchesne (1984) and Howard and Polich (1985) defined P3 between 225 and 400 ms. Using a more fine-grained approach, Polich, Howard and Starr (1985) defined the earliest portion of P3 as "P3a" (from 220 to 350 ms); if a second positive wave occurred immediately after "P3a," subjects were said to have a "P3b" waveform (if evident between 280 and 500 ms). Measurement procedures for the P3 are so diverse that detailed comparisons between studies often are not practicable. A major benefit of a study involving younger subjects is to document the range and standard deviations for each ERP in the four-wave N1-P2-N2-P3 complex.

Auditory ERPs and Development

The auditory P3 has been used to assess basic information processing capabilities in children and adults. Several studies have contributed to a general profile of ERPs across the lifespan (Brown et al., 1983; Courchesne, 1978; Goodin et al., 1978; Pfefferbaum, Ford, Wenegrat, Roth, & Kopell, 1984; Picton et al, 1984; Polich, 1991). Children between six years old and mid-adolescence exhibit a progressive decrease in P3 latency. Most studies of children in this age range, however, have limited samples of young subjects. Below age eight, for example, Goodin, Squires, Henderson, and Starr, (1978) reported one child;

Finley, Faux, Hutcheson and Amstutz, (1985), eight; Howard and Polich (1985), five; and, Pearce, Crowell, Tokioka and Pacheco (1989), nine.

More recent studies have included larger samples of young subjects. Satterfield, Schell, Nicholas, Satterfield and Freese (1990) compared 15 normal and 15 attention-deficit hyperactivity disorder (**ADHD**) boys who were first tested as 6-year-olds and retested later as 8-year-olds. An abnormally small P3b to target stimuli was observed in the ADHD sample. Satterfield et al. (1990) concluded that the small P3b in ADHD subjects may relate to reduced levels of noradrenergic activity. The study included both Ignore and Attend conditions. Auditory stimuli were 1 kHz sine wave tone bursts of 10 ms duration at 75 dB (nontargets) or 85 dB SPL (targets). As 6-year-olds the normal and ADHD subjects had average P3b amplitudes of about 5 μV for the Ignore condition. By age eight, P3b amplitude decreased to about 4 μV in each group. The 6-year-olds' P3b amplitude for the Attend condition averaged 11 μV for normals and about 7 μV for ADHD subjects. These values suggest that with subjects less than 6-years-old, if a P3 is observed in an Ignore condition, the peak amplitude for some subjects may be in the 4-to-7 μV range. Ivey (1992) examined 45 normal 6- and 8-year-old subjects and 110 children suspected of central auditory processing deficits. Tone

pips were used (a 500 Hz nontarget and a 2 kHz target) with an interstimulus interval (ISI) of 2 s. Ivey (1992) did not report results by age or number (only by percentages and quartile ranges) and data were based on only one site (Cz). However, Ivey does report a P3 mean latency of 335 ms (SD = 35) and a mean amplitude of 10.1 μV (SD = 3.5) for the normals (N = 45). In a study of older children (age range = 9.2 to 11.6 years), Jirsa and Clontz (1990) examined 18 subjects with central auditory processing disorders (CAPD) and 18 normal comparison subjects. Tone pips at 65 dB HL were used in the 20% oddball paradigm (target = 2 kHz; nontarget = 1 kHz) that revealed significant P3 differences between groups for latency (315 vs. 429 ms) and amplitude (8.7 vs. 5.2 μV) for the normals compared to the CAPD subjects. Latencies differences also were significantly shorter for the normals for N1 (88 vs. 119 ms) and P2 (171 vs. 220 ms)($p < .01$). Jirsa and Clontz (1990) also reported the slope (in years) for N1, P2, and P3 (based on the regression line for normals) with each ERP revealing an increased negative slope (9, 22, and 40 ms, respectively). Subjects counted the occurrence of each target silently.

By mid-to-late adolescence, P3 waveforms are equivalent to or approximate latencies and amplitudes of adults (Goodin et al., 1978; Finley et al., 1985; Howard &

Polich, 1985; Pearce, Crowell, Tokioka & Pacheco, 1989; Polich, 1991; Polich, Ladish, & Burns, 1990). Examination of the slope of the latency decrease from middle childhood to adolescence reveals a range from as small as 3.6 ms per year (Finley et al., 1985) to notably larger yearly slopes of about 20 ms per year. Goodin, et al. (1978) reported an 18.4 ms per year decrease at Cz, and Pearce et al. (1989) reported 20.4 ms for Cz and 19.3 ms for Pz. Other studies reported values between about 7 and 15 ms per year through adolescence (Enoki, 1990; Howard & Polich, 1985). By late adolescence or early adulthood, P3 latency reaches a plateau after which it begins to slow down slightly at a rate of about 1.3 ms per year across the span of adulthood (Polich, 1991).

Current understanding of the developmental trajectory of ERPs in infancy and early childhood is quite limited. In a sample of 30 infants Tokioka (1987) examined possible precursors of the auditory P3 in subjects between one and three months old. Twenty infants were normal term (**NT**) and 10 were low-risk preterm (**PT**). All were tested using a standard auditory "odd-ball" paradigm (Rare targets $p = .2$) with pure tones presented at 65 dB SPL.

The infants in Tokioka's study (1987) exhibited a consistent ability to distinguish Rare from Common tones.

Two distinct positive ERPs were evident: late positive component one (**LPC1**) and two (**LPC2**). LPC1 occurred between 548 and 608 ms, and LPC2 appeared between 788 and 813 ms. Differences in mean latencies between NT and PT subjects were not significant, but mean amplitude values for NT infants were significantly greater at LPC1 and LPC2. Thus, rudimentary auditory information processing skills are observable at least by three months old (Tokioka, 1987). Between groups differences in amplitude indicate that ERPs can detect functional processing differences in relation to birth status in the early postnatal period.

Speech stimuli also have been used with infants. Of particular interest is the work of Kurtzberg and Vaughan (1985), Kurtzberg, Stone, and Vaughan (1986), and Molfese, Morse, and Peters (1990). For example, Kurtzberg and Vaughan (1985) demonstrated notable differences for speech compared to tonal stimuli by recording late cortical auditory evoked potentials (**CAEP**) in neonates. The production of / da / and / ta / speech sounds yielded a notable negative ERP at approximately 800 ms in infants who were born very low birth weight (**VLBW**) and in normal full-term newborns. By testing both groups at the equivalent postconceptional age of 40 weeks, it was possible to show that in VLBW infants the CAEP was significantly less mature

than that of the term babies. Differences between NT and VLBW subjects were less marked for pure tones (than for speech stimuli). Kurtzberg and Vaughan (1985) concluded that CAEPs may serve to evaluate higher order auditory processing in infants.

In a longitudinal follow-up that included 10 time points across infancy, Kurtzberg et al. (1986) systematically assessed 21 NT infants through two years old (with monthly testing the first 6 months, then at 9, 12, 18, and 24 months). Stimuli were presented via a loudspeaker with a peak intensity of 85 dB SPL at the infant's head. Three consonant/vowel presentations (/da/, /ba/, and /ta/) were employed. Results showed that an initial positive peak occurred around 120 ms for /da/ and /ba/, but not before 220 ms for /ta/. This 100 ms difference underscores the importance of interpreting differences between studies with considerable caution. In early infancy (based on term birth or its equivalent), Kurtzberg et al. (1986) also showed that midline central positivity to /da/ corresponded to concomitant negativity overlying the lateral temporal regions. By the end of the first postnatal month, however, these lateral temporal waveforms had shifted to surface positive. The longer latency ERP showed a negative peak near 600 ms for /da/ and /ba/ and 700 ms for /ta/.

Neonates discriminated between speech sounds that differed along specific phonetic dimensions: consonant-vowel syllables /da/ and /ta/, which differ in terms of voice onset time (**VOT**). Whichever stimulus was the Rare target (p = .14) yielded a distinct negativity ERP at 880 ms for /da/ and 820 ms for /ta/. Amplitude was greatest at Fz. Somewhat similar findings were reported by Courchesne, Ganz, and Norcia (1981) in a study of 4-to-7-month-old infants. However, Courchesne et al (1981) employed an infrequent visual stimulus (p = .12) and found a large negative ERP (called Nc) at Fz at 700 ms. This correspondence across modalities seems to support the possibility of non-modality-specific processing for visual and auditory Rare stimuli (Kurtzberg et al., 1986). The variety of longitudinal changes noted by Kurtzberg et al. (1986), in early infancy along with subsequent findings of auditory and visual modality differences by Courchesne (1990) suggest that this view may be an oversimplification. In fact, most recent studies of cross-modal ERP processing support the view of modality independent generators for the P3 (Johnson, 1989a, 1989b).

Another salient finding of Kurtzberg et al. (1986) was that the lateral temporal pattern of response developed on a different maturational time course (compared to midline ERPs) during the first 24 months. This differential

maturation between midline and lateral responses was most notable for /da/ compared to /ta/, helped to distinguish preterm from early post-term development, and continued on distinct developmental trajectories (midline vs. lateral) during the first two years.

This pattern of development is consistent with the findings of Molfese et al. (1990) who employed ERPs to examine the effects of an operant training paradigm in which parents consistently named novel objects (either "gibu" or "bidu") that their 14-month-old infants held. The ERPs collected in the posttraining period differed specifically from pretraining ERPs along the lines of a "match" versus a "mismatch." Two regions of the ERP waveform varied reliably: an early component that changed bilaterally over the frontal regions of both hemispheres, and a late-occurring lateralized response that only occurred at left hemisphere sites. The bilateral ERP was positive, frontally distributed, and only occurred when there was a "match" between the auditorily presented word and the object that the infant held. This peak was evident between 20 and 100 ms following the auditory onset of the object name. In cases of a "mismatch" the polarity of this early waveform inverted and produced a negative deflection within the same basic time frame. Between 520 and 600 ms, a large positive ERP occurred, but only over the three left

hemisphere sites when the infant listened to a stimulus that did not name the object being held.

A similar pattern of early bilateral response that is followed in time by a lateralized (left hemisphere) change in the ERP had been noted in earlier studies by Molfese (1984) and colleagues (Molfese & Hess, 1978; Molfese & Molfese, 1988). The present extension to semantic content at 14 months of age suggests that the processing of a variety of types of materials during speech perception and word discrimination reflects multiple levels of involvement within the central nervous system and not simply a left- or right-hemisphere response. In short, brain responses to speech and language input are multidimensional and interactive, activate various distinct processes, and occur both sequentially and in a parallel during the processing of information (Molfese et al., 1990).

The N1-P2 complex in children is not well-documented. Relatively little is known about N1 or the auditory vertex potential, as it is also known. No longitudinal or cross-sectional studies of N1 span childhood in awake subjects (Courchesne, 1990). According to Courchesne (1990), N1-P2 that is evoked by speech stimuli in adults is not readily identifiable before age 10 (years) or older. This claim is puzzling in light of Molfese et al.'s (1990) findings with

the speech segments /ba/, /da/, and /ta/. In light of how little is known about the developmental trajectory of N1 (and P2) in infancy and early childhood, statements about patterns of ERP development between birth and age five are best regarded as tentative and in need of corroboration.

The work of Molfese and colleagues with young subjects is quite revealing in relation to speech and language stimuli (Molfese, 1984; Molfese & Hess, 1978; Molfese & Molfese, 1988). There is also evidence that the vertex potential in infants exposed to tone pips occurs in a time frame that is quite similar to that of adults (Shucard, Shucard, & Thomas, 1987 & 1988). Compared to young adults, latencies to tone pips for 1-month-, 3-month-, and 6-month-old infants (12 in each category) were 105, 118, and 136 ms, respectively (vs. 94 ms for the adults). Unpublished data of 17 5-to-7-year-olds by Todorovich, Pearce, and Crowell (1990) consistently observed the N1 in the 80-150 ms range. Other studies also report that N1 and P2 reach or approximate adult latencies by five or six years, if not earlier (Goodin, 1986; Goodin et al., 1978).

These findings raise several questions about N1. What is its developmental trajectory prior to age five years? Does N1 approach adult values to tonal stimuli before age five? Is N1 on an earlier developmental trajectory than

the P3? That is, does N1 approach adult values before P3 does? Is N1 less dependent on factors associated with learning than is the P3? If so, do the latency and amplitude for N1 develop independently of those associated with P3? In a broader context, what characterizes the normal developmental trajectory for N1-P2-N2-P3? Is this ERP complex tightly linked and interdependent, or do the different components evolve along unique pathways that are functionally and morphologically independent?

There is no simple answer to such questions. It is not always possible to specify that a particular component recorded under one set of circumstances is the same as that recorded under differing circumstances (Coles et al., 1990), especially with young subjects. How certain can an investigator be that the latency of a particular peak that varies between two experimental conditions is the same component versus two different components that are present in two distinct (though similar) conditions? The results obtained need to be examined carefully and compared with what is already known about the ERP(s) in question. Procedurally, this requires a careful blending of several empirical and theoretical factors in order to arrive at the definition of each component, including: polarity, latency, scalp site, and sensitivity to experimental manipulation (Coles et al., 1990; Polich, 1993; Rosler, 1983).

Different ERPs seem to emerge along modality-distinct pathways. For example, P3b can be elicited to visual target events in normal 3-year-olds. However, differences between auditory and visual P3 development are notable (Courchesne, 1990). Auditory P3b latencies ranged from 474 to 550 ms between 4.8 and 10.9 years, and then dropped sharply to 344 ms by 12.3 years old. Although the amplitude for a well defined visual P3b was evident between 3.0 and 3.7 years, it occurred much later (800-900 ms), decreased gradually, and did not reach 400 ms until adolescence. The possibility of distinct developmental trajectories for the auditory P3 and the visual P3 needs further study and underscores the importance of modality-specific documentation of ERPs from birth through age five.

Attempts to delineate the emergence and functional significance of the P300 complex should recognize: (a) the emergence of P3 varies as a function of modality (Courchesne, 1990); (b) it is unclear how P3 may vary in relation to task condition--whether or not the non-task Ignore condition may induce an earlier P3a than the "equivalent" P3a in a task-related paradigm with identical stimulus parameters; and, (c) P3b may emerge before it can be clearly delineated experimentally due to young subjects limited ability to respond behaviorally to verify discrimination of the Rare versus the Common tone.

Childhood ERP investigations are likely to elucidate patterns of early cognitive development. However, gaps in current understanding of ERP development reflect a need for much more work in this area. In particular, studies of infants and toddlers need larger samples.

Enhancement of P3 amplitude in the task-related (Attend) condition has been substantiated in a multitude of studies since Sutton et al.'s original publication (1965). The host of variables and task conditions that elicit the P3b is extensive (Donchin & Coles, 1988). The Attend condition consistently induces an enhancement in the amplitude associated with P3b. Conversely, the primary function of the Ignore condition is ostensibly to establish a baseline for the anticipated enhancement of the ERPs in the Attend condition. In fact, Shibasaki and Miyazaki (1992) suggest that P3 (presumably the P3b) is not evident before age five (years). This very likely underestimates the utility of the Ignore condtion.

In younger subjects the Ignore condition may offer considerable insight into the ontogeny of auditory information processing. The use of a finger signal to verify detection of an auditory target is problematic with 3- or 4-year-olds. Thus, a basic premise of this study is that the nontask Ignore condition is the preferred starting point for examining the emergence and progressive development of the entire N1-P2-N2-P3 complex.

Statement of the Problem

Several challenges are evident for investigations of ERPs in infants or young children. First, is the need for a definitive childhood profile of ERP morphology (Shibasaki & Miyazaki, 1992). In order to create an ERP profile, a uniform procedure for ERP identification and measurement is needed that incorporates latency, polarity, amplitude, and site for a particular experimental condition. If N1 is consistently evident in infants by 150 ms or earlier, as suggested by Goodin (1986) and Shucard and Shucard (1987), but exhibits an amplitude of less than 5 μV, failure to identify N1 may falsely push the entire four-wave complex into a much later latency window.

Second, to determine if the developmental trajectories of ERPs can be sufficiently delineated in the Ignore condition. If so, does the ontogeny of N1-P2-N2-P3 differ notably in relation to the Common versus Rare condition?

Third, what is the developmental status of the auditory N1-P2-N2-P3 complex in three-year-olds, and how does it evolve by age five years? Is the entire N1-P2-N2-P3 complex interdependent, or do the ERPs preceding P3 develop along independent pathways?

Fourth, the age at which the P300 complex emerges and is consistently evident has not yet been clearly ascertained. Studies with larger samples are needed to clarify the developmental status of the auditory and visual P3 in this age range. When is the P3 clearly evident in each modality? Does its ontogenetic timetable differ notably for different modalities?

Fifth, once the earliest occurrence of P3 is better understood, more fine-grained designs will need to address variations that can be induced as a function of stimulus conditions. For example, how amenable to variations in stimulus parameters is the P3 in any modality? How much does P3 differ in relation to the Ignore versus the Attend condition? Given the task-dependent nature of P3b, does P3a exhibit a developmental timetable independent of P3b?

Sixth, different investigators need to corroborate findings related to the entire N1-P2-N2-P3 complex by age, condition, modality, and sex. There is a need for a greater variety of designs (longitudinal, cross-sectional, cross-sequential, or even a cross-modal case study approach) in childhood ERP studies. Longitudinal studies are especially needed in order to delineate the ontogeny and stability of ERPs across childhood.

Finally, theorizing related to childhood ERP development is overly speculative. Modality specific findings need to be replicated by different investigators. Until this occurs it is not feasible to ascertain if any specific ERP may predict subsequent information processing abilities as has been indicated by non-ERP investigative approaches (Bornstein, 1985; Rose, Feldman, Wallace, & McCarton, 1991).

It is important to capitalize on the ability of ERPs to measure the ongoing stream of information processing (Nelson & Collins, 1991), especially if ERP studies of infancy and early childhood intend to shed light on the interplay between early maturational and environmental influences in the development of cognition.

The purposes of this study were:

1. To examine the developmental status of the auditory N1-P2-N2-P3 complex in 3-year-olds and to delineate its ontogeny through age five years.

2. To establish a definitive childhood profile of auditory ERP morphology by developing and applying a uniform measurement procedure for ERP identification.

3. To determine if the developmental trajectories of auditory ERPs can be sufficiently delineated in the Ignore condition. If so, does N1-P2-N2-P3 differ significantly as a function of the Common versus Rare tone?

4. To examine the extent to which the P300 complex emerges and is consistently evident in 3-to-5-year-olds in the nontask, Ignore condition.

5. To compare the morphology of the nontask auditory P3 with current developmental findings of the auditory P3b.

The age range designated for this study is based on several considerations. First, documentation of auditory ERP development below five years old is inadequate. Second, although the entire span between birth and five years merits closer study in all modalities, there is sufficient uncertainty about when the four-wave N1-P2-N2-P3 complex (especially the P3) is consistently evident to warrant a "work-backwards-until-found" approach. Third, 3-to-5-year-olds were more likely to cooperate with testing conditions than 1- or 2-year-olds. Fourth, expansion of the ERP data base in the 3-to-5-year-old range would help

close the gap between infant ERP studies (Courchesne, 1990; Kurtzberg et al., 1986; Molfese et al., 1990; Tokioka, 1987) and studies of older subjects.

This study examined morphological patterns of auditory ERP development from 36 to 69 months old. Primary variables of interest included latency (from 70 to 700 ms), polarity, amplitude, scalp site, and stimulus condition. The study was designed to: (a) develop a profile of the classic N1-P2-N2-P3 complex in 3-to-5-year-olds; (b) to pilot a consistent and replicable ERP measurement system (i.e., an ERP template); (c) to explore the status of and possible emergence of the auditory Rare/P3 waveform in 3-year-olds; and (d) to begin to delineate patterns of stability and change within and between individual waveforms of the classic N1-P2-N2-P3 complex.

II. METHOD

Design

A two phase cross-sectional design was employed: A preliminary phase involving 16 subjects, followed by a primary phase with 60 additional subjects. The intent of the preliminary phase was twofold: (a) to ascertain viable stimulus parameters for data collection with 3-to-5-year-olds, and and, (b) to develop basic criteria for systematic identification and quantification of the four-wave (N1-P2-N2-P3) ERP complex between 70 and 700 ms. Subjects tested in the preliminary phase were not included in the statistical analyses.

The primary study used the basic measurement criteria that were piloted in the primary phase of the study and attempted to identify and measure the latency, polarity, and amplitude of ERPs at three scalp sites (Fz, Cz, and Pz) in 15 or more subjects per age group.

Subjects

All subjects were between three and five years old (Table 1). Sixteen subjects were tested in the preliminary Study. The primary study included 60 additional subjects,

although 12 were dropped due to data loss, noisy data, extreme fidgetiness, or failure to pass a hearing test. Subjects were drawn from a variety of community sources. The majority were recruited from eight preschools within three miles of the research site. Six referrals also came from the Department of Pediatrics at Straub Clinic and Hospital, Inc., Honolulu, Hawaii.

Subjects were healthy, had normal hearing and no record of neurological or auditory problems at the time of testing. Based on parental report and the pretesting orientation session between parent, child and the investigator, each child's language development was considered to be in the normal range. A detailed consent form was explained to and signed by the parent(s) or guardian. The family of each subject was paid $12 through a research grant from the Pacific Health Research Institute in affiliation with the Straub Trust Foundation.

Table 1. Subjects included in preliminary and primary phases of study are listed by their age (in years).

Age (in years)	3	4	5
Preliminary phase	4	5	7
Primary phase	22	20	18

Apparatus

A Nicolet Pathfinder II was used for all ERP data collection. The Pathfinder II was equipped with two amplifiers, an SM200 and an SM200L. Each amplifier collected data independently in two separate channels. Stimuli were delivered via the Auditory Stimulator (SM400). An SM100 Stimulus Controller module controlled the stimulus rate, the duration of each stimulus, the system sensitivity, and the high and low bandpass filter settings. Data acquisition was displayed on-line throughout each testing session via a 15-inch video monitor capable of displaying up to 16 channels of data simultaneously. The Pathfinder II is equipped with a dual cursor system for waveform measurement and identification.

Pathfinder II software established a communication link between the main processor (1280) and the microcomputers (Z80s) used in the stimulus and amplifier modules. Communication between these units was carried over a standard IEEE-488 bus interface. A special software program developed by Nicolet allowed for independent control of stimulus parameter settings for each channel. The Pathfinder II can be controlled via an automated program mode or by manually setting the stimulus and

amplifier parameters. This study used the automated mode.

Stimulus characteristics and data collection procedures included: a time base of 1024 ms with a 100 ms prestimulus epoch; a digitization rate of 2 ms per data point; bandpass filter settings of 0.5 Hz (low) and 30 Hz (high) for all mid-line leads (Fz, Cz, and Pz) and a 1 Hz LBP for the EOG channel. The system sensitivity was 500 μV. The automatic artifact reject level was preset to discard all subject output that exceeded 95% of the system sensitivity. The 500 Hz and 2000 Hz pure tone stimuli were presented at 70 dB SPL with a rise/fall time of 9.9 ms and a 50 ms plateau. The interstimulus interval was 3.3 s. All stimuli were presented binaurally via Nicolet tubal insert phones (TIPS) with disposable 13 mm Axon Systems foam attachments for each subject.

Procedure

Active EEG leads were placed at Fz, Cz, and Pz, according to the International 10-20 system (Jasper, 1958). All leads were referenced to a linked (right) mastoid. The forehead (Fpz) was the ground. Subject impedances were $\leq$ 7 kΩ for mid-line leads, the EOG lead and reference electrode. Each subject's EOG was monitored via a lead

placed at the outer canthus of the right eye. The EOG data verified whether eye movement artifact contaminated the mid-line (Fz, Cz, Pz) leads. A standard oddball paradigm based on pure tone stimuli was used: $\underline{p}$ = .8 (Common) and .2 (Rare) in the preliminary study, and $\underline{p}$ = .7 (Common) and .3 (Rare) in the primary study. The probability level for the Rare tone was increased to 30% in the primary study to improve the signal-to-noise ratio. Each subject served as his or her own control by receiving a pseudo-random set of pure tones presented binaurally at 500 and 2000 Hz.

Prior to the ERP testing session, a two minute hearing test was administered to minimize the likelihood of notable hearing difficulties for each subject. Pure tones of 500 Hz, 1 kHz and 2 kHz were presented independently to each ear at an intensity of 50 dB SPL. The tones occurred in a random sequence that included two presentations of each tone to each ear. Thus, the hearing test included 12 tones with a five second pause between each tone. The subject was instructed to point to the ear in which each sound was heard. If a child correctly identified less than 10 of the 12 tones, an alternate sequence of 12 tones was presented. Subjects who identified the correct ear of stimulus presentation for less than 10 tones for <u>both</u> tone sequences were not included in the final study.

Preliminary phase of study

The purposes of the preliminary study were twofold: to establish acceptable stimulus parameters for auditory ERP data acquisition with 3-to 5-year-olds, and to pilot a uniform set of measurement criteria for the identification of the four-wave N1-P2-N2-P3 complex.

The stimulus parameters that were used at the start of the preliminary phase are summarized on the left side of Table 2.

Table 2. Stimulus parameters used in this study

Parameter	Preliminary Phase	Primary Phase
Band pass	2 Hz to 30 Hz	.5 Hz to 30 Hz
EOG	.5 Hz	1 Hz
Tone	2000 Hz target	2000 Hz target
	500 Hz nontarget	500 Hz nontarget
Intensity	70 dB SPL	70 dB SPL
Sensitivity	200 μV	500 μV
Probability	20% Rare	30% Rare
	80% Common	70% Common
Rares (total)	30 stored (max)	$\geq$ 8 - 20 stored
Commons (total)	120 stored (max)	$\geq$ 14 - 68 stored
Test period	11 min	11 min 40 s
Pause	none	mid-train
Eyes	open	closed

Several modifications in stimulus parameters occurred during the preliminary study. Based on an initial bandpass settings of $\geq$ .2 Hz for the low bandpass (**LBP**) and $\leq$ 30 Hz for the high bandpass (**HBP**), a system sensitivity of 200 μV, and scalp impedances below 7 kΩ, artifact rejection rates for Common and Rare tones exceeded 80%. The signal-to-noise ratio was persistently low for preliminary phase subjects. For example, 107 out of 120 Rare tones were rejected for the four 3-year-olds who were tested in the preliminary phase. The mean number of accepted Rare tones for the first 12 preliminary subjects tested with the 20% oddball paradigm was 10.58.

Five areas were identified as major sources of difficulty. First, the uninterrupted 11-minute duration of the original stimulus train was very long, especially for the 3- and 4-year-olds. Second, the signal-to-noise ratio was very low and clearly needed to be increased. Third, the .2 Hz LBP settings for Pz, Cz, Fz, and the EOG seemed to accentuate high artifact rates. Fourth, the system sensitivity of 200 also appeared to contribute to high rates of artifact rejection. Fifth, subjects were not able to keep their eyes open and fixate on a specific spot on the wall for 11 minutes.

Design changes related to all of the above were implemented prior to completion of the preliminary study. The first and second problems (above) were resolved as follows. In order to increase the signal-to-noise ratio within the stimulus train, the probability of occurrence of the Rare tone was increased from $p = .20$ to $p = .30$. The revised stimulus train included 160 stimuli (112 Common and 48 Rare tones) and ran for 11 min 45 s. This was about 40 s longer than the original program. However, by inserting a system pause at the half-way point, 80 tones (56 Commons and 24 Rares) were generated by the stimulus modulator. Then after 5 min 50 s, a system pause occurred in order to give each subject a 3-5 minute break. During the break a game-like stretching activity was conducted. A drink of water was also offered to each child. If necessary, the parent took the child to the restroom. Prior to restarting the program, all impedances were rechecked. When restarted, the program generated a different train of 80 tones, 56 that were Common and 24 that were Rare. However, once the Nicolet Pathfinder II processed and stored 20 Rare tones, data acquisition stopped automatically.

The decision to limit the maximum number of Rare targets to 20 was based on several factors: (a) empirical findings indicate that adequate waveform delineation can be based on 20 Rare stimuli (Polich, 1993; Ladish & Polich,

1989); (b) not wanting to skew results based on a subset of highly cooperative subject who might have higher numbers of Rares accepted, but who behaviorally might not be representative of their age group; and, (c) the obvious inverse relationship between length of time in the testing setting and the likelihood of collecting good data--after 30-40 min most subjects became increasingly restlessness, fidgety, and uncooperative.

Problems associated with the band-pass settings and the system sensitivity setting were resolved as follows. The initial low band-pass (LBP) settings of .2 Hz for Fz, Cz, and Pz were increased to .5 Hz due to persistent artifact rejection rates of 80% or higher in 9 of the first 12 subjects tested in the preliminary phase. The LBP setting for the EOG also was increased to 1 Hz. Continued difficulty with artifact resulted in resetting the system sensitivity from 200 to 500. This resulted in a notable reduction in the artifact rejection rate. In three cases involving highly compliant subjects, initial data acquisition based on a system sensitivity of 500 yielded good data with artifact rejection rates below 20%. Following a five minute break, a replication run was begun with only one change: the system sensitivity was reduced to 200. In all three cases, the replication run was aborted after 40 to 50 tone presentations because the artifact

rejection rate exceeded 95% for all stimuli. There was no apparent change in subject compliance during any replication run.

The last area of apparent difficulty in data collection related to children not being able to keep their eyes open and focused on a single spot on the wall for 11 m. By asking subjects to close their eyes, artifact rejection rates associated with excessive eye movements were reduced substantially. Additional procedural details related to stimulus parameters used for the primary study are found in Appendix B.

In summary, several procedural modifications occurred for the express purpose of overcoming preliminary phase data collection difficulties. First, the stimulus train was changed to include a mid-train pause and an interrupt loop which stopped the program as soon as 20 artifact-free Rare tones were collected. Second, an attempt was made to improve the signal-to-noise ratio by increasing the occurrence of Rare tone to $p = .3$ which exposing each subject to a maximum of 48 Rare tones instead of 30 in a 40 sec longer testing period. Third, LBP settings for Fz, Cz, and Pz were changed to .5 Hz and the EOG to 1 Hz. Fourth, the system sensitivity was set at 500. Fifth, all primary phase subjects were tested with their eyes closed.

The modified stimulus parameters employed in the primary study are summarized on the right side of Table 2.

The study was designed to acquire all data within 60 minutes of the subject's arrival: 15 min to get acquainted and learn about procedural details, 20 min to prepare the subject for testing, and 25 min to acquire and store data and to plot the child's ERP record. In cases involving subject restlessness or system problems resulting in increased rates of artifact rejection, fewer than 20 Rare tones were accepted. Subject records based on less than 20 target tones were included in the study, as long as identifiable waveforms were evident and the subject complied with the testing conditions--especially keeping eyes closed, staying awake, and sitting still during the testing period.

Measurement of N1-P2-N2-P3 Waveforms: Preliminary Study

The second purpose of the preliminary study related to piloting a uniform set of measurement criteria for the identification of the ERPs associated with the classic four-wave (N1-P2-N2-P3) complex. Specification of the preliminary phase measurement criteria was based on published studies (Brown et al., 1983; Courchesne, 1978; Pearce et al., 1989; & Polich et al., 1990), and unpublished data from this laboratory (n = 17 5-to-7-year-olds). A "latency window" with upper and lower limits (in ms) was specified for each ERP: **N1**, 70-200; **P2**, 140-300; **N2**, 150-350; and, **P3**, 240-700. Within these windows, an **ERP template** based on minimum latency and peak-to-peak

amplitude changes of $\geq$ 40 ms and $\geq$ 4 microvolts was used to measure N1-P2-N2-P3 for all Common and Rare tones at Fz, Cz, and Pz. All data acquisition was based on the non-task Ignore condition. Rare and Common ERPs from the subjects in the preliminary phase ($\underline{n}$ = 16) served as the basis for piloting an **ERP template** to establish basic latency/amplitude windows for N1, P2, N2, and P3 between 70 and 700 ms post-stimulus.

The grand average for five preliminary phase subjects (4 females and 1 male with a mean age of 5 yr and 2 m) is illustrated in the upper panel of Figure 1. This plot, referred to as **GAPS20**, shows that the N1-P2-N2-P3 complex is better defined at Cz/Common. Identical latencies for the P3 at Cz for both the Common and Rare tones (322 ms) argue against assigning P3 to the subsequent waveform (near 600 ms) in the Rare condition. The GAPS20 plot also illustrates that each ERP in the N1-P2-N2-P3 complex in the Common condition at Cz and Fz surpasses ERP template minima. This supports assignment of comparable latencies for the less well-defined Pz/Common waveforms (based on multi-site coherence), despite the low P2-N2 amplitude at Pz. Conversely, the diminished amplitudes for the Rare P2-N2 complex at Cz and Pz both fall short of the ERP template minimina and are not identified. Finally, no 3-year-olds were included in the GAPS20 plot due to artifact rejection rates which averaged 89% for the four 3-year-olds in the preliminary phase.

Figure 1. Preliminary study Grand Average (GA) based on 20% oddball paradigm (**GAPS20**) (upper panel) with N1 and P3 latencies identified (*) for Common and Rare tones. The GAPS20 plot was based on five subjects (mean age = 5 yr 2 m). The lower panel (**GAGO30**) was a modified GA replication based on the 30% oddball paradigm. It included five different subjects (mean age = 4 yr 10.5 m) who were tested with the revised stimulus train, which included a mid-train pause to give subjects a 3 min rest. Positive is down in all plots.

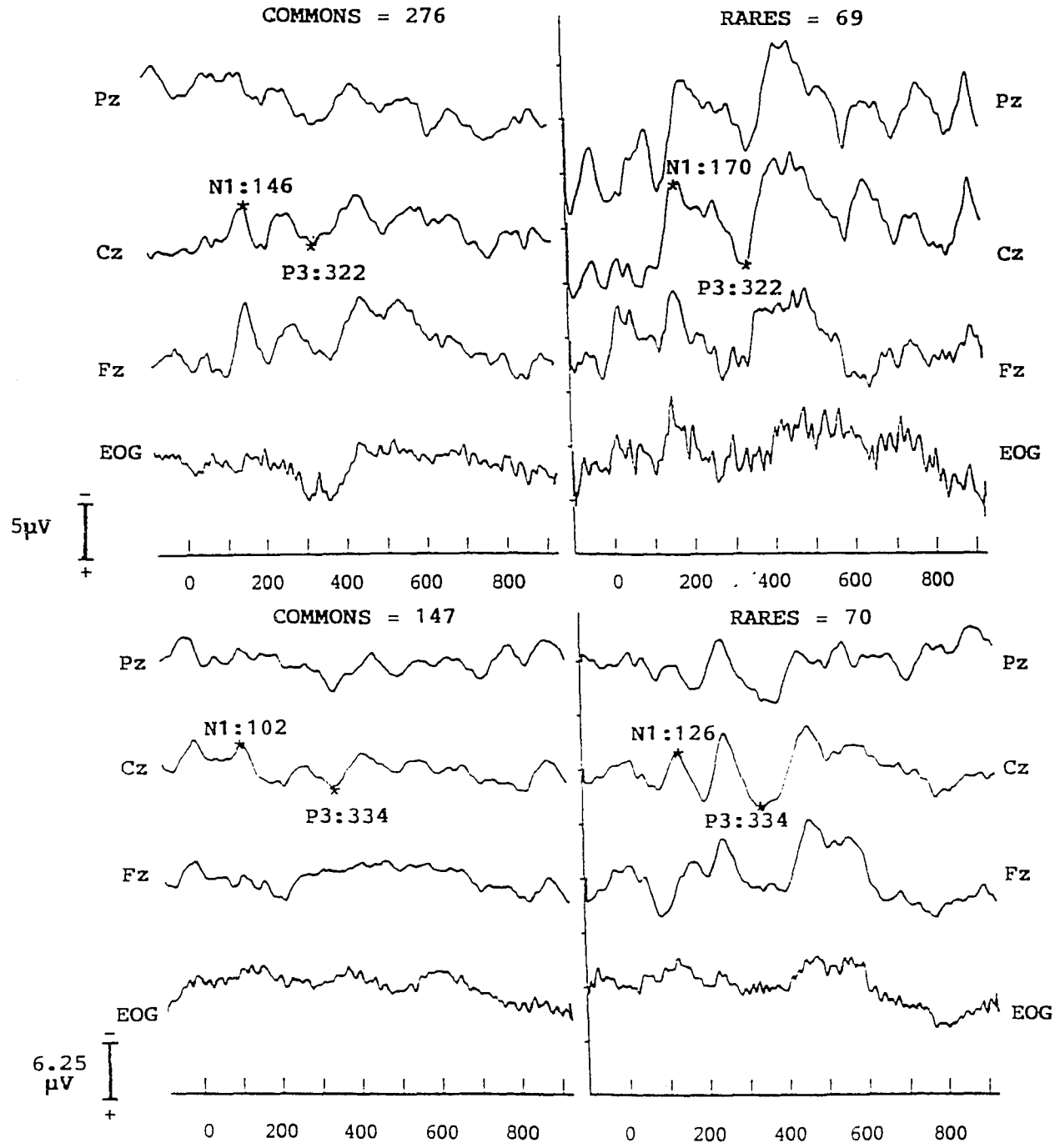

COMMONS = 276
RARES = 69
Pz
Cz
Fz
EOG
N1:146
P3:322
N1:170
P3:322
5µV
0
200
400
600
800
COMMONS = 147
RARES = 70
N1:102
P3:334
N1:126
P3:334
6.25 µV

Figure 1

In order to confirm the feasibility of efficient data collection in the primary study, the modified stimulus parameters, as summarized in Table 2, were used to create a second preliminary phase Grand Average. This second Grand Average, referred to as **GAGO30**, was created to determine with as much accuracy as possible if a non-statistical but empirical replication of the data profile represented in 20% Rare GAPS20 plot could be demonstrated with the 30% Rare stimulus parameters (Figure 1). In order to minimize differences between these Grand Averages (the upper panel, GAPS20 plot, and the lower panel, GAGO30 plot, Figure 1), the latter was matched as closely as possible for mean age, sex, and number of accepted Rare targets. The GAPS20 plot included 69 Rare tones derived from five subjects (mean age was 5 yr 2 m). The GAGO30 replication (Figure 1, lower panel) was based on five <u>different</u> subjects, including two early subjects from the primary study, and was based on 70 Rares. Mean subject age was 4 yr 10.5 m (3.5 m younger than GAPS20 subjects). Each plot included one male and four females.

Similarities between the 30% Rare tone GAGO30 plot and the GAPS20 plot (with the 20% Rare tone) corroborated the efficacy of the ERP template with the 30% Rare tone. As a pilot of the modified stimulus parameters planned for the primary study, the GAGO30 plot also helped resolve several

issues that emerged during the early part of the preliminary study. First, it helped confirm the use of reduced ERP template minima of 30 ms and 3 μV for low amplitude ERPs (see following paragraph). Second, it expedited data collection within 60 minutes. Third, it improved individual subjects' signal-to-noise ratio. Fourth, it documented the existence of the entire N1-P2-N2-P3 complex in the non-task Ignore Condition before age five based on a 30% Rare tone. In short, the GAGO30 plot supported use of the 30% oddball paradigm for the primary study.

Findings derived from the preliminary study indicated the latency windows effectively categorized the ERPs with two minor variations. First, no waveform, namely the P3, occurred beyond 600 ms. Thus the maximum latency for P3 in the primary phase was reduced to 600 instead of 700 ms. Second, it was apparent that for some waveforms, the ERP template minimums of 40 ms and 4 μV were too restrictive. In such cases it was necessary to reduce template minimums about 25% whenever an ERP could not be readily identified. This was only done when multi-site coherence was evident. That is, when an ERP of reduced amplitude occurred within approximately $\pm$ 10 ms of a better defined ERP at another scalp site for the same condition (Common or Rare). Thus, a minimum peak-to-peak duration of 30 ms and 3 μV became the operational minima for the primary study.

The Primary Study

The primary study used the basic measurement criteria derived from published studies (Goodin et al., 1978; Finley et al., 1985; Howard & Polich, 1985; Pearce et al., 1989; & Polich, 1993), the preliminary phase of the present study, and unpublished data from a previous study in this laboratory (Todorovich, Crowell, & Pearce, 1990) to identify and measure the latency, polarity, and amplitude of ERPs at three scalp sites (Fz, Cz, and Pz). Data collection also include one EOG lead (the outer canthus of the right eye). EOG data were inspected visually for each individual record, but not analyzed statistically

Criteria for Inclusion in the Study

Not all subjects tested were included in the final study. Subjects were dropped for several reasons. Some were non-compliant with the testing conditions--refusing to sit still or to keep eyes closed. Others were compliant, but had notable anomalies in one or more EEG channels (e.g., one lead was so discrepant that the ERPs for that site were not identifiable). Appendix A summarizes the general performance of each subject during the testing session, including file name, sex, age (in months), number correct out of 12 on the hearing test, percentage of Common and Rare tones accepted and rejected, and "state" ratings for each 3 min interval during data acquisition.

Summary of Subject Attrition From the Primary Study

A profile of the 12 subjects dropped from the primary study (n = 8 males and 4 females) follows. Appendix B provides additional details related to subjects who were dropped due to an unaccounted for offset spike between 18 and 32 ms post-stimulus.

3-year-olds. Three males and three females were dropped. Each male was extremely restless during data collection. In one case the entire record was lost after six system pauses caused a system halt. One female failed the hearing test; another had anomalous Cz data (possibly due to a faulty Cz lead). The third had an offset spike and failed to meet all criteria for inclusion (15 or more Rare tones in the final record).

4-year-olds. Two males were dropped. One had an offset spike, was non-compliant with the testing conditions and had fewer than 15 Rare tones accepted. The other male had occasional seizures during infancy and was still taking an anti-seizure medication (clonazepam) twice daily. Clonazepam is known to suppress EEG activity.

5-year-olds. Four 5-year-olds were dropped. One male and one female failed the hearing test. A second male had an offset spike and fewer than 15 Rares accepted. A third male who was very restless had an intact record (19 Rares accepted), but his ERP profile was so disparate across all mid-line leads (Pz, Cz, and Fz) that he was dropped.

Subjects remaining in the primary study are summarized in Table 3 by age (in years) and sex.

Table 3. Subjects included in the primary study are summarized by age and sex.

Age (in yrs)	**3**	**4**	**5**	**TOTAL BY SEX**
Males	9	7	6	22
Female	7	11	8	26
TOTAL BY AGE	16	18	14	**48**

Primary Study Data Acquisition

A train of 160 pure tone stimuli was generated at 2 kHz for the Rare targets (p = .3) and 500 Hz for the Common tones (p = .7) with a system pause built in after subjects were presented an initial train of 80 pure tones. After a short break, a different train of 80 more tones was presented. The stimulus train was pseudo-random to preclude the presentation of successive Rare tones. Stimulus intensity was 70 dB SPL. The Ignore condition was employed. Each subject was instructed to close his or her eyes, sit quietly, and listen to the sounds.

Each subject was seated in a reclining chair with arm rests. Most preferred to sit on their parent's lap. The Nicolet Pathfinder II collected, averaged, and stored separately the Common and Rare tones for each subject. Artifact trials were rejected automatically whenever the ERP exceeded 95% of the maximum sensitivity. All subjects received the same sequence of tone presentations. However, the stimulus train ended automatically as soon as 20 artifact-free Rare tones were stored.

Individual differences in artifact rejection rates resulted in considerable variability in the final number of accepted and rejected Common and Rare tones. Some subjects were exposed to the entire stimulus train of 160 tones (112 Commons and 48 Rares). On the other hand, four subjects complied with the testing conditions so well that 20 (out of the first 24 Rares) were accepted and the second half of the stimulus train was not needed. The final number of accepted tones ranged from 14 to 68 for the Commons and from 8 to 20 for the Rare tones.

Prior to saving the summated average for each subject, the digitized record was smoothed (via a standardized 9-point averaging algorithm) and base line corrected (BLC). The BLC procedure subtracts the mean

voltage of the entire waveform from each data point in the waveform. This normalizes the entire ERP in relation to fluctuations in low frequency (slow wave) EEG (Polich, 1993). The data acquisition device (Nicolet Pathfinder II) has a cursor which allowed precise measurement of the base line-corrected peak-to-peak amplitude change at 2 ms intervals across the system time base (1024 ms, including the 100 ms prestimulus epoch).

Analysis

Measurement of N1-P2-N2-P3 Waveforms: Primary Study

Two changes related to ERP measurement criteria were implemented following the preliminary study. The upper limit on P3 latency was reduced to $\leq$ 600 ms (rather than $\leq$ 700 ms). Otherwise, the latency windows for the measurement of N1-P2-N2-P3 waveforms was unchanged: **N1**, 70-200; **P2**, 140-300; **N2**, 150-350; and, **P3**, 240-600. In addition, the ERP template was reduced by 25% (based on the preliminary study) so that minima of 30 ms between ERPs with amplitude differences $\geq$ 3 microvolts were allowed for ERP waveform identification based on explicit constraints related to low amplitude ERPs.

Prior to identifying any Common or Rare ERPs, the entire record for each subject was examined for multi-site coherence (evidence of the same waveform in the same basic latency range at $\geq$ 2 EEG sites). If an analogous waveform (that is, an ERP at an alternate site for the same stimulus condition) occurred within $\pm$ 20 ms, then the minimum criteria for the ERP template could be waived.

Identification of the N1-P2-N2-P3 waveforms proceeded in a forward direction beginning at 70 ms. Waveforms in the N1-P2-N2-P3 complex were measured and labeled up to 600 ms. Whenever a particular waveform could not be identified clearly and multi-site coherence was not evident, a three-step alternative procedure was employed:

First, switch to the opposite stimulus condition (e.g., if measuring a Rare ERP, examine the analogous Common waveform for the same site). If an equivalent ERP was found, the closest ERP (within $\pm$ 20 ms) that exhibited the same polarity in the initial channel was tagged (even though the amplitude was $< 4\ \mu V$). If this failed to identify the ERP in question, a second option was employed.

Second, work backwards from the first positive ERP beyond 240 ms, assign this waveform the P3 tag, and continue in a

reverse direction until all possible ERPs in the N1-P2-N2-P3 complex were identified. The ERP template was still applied when working in the reverse direction.

Finally, in cases where no alternate procedure effectively identified part or all of the waveform in question, no ERP was tagged, a value of "0" was assigned for amplitude, and the latency measure was left blank.

Reliability Check

In order to corroborate the accuracy of the entire measurement procedure, including the ERP template, a reliability check was conducted that included two independent raters with considerable expertise in the area of ERPs (Table 4). For the reliability check, each rater was provided with the measurement criteria stated above, the minimum and maximum "latency windows" for each ERP in the N1-P2-N2-P3 complex, and instructions related to basic procedures for component identification.

The reliability check included five subjects per group (drawn at random via numbered plastic chips matched to subjects). The reliability check included N1-P2-N2-P3 waveform assignment at Fz, Cz, and Pz for both Common and Rare tones.

The composite rating for the reliability check was calculated by comparing the concurrence for each rater with the values assigned by the original investigator. As long as the composite average for the two raters exceeded 80%, the ERP values originally assigned by the investigator remained unchanged. Otherwise, ERPs assigned a different value by both raters would be reconciled by mutual consensus.

Table 4. Percentage of agreement for each rater who participated in the ERP reliability check.

	COMMON	RARE
Rater A	87%	89%
Rater B	77%	81%
Ave. of A + B	82%	85%

Statistical Analyses

As indicated, data from the 16 subjects in the preliminary study were not analyzed statistically. Statistical analyses of the primary study included 48 subjects. The main dependent measures related to either latency or amplitude of the four-wave N1-P2-N2-P3 complex. Latency measures were referred to as **ERPs** and included N1, P2, N2, and P3. Amplitude measures were referred to as **AMPS** and included **Amp1**, **Amp2**, and **Amp3**. **Amp1** refers N1-P2, **Amp2** to P2-N2, and **Amp3** to N2-P3. Statistical analyses used MVS SAS Version 6.08 (Copyright 1990, 1991, 1992).

The overall analysis included nine steps. The first step reported means and standard deviations for each age group (based on the univariate procedure of the SAS General Linear Model (GLM). The second step represents a graphic portrayal of two types of ERP plots: one involves sample plots of individual subjects (one from each age group); the other represents Grand Average plots for all subjects within each age group. The digitized record for all subjects within each group was combined to create the GATOT plots: **GATOT3** for 3-year-olds, **GATOT4** for 4-year-olds, and **GATOT5** for 5-year-olds. The Cz data represented in Figure 3 was then extracted for each age group to create

a **GATOT** file to portray the data for the vertex lead (Cz) in a single composite plot representing the Cz morphology for the 3-, 4-, and 5-year-olds in the Figure 4 plot.

The third step employed repeated measures MANOVA to examine ERP latency measures as a function of age in months (**AGEMON**) and **SEX**. Within factors for latency included: **SITES** (Fz, Cz, & Pz); **COMRAR** for stimulus probability: Common, 70% versus Rare, 30%; and, **ERPs** for N1, P2, N2, and P3.

The fourth step employed the same repeated measures MANOVA with **AMPS** (Amp1, Amp2, Amp3) replacing ERPs. Thus, the within factors included **SITES, COMRAR, and AMPS.** If the between factor for SEX was significant for step three or four, subsequent analyses would include SEX as a separate measure. If not, the model reduced to AGEMON.

The fifth analytic step employed repeated measures MANOVA to examine the ERP latency measures for differences within age groups. This step examined the effect of COMRAR tones on each age group and included one between factor (**AGE_GRP**, for 3-, 4-, & 5-year-olds) and three within factors **SITES**, for Fz, Cz, & Pz; **COMRAR**, for stimulus probability; and, **ERPs** (N1, P2, N2, and P3).

The sixth step used the same model with AMPS replacing ERPs as the third within factor. This examined patterns of age-related amplitude change to the COMRAR tones.

The seventh step employed repeated measures MANOVA to examine the nature and extent of latency changes across age groups. Thus, 3-year-olds were compared to 4-year-olds; and, the 4-year-olds were compared to 5-year-olds. The between factor was AGE_GRP. Within factors for latency included: **SITES** (Fz, Cz, & Pz), **COMRAR** for stimulus probability, and **ERPs** (N1, P2, N2, AND P3).

The eighth step was the same as step seven, except that **AMPS** replaced **ERPs** as one within factor. This step examined age-related changes in amplitude response to the COMRAR tones.

The ninth and final step used regression analyses to examine age-related changes in peak latency (**ERPs** by **SITE** by **COMRAR**) across the 36 to 69 month age span of subjects. Each ERP by SITE by COMRAR tone was regressed on AGEMON to examine age-related patterns of latency decrease.

III. RESULTS

Step 1. The means and standard deviations (SDs) for peak N1-P2-N2-P3 latencies are summarized in Table 5 for Common and Rare tones by age group (3-, 4-, and 5-year-olds) and site (Pz, Cz, and Fz). Several patterns were noted. First, in the 3- and 4-year-old groups, mean peak latencies for Rare versus Common tones were shorter for 21 out of 24 ERPs by SITES. Second, for 5-year-olds, all N1 and P2 mean latencies collapsed for SITES were an average of 19 ms faster to the Common tone. Third, COMRAR latency differences within age group showed minimal variation for two ERPs (collapsed for SITE). All N1 values for 3-year-olds were between 146 and 153 ms. Likewise, all P3 means in 5-year-olds were between 317 and 325. All other Rare and Common ERP ranges within age groups varied from 26 to 51 ms. Fourth, within group variability based on SDs yielded 14 SDs > 50 ms in 3-year-olds, seven in 4-year-olds, and none in 5-year-olds. Finally, the only ERP for each group in which the Rare SD was always less than the Common SD was the P3. Averaged across SITES, the Rare (vs. Common) SDs were 30 ms less for 3-year-olds, 22 ms less for 4-year-olds, and 8 ms less for 5-year-olds.

Table 5. Mean latency and SDs (in parentheses) for Common (COM.) and Rare waveforms (N1, P2, N2, & P3) are reported by age group. **Rare** values are displayed in **bold** print.

Age group: 3-yr-olds (N = 16)

	N1 COM.	N1 RARE	P2 COM.	P2 RARE	N2 COM.	N2 RARE	P3 COM.	P3 RARE
Pz	146	**150**	228	**218**	299	**278**	377	**340**
	(43)	**(49)**	(58)	**(57)**	(80)	**(66)**	(84)	**(58)**
Cz	150	**147**	228	**214**	310	**269**	391	**344**
	(28)	**(46)**	(46)	**(48)**	(64)	**(61)**	(90)	**(64)**
Fz	151	**153**	239	**213**	318	**275**	396	**346**
	(38)	**(37)**	(45)	**(47)**	(80)	**(67)**	(95)	**(57)**

Age group: 4-yr-olds (N = 18)

	N1 COM.	N1 RARE	P2 COM.	P2 RARE	N2 COM.	N2 RARE	P3 COM.	P3 RARE
Pz	134	**119**	220	**175**	282	**253**	361	**346**
	(43)	**(21)**	(48)	**(40)**	(55)	**(55)**	(64)	**(44)**
Cz	138	**127**	216	**185**	286	**258**	360	**360**
	(40)	**(23)**	(47)	**(41)**	(53)	**(43)**	(66)	**(39)**
Fz	152	**138**	225	**194**	292	**249**	376	**334**
	(38)	**(25)**	(46)	**(41)**	(60)	**(41)**	(60)	**(41)**

Age group: 5-yr-olds (N = 14/PZ & Cz; N=13 at Fz for N1)

	N1 COM.	N1 RARE	P2 COM.	P2 RARE	N2 COM.	N2 RARE	P3 COM.	P3 RARE
Pz	110	**135**	178	**206**	244	**263**	317	**324**
	(20)	**(37)**	(45)	**(42)**	(43)	**(49)**	(43)	**(33)**
Cz	114	**140**	182	**205**	258	**257**	320	**325**
	(30)	**(34)**	(29)	**(47)**	(31)	**(39)**	(43)	**(34)**
Fz	126	**133**	176	**181**	256	**235**	320	**317**
	(23)	**(29)**	(33)	**(39)**	(37)	**(38)**	(42)	**(37)**

Mean amplitudes and SDs are summarized in Table 6 for Common and Rare tones by age group and site. Highlights follow. First, the basic pattern for amplitude means was highly consistent for the 3-year-olds and 4-year-olds. Within each age group, all nine Rare means for **SITES** by **AMPS** exceeded the Commons, although in 4-year-olds, the Amp1 COMRAR differences were less than 1 μV. Second, in the 5-year-olds, multi-site consistency for Rare amplitude means was only evident for the Amp3 measures; although differences were negligible, Common Amp1 and Amp2 means exceeded the Rares in 3 out of 6 cases. Third, in three cases the mean peak amplitudes $\geq$ 19 μV: Amp3/Rare at Pz and Cz in the 4-year-olds (19.26 and 20.71 μV, respectively), and Amp1/Rare in 3-year-olds: 19.16 μV. Fourth, the 3-year-old mean for all three Amp1/Rares (computed across SITES) was 17.3 μV. Comparable Amp1/Rare means were 13.1 μV for 4-year-olds, and 15.1 μV for 5-year-olds. Fifth, peak amplitude means for Amp2/Rare and Amp3/Rare (computed across SITES) were both largest for 4-year-olds (14.3 μV and 19.4 μV, respectively). Sixth, when Amp1, Amp2 and Amp3 Rares are averaged across SITES and then ranked for each group, the only case that favors the youngest group is Amp1. As the initial ERP in the youngest group, this may relate to the emergence of the entire N1-P2-N2-P3 complex.

Table 6. Amplitude means and SDs (in μV) are summarized for N1-P2 (**Amp1**), P2-N2 (**Amp2**), and N2-P3 (**Amp3**) for Common and Rare tones by Site (Pz, Cz, Fz) and age group. Rare values appear in **bold** print.

Age group: 3-yr-olds (N = 16)

	Amp1 COM.	**Amp1 Rare**	**Amp2 COM.**	**Amp2 Rare**	**Amp3 COM.**	**Amp3 Rare**
Pz	12.90 (7.99)	**16.85 (7.78)**	9.31 (6.71)	**13.31 (6.32)**	10.36 (6.31)	**16.69 (8.90)**
Cz	13.13 (7.90)	**15.89 (5.91)**	9.32 (6.78)	**12.64 (6.40)**	10.12 (6.64)	**13.84 (8.71)**
Fz	15.90 (9.12)	**19.16 (10.17)**	11.43 (6.96)	**12.86 (7.27)**	13.24 (8.10)	**13.99 (7.20)**

Age group: 4 yr-olds (N = 18)

	Amp1 COM.	**Amp1 Rare**	**Amp2 COM.**	**Amp2 Rare**	**Amp3 COM.**	**Amp3 Rare**
Pz	12.33 (6.12)	**12.76 (6.41)**	8.49 (4.58)	**13.27 (7.02)**	10.29 (4.18)	**19.26 (11.30)**
Cz	13.17 (5.78)	**13.78 (8.10)**	10.96 (6.34)	**17.22 (9.76)**	9.96 (5.64)	**20.71 (11.33)**
Fz	12.61 (7.02)	**12.72 (8.08)**	10.36 (6.14)	**12.25 (6.90)**	11.67 (7.05)	**18.35 (8.57)**

Age group: 5 yr-olds (N = 14 at PZ & Cz; N=13 at Fz/Ampl)

	Amp1 COM.	**Amp1 Rare**	**Amp2 COM.**	**Amp2 Rare**	**Amp3 COM.**	**Amp3 Rare**
Pz	12.8 (8.81)	**17.41 (9.61)**	8.18 (4.76)	**11.61 (8.15)**	8.58 (5.11)	**17.48 (7.01)**
Cz	14.14 (8.65)	**13.62 (6.43)**	10.43 (3.80)	**9.70 (7.98)**	8.30 (5.18)	**15.32 (5.12)**
Fz	13.73 (10.64)	**14.13 (8.33)**	13.82 (6.21)	**12.27 (7.85)**	12.48 (8.85)	**16.37 (10.15)**

Descriptive profiles of each age group for mean age in months (AGEMON), Common and Rare tones accepted and rejected, Total Common and Total Rare Tones (accepted plus rejected tones) are summarized in Table 7. The mean age was 3 yr 7.8 mo, 4 yr 4.4 mo, and 5 yr 4.5 mo, for the 3-, 4-, and 5-year-old groups, respectively. The mean difference between 3- and 4-year-olds was 8.6 months compared to 12.1 months difference between 4- and 5-year-olds. The mean number of Rare tones accepted (Rare/Go) was largest for the 4-year-olds (18.7) and smallest for 3-year-olds (17.5). The Common/Go means was greatest for 5-year-olds (44.6) and smallest for 3-year-olds (42.8). The ranges for Rare/Go and Common/Go both reflect mean differences of 1.9 or less.

Step 2. This step presents sample plots of three individual subjects (Figure 2) and Grand Average plots which reflect the composite record for all subjects included in each age group (Figures 3 and 4). The records of the three individual subjects presented in Figure 2 represent an intact record for one subject per age group. The consistency of N1 for Common and Rare tones in each record attests to the feasibility of employing a measurement system which begins with the first wave, N1, and proceeds sequentially to P2, N2, and then P3.

Table 7. Means by age group (Age_Grp3, Age_Grp4, Age_Grp5) are summarized for subject age in months **(AGEMON)**, Common and Rare tones accepted **(COMMON/GO** and **RARE/GO)**, and for rejected Common and Rare tones **(COMMON/NO** and **RARE/NO)**. **COMMON/TOTAL** and **RARE/TOTAL** means include all accepted and rejected tones for that condition.

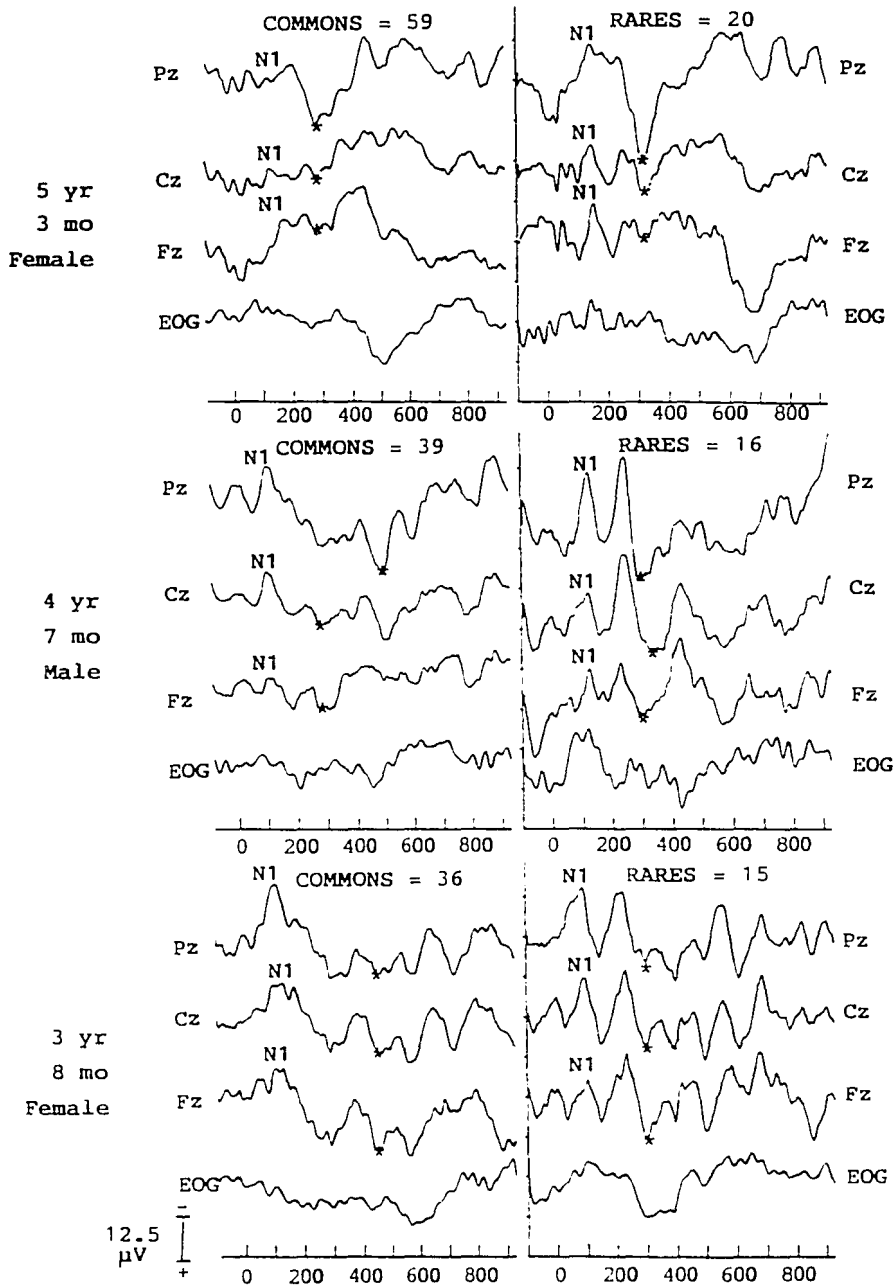
	AGE Grp3 (n=16)	**AGE Grp4** (n=18)	**AGE Grp5** (n=14)
AGEMON	43.8 (3.2)	52.4 (3.1)	64.5 (2.7)
COMMON/GO	42.8 (10.8)	43.1 (11.1)	44.7 (10.6)
COMMON/NO	46.8 (26.1)	40.3 (27.0)	40.4 (25.4)
COMMON/TOTAL	89.6 (18.3)	83.3 (21.7)	85.3 (19.6)
RARE/GO	17.5 (3.9)	18.7 (2.8)	18.4 (3.5)
RARE/NO	20.2 (12.0)	16.6 (11.7)	17.7 (11.2)
RARE/TOTAL	38.4 (8.8)	35.2 (9.6)	36.1 (8.6)

The advantage of recording data from three sites is illustrated in the record of the 5-year-old female, Figure 2 (upper panel). The similarity of the ERP profile for the Rare waveforms at Fz and Cz supports identifying P3 at Pz at the same relative time, despite poor delineation of the P2-N2 complex at Pz.

The Grand Average (GA) plots (Figures 3 and 4) summarize in graphic form the patterns of ERP stability and change by SITE and stimulus probability (COMRAR). Figure 3 represents the GA plot for each age group: **GATOT3** for 3-year-olds, **GATOT4** for 4-year-olds, and **GATOT5** for 5-year-olds. The lower portion of each plot also includes the EOG for each tone. The N1 peaks in Figure 3 are marked above the first ERP in each record for Common and Rare tones. An asterisk (*) marks the P3 peak. Positive is down.

The occurrence of N1 (between 110 and 178 ms) at all sites for all age groups for both Common and Rare tones is noteworthy. All P3 waveforms occurred prior to 400 ms, although at Fz in the GATOT3 Rare plot it could be argued that the P3 is the positive waveform that <u>follows</u> the peak that is marked in Figure 3. Visual inspection of the GA plots indicates that N1 and P3 are consistently evident and that the entire N1-P2-N2-P3 complex is recognizable in response to the Common and Rare tones for all age groups.

Figure 2. Sample plots represent one subject from each age group. N1 is listed above the first identified ERP for each site. The star (*) identifies the P3 at each site for the Common tones (on the left) and the Rare tones (on right). Note the consistency of N1 at all sites for each tone.



* Represents P3

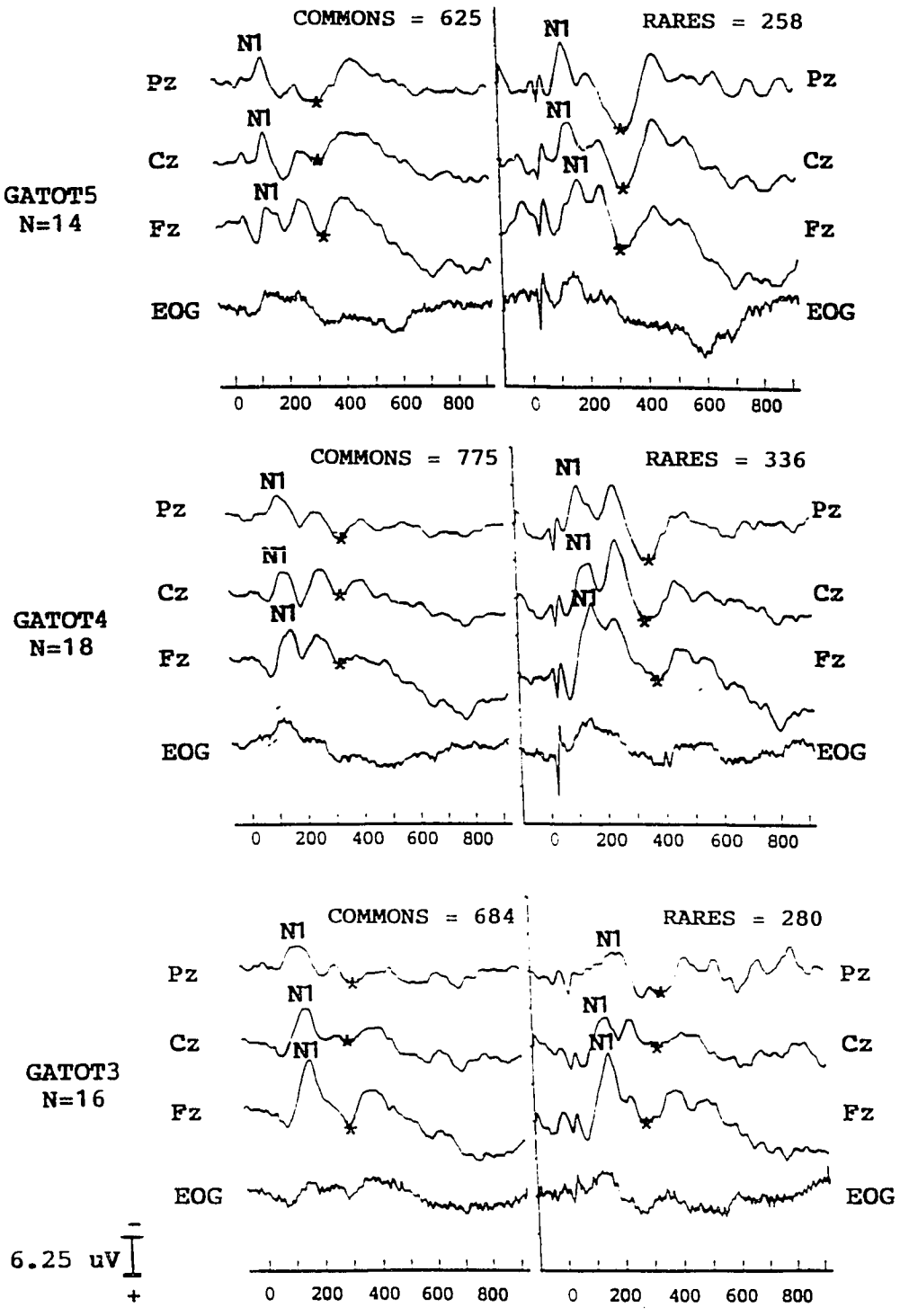
Figure 2

In general, N1-P2-N2-P3 becomes progressively better defined in each older group, although N1 amplitude for Common and Rare tones is large at Fz in the 3-year-olds (Figure 3).

The composite Grand Average Total(**GATOT**), Figure 4, is based on the Cz record from each age group. Negative ERPs (N1 and N2) are placed above the identified wave and positive waves (P2 and P3) below. In the Common condition, the delineation of the N1-P2-N2-P3 complex is more clearly defined in 4- and 5-year-olds compared to the 3-year-olds, except for N1 which is clearly evident in all groups. A similar pattern is observed in the Rare plots. One other pattern in the Rare plots stands out: the emergence of a well-delineated ERP subsequent to the Rare/P3 in 4- and 5-year-olds. This negative N4 peak occurs between 400 and 450 ms, and at Cz becomes is increasingly evident for each older group. Could this N4 to a pure tonal stimulus be a concomitant of the emerging P3?

Plots of individual subjects in Figure 2 and the GA plots (Figures 3 & 4) provide graphic support for several findings borne out by this study: (a) the stability of N1 for COMRAR across SITES and age-groups; (b) the feasibility of forward identification of ERPs in young subjects from the N1 through the P3 according to the ERP template minima;

Figure 3. Grand Average Total (**GATOT**) plots for each age group demonstrate the consistent occurrence of N1 before 200 ms and P3 (noted by *) prior to 400 ms for each GATOT.



* Represents P3

Figure 3

Figure 4. Composite Grand Average Total (GATOT) plot derived from the Cz record for each age group (3-, 4-, and 5-years-old). Negative ERPs (N1 and N2) are indicated above the identified wave and positive waves (P2 and P3) are noted below each identified wave. Positive is down.

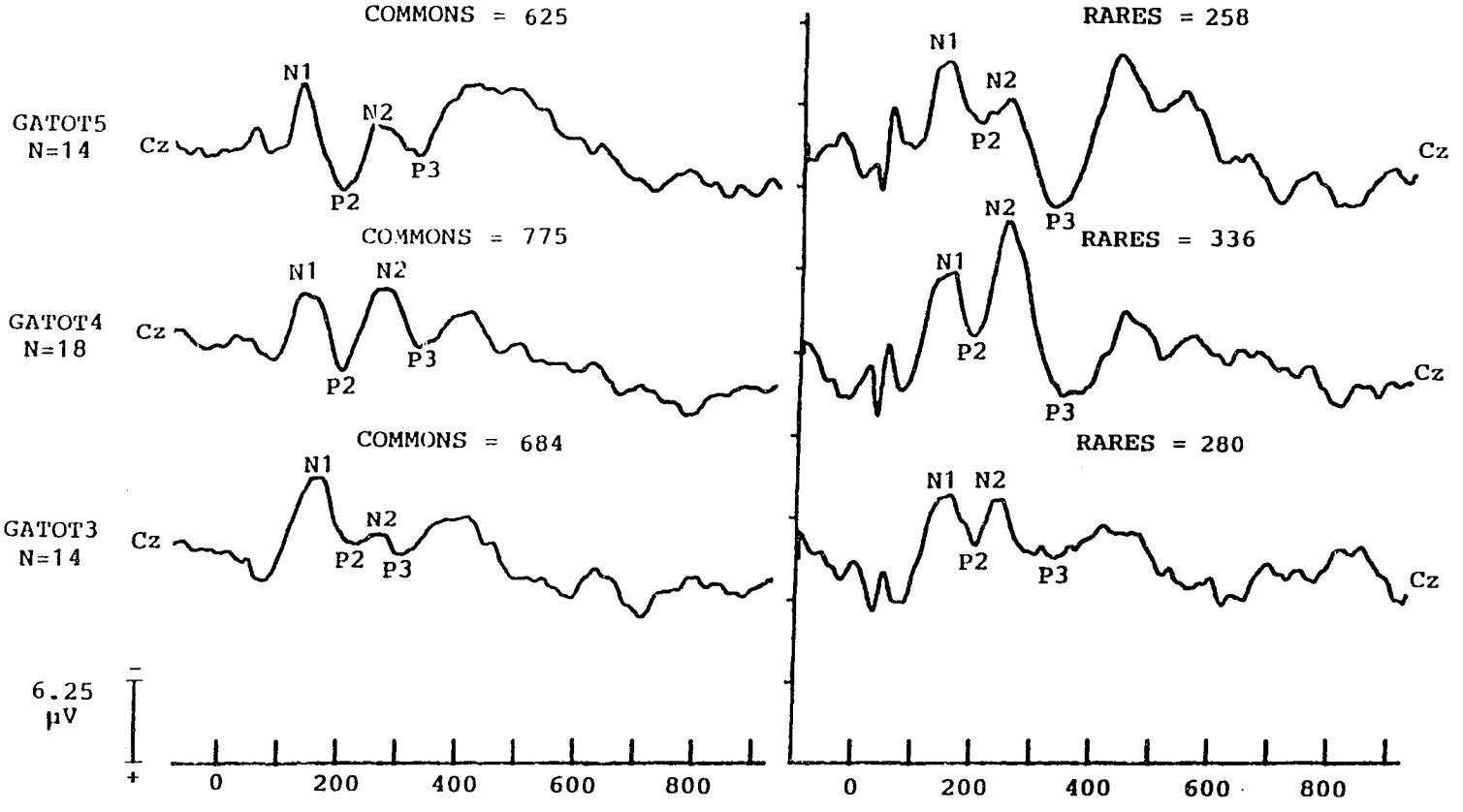

COMMONS = 625
RARES = 258
GATOT5
N=14
Cz
N1
N2
P2
P3
COMMONS = 775
RARES = 336
GATOT4
N=18
COMMONS = 684
RARES = 280
GATOT3
N=14
6.25
μV
0
200
400
600
800

Figure 4

(c) accentuation of Rare/Amp3 morphology in 4- and 5-year-olds compared to 3-year-olds, except for fairly homologous N1 Common and N1 Rare in 3-year-olds; and, (d) based on Figures 2 and 3, the overall profile of the EOG does not appear to notably contaminate Fz, Cz, or Pz records during the 70-600 ms interval of interest.

Latencies derived from the Grand Average for each age group in Figure 3 are summarized in Table 8. These values are based on the digitized summation of each subject's record by age group. Measurement and identification of N1-P2-N2-P3 for the Grand Average occur only once--after all individual digitized records are summated. This differs markedly from the individual identification and measurement of each subject record based on the ERP template (Table 5). Although the Grand Average for each age group helps corroborate the efficacy of the ERP template, direct comparisons between Table 5 latencies and those based on the digitized summation of all records within each age group (Table 8) are inappropriate.

Table 8. Grand Average ERP latencies are summarized for each age group. **Rare** tone latencies are in **bold** print. The data for 3-year-olds appear at the bottom and for 5-year-olds at the top to match the panels displayed in Figure 3.

Age group: 5-yr-olds (N = 14)(625 Common & 258 Rare tones)

	N1 COM.	N1 RARE	P2 COM.	P2 RARE	N2 COM.	N2 RARE	P3 COM.	P3 RARE
Pz	112	**116**	182	**166**	230	**200**	288	**318**
Cz	114	**132**	184	**190**	236	**238**	310	**316**
Fz	120	**158**	184	**194**	236	**236**	312	**306**

Age group: 4-yr-olds (N = 18)(775 Common & 336 Rare tones)

	N1 COM.	N1 RARE	P2 COM.	P2 RARE	N2 COM.	N2 RARE	P3 COM.	P3 RARE
Pz	110	**110**	194	**184**	240	**234**	332	**334**
Cz	122	**144**	188	**182**	250	**238**	316	**334**
Fz	148	**150**	188	**200**	240	**226**	312	**380**

Age group: 3-yr-olds (N = 16)(684 Common & 280 Rare tones)

	N1 COM.	N1 RARE	P2 COM.	P2 RARE	N2 COM.	N2 RARE	P3 COM.	P3 RARE
Pz	126	**178**	216	**276**	256	**304**	318	**338**
Cz	150	**150**	218	**194**	252	**234**	290	**324**
Fz	158	**154**	--	--	--	--	292	**278**

Analytic Data. For each phase of MANOVA, results are presented for latency (**ERPs**) followed by amplitude (**AMPS**).

Step 3. The MANOVA for ERPs was significant for the AGEMON effect, $F(1,44) = 11.27$, $p < .01$, but not for SEX, $F(1,44) < 1.0$, $p = .56$. Three repeated measures also were significant: COMRAR, $F(1,44) = 7.75$, $p < .01$; ERPs, $F(3,132) = 26.1$, $p < .001$; and the COMRAR by AGEMON interaction, $F(1,44) = 5.99$, $p < .05$. Latency not only decreased with increasing age, but the rate of this decrease differed significantly as a function of COMRAR stimulus probability. These effects are examined further via regression analyses.

Step 4. The MANOVA for amplitude with AGEMON and SEX as between factors did not differ significantly for AGEMON, $F(1,44) < 1.00$, $p = .81$, or for SEX, $F(1,44) = 1.34$, $p = .25$. One repeated measure was significant: the AMPS by SEX interaction, $F(2,43) = <.05$. However, since neither main effect for the Step 3 or Step 4 MANOVA (for AGEMON and SEX) yielded significant sex differences, the subsequent MANOVAs dropped SEX as an independent variable.

Step 5. When MANOVA was run for ERPs within age groups, statistical significance for the main effect (AGEMON, within each age group) was not attained for AGE_GRP3 or

AGE_GRP4. The between factor (AGEMON) for 3-year-olds did not differ significantly, $F(1,14) = 1.59$, $p = .23$, although the repeated measures for ERPs, $F(3,12) = 3.84$, and for ERPs by AGEMON, $F(3,12) = 3.45$, were significant ($p < .05$).

The MANOVA for the 4-year-olds also failed to reach significance, $F(1,16) = 1.80$, $p = .20$). No within factors were significant.

The MANOVA for the 5-year-olds was significant, $F(1,11) = 6.64$, $p < .05$. No within factor was significant.

Step 6. When MANOVA was run for AMPS within age groups, statistical significance was not attained for the main effect (AGEMON) for any group. For the 3-year-olds, $F(1,14) < 1.0$, $p = .52$. No repeated measures were significant.

AGE_GRP4 MANOVA was similar: $F(1,16) < 1.0$, $p = .45$, with no significant repeated measures.

The AGE_GRP5 MANOVA also was nonsignificant, $F(1,11) < 1.0$, $p = .59$. However, two interactions were significant: SITES by AMPS, $F(4,8) = 4.54$, and, SITES by AMPS by AGEMON, $F(4,8,) = 4.57$, $p = < .05$, respectively.

Step 7. The MANOVA that examined ERPs differences across age groups first compared AGE_GRP3 with AGE_GRP4 and then, AGE_GRP4 versus AGE_GRP5. Differences between AGE_GRP3 and AGE_GRP4 were not significant $F(1,32) = 2.57$, $p = .12$.

This suggests that decreases in mean peak latencies, though evident in 4-year-olds compared to the 3-year-olds, do not account for the major latency decrease reported in the MANOVA for ERPs with AGEMON as the independent variable. Nevertheless, two repeated measures attained significance: the COMRAR effect, $F(1,32) = 6.88$, $p = .01$; and, the ERPs effect, $F(3,30) = 375$, $p < .0001$. Two Bonferroni comparisons for specific variables differed significantly ($p < .05$). The latency for the Rare/N1 at Pz was 150 ms for AGE_GRP3 versus 119 ms for AGE_GRP4. The following waveform differences at Rare/P2 for Pz also were significant ($p < .05$): 218 ms for AGE_GRP3 compared to 175 ms for AGE_GRP4.

The MANOVA for AGE_GRP4 versus AGE_GRP5 was significant for ERPs, $F(1,29) = 4.78$, $p < .05$. One repeated measures main effect and two interactions were significant. The ERPs effect, given distinct latency "windows" for N1, P2, N2 and P3, yielded an huge F value: $F(3,27) = 707.8$, $p < .0001$. Significant interactions included COMRAR by AGE_GRP, $F(1,29) = 6.36$, $p < .05$); and, ERPs by AGE_GRP, $F(3,27) = 3.35$, $p < .05$. The COMRAR by AGE_GRP interaction yielded six significant differences by AGE_GRP for Common tones and two for Rare tones (Table 9), based on Bonferroni's t-test. Six differences were evident for the Common tone: N1/Fz, P2/Pz, P2/Cz, and all three

sites for P3/Common, Pz, Cz, and Fz (Table 9). All six latency differences were shorter for AGE_GRP5. Two significant COMRAR differences were observed for Rare tones: P2/Pz and P3/Cz, (Table 9). The P2/Pz mean was shorter for the 4-year-olds (175 ms vs. 206 ms). The P3/Cz mean was shorter for the 5-year-olds (324 ms vs. 360 ms).

The ERPs effect and the interaction between ERPs and AGE_GRP were analyzed subsequently via regression analyses.

Step 8. The MANOVA for amplitude differences between AGE_GRP3 and AGE_GRP4 was not significant: $F(1,32) < 1.0$, $p = .97$. However, three repeated measures factors were significant: COMRAR, $F(1,32) = 24.1$, $p < .0001$; the AMPS effect, $F(2,31) = 6.83$, $p < .01$; and an interaction for SITES by AGE_GRP, $F(2,31) = 3.73$. $p < .05$. Bonferroni's t-test for Fz Rare Amp1 was significantly greater for AGE_GRP3 (19.16 μV) versus AGE_GRP4 (12.71 μV).

Amplitude differences between AGE_GRP4 and AGE_GRP5 were not significant, $F(1,29) < 1.0$, $p = .68$. However, four repeated measures were significant: the COMRAR effect, $F(1,29) = 18.7$, $p < .001$; AMPS, $F(2,28) = 4.59$, $p < .05$; COMRAR by AMPS, $F(2,28) = 4.17$, $p < .05$; and, SITES by AGE_GRP, $F(2,28) = 3.35$, $p < .05$. The Amp2 variable for the Cz/Rare difference between 4- and 5-year-olds was significant ($p < .05$, Bonferroni's t-test): 17.2 versus 9.89 μV, respectively.

Table 9. Mean latencies and standard deviations (SDs) for N1, P2, N2, and P3 Common and Rare waveforms are summarized for 4-year-olds compared to 5-year-olds. **GP4** represents the 4-year-olds and **GP5** the 5-year-olds.

COMMON TONES

	N1 GP4	**N1 GP5**	**P2 GP4**	**P2 GP5**	**N2 GP4**	**N2 GP5**	**P3 GP4**	**P3 GP5**
Pz	134 (43)	110 (20)	220* (48)	178* (45)	282 (55)	244 (43)	361* (64)	317* (43)
Cz	138 (40)	114 (30)	216* (47)	182* (29)	286 (53)	258 (31)	360* (66)	320* (43)
Fz	152* (38)	126* (23)	225 (46)	176 (33)	292 (60)	256 (37)	376* (60)	320* (42)

RARE TONES

	N1 GP4	**N1 GP5**	**P2 GP4**	**P2 GP5**	**N2 GP4**	**N2 GP5**	**P3 GP4**	**P3 GP5**
Pz	119 (21)	135 (37)	175* (45)	206* (42)	253 (55)	263 (49)	345 (44)	324 (33)
Cz	127 (23)	140 (34)	185 (41)	205 (47)	258 (43)	257 (39)	360* (39)	325* (34)
Fz	138 (25)	133 (29)	194 (41)	181 (39)	249 (41)	235 (38)	334 (41)	317 (37)

* $p < .05$ (Bonferroni's t-test)

Step 9. Regression analyses examined patterns of latency change across the entire sample (N = 48) based on age in months (AGEMON). Equations for each ERP by Site for the Common and Rare tones are summarized in Table 10. The adjusted R-square, slope, standard error of estimate (SEE) and p values are summarized for each ERP by Site by Condition. The linear REGRESSION for N1, P2, N2 and P3 on AGEMON (age in months) revealed a strong inverse relationship between ERP latency and age (AGEMON) for Common tones. All 12 equations for the Common condition were significant, $p < .05$. In the Rare condition, only N2/Fz was significant, $p < .05$.

The yearly slope for each ERP is calculated by multiplying the slope for each equation by 12 months. Table 11 summarizes these slopes by TONE (Common and Rare). Several distinct patterns were evident. First, there was a consistent inverse relationship for all ERPs for either TONE (Common or Rare) across the age span (36-69 months) of this study. Second, This pattern was statistically significant for the slope for all 12 ERPs by Sites in response to the Common tones, $p < .05$. Third, the negative ERP slopes accelerated in opposite directions. The Common N1 slope increased posteriorly (19 ms/yr at Fz, 22 at Cz, and 26 at Pz), whereas, the slopes for P2, N2, and, P3

accelerated anteriorly: from 27 to 38 ms/yr for P2, from 28 to 38 ms/yr for N2, and from 33 to 44 ms/yr for P3. Fourth, the overall rate of acceleration for the Common slope was greatest for P3: 33 ms/yr at Pz, 40 at Cz, and 44 at Fz. This averaged to 39 ms/yr when collapsed across sites. Corresponding values for the Rare P3 were 10 ms/yr at Pz, 12 at Cz, and 15 at Fz which averages 12 ms/yr when collapsed across sites. Fifth, if each ERP was viewed as a composite N1, P2, N2, and P3 (by averaging the yearly slope across Pz, Cz, and Fz, but within the Common or Rare tone condition), the composite slope for the Common tone was 23 ms/yr for N1, 31 ms/yr for P2, 33 ms/yr for N2, and 39 ms/yr for P3. The corresponding composite slopes for the Rare ERPs were 4 ms/yr for N1, 7 ms/yr for P2, 11 ms/yr for N2, and 12 ms/yr for P3. When Expressed as composite ratios (the Common slope compared to the Rare slope), a threefold or greater difference was apparent: 5.65 for N1, 4.47 for P2, 3.0 for N2, and 3.25 for P3.

Table 10. The adjusted R-square, slope, standard error of estimate (SEE) and p levels are listed for the linear regression of peak latency on age (in months) for each **ERP** by **Site** by **Condition**. Analyses are based on 48 subjects.

ERP/SITE/COND.	**Adj R2**	**Slope**	**SEE**	**p Level**
N1/Pz/Common	0.22	-2.17	0.58	< 0.001
N1/Pz/Rare	**-0.01**	**-0.41**	**0.64**	**0.52**
N1/Cz/Common	0.20	-1.88	0.53	< 0.001
N1/Cz/Rare	**-0.02**	**-0.02**	**0.60**	**0.97**
N1/Fz/Common	0.13	-1.60	0.57	< 0.01
N1/Fz/Rare	**0.00**	**-0.58**	**0.53**	**0.28**
P2/Pz/Common	0.12	-2.27	0.84	< 0.01
P2/Pz/Rare	**-0.02**	**-0.12**	**0.83**	**0.89**
P2/Cz/Common	0.20	-2.43	0.67	< 0.001
P2/Cz/Rare	**-0.02**	**-0.28**	**0.78**	**0.72**
P2/Fz/Common	0.31	-3.16	0.68	< 0.001
P2/Fz/Rare	**0.04**	**-1.23**	**0.71**	**0.09**
N2/Pz/Common	0.08	-2.34	1.02	< 0.05
N2/Pz/Rare	**-0.02**	**-0.40**	**0.95**	**0.67**
N2/Cz/Common	0.18	-2.78	0.83	< 0.01
N2/Cz/Rare	**-0.01**	**-0.60**	**0.20**	**0.45**
N2/Fz/Common	0.17	-3.20	1.0	< 0.01
N2/Fz/Rare	**0.07**	**-1.81**	**0.83**	**0.05**
P3/Pz/Common	0.10	-2.76	1.10	< 0.05
P3/Pz/Rare	**0.00**	**-0.81**	**0.80**	**0.29**
P3/Cz/Common	0.14	-3.36	1.13	< 0.01
P3/Cz/Rare	**0.10**	**-0.96**	**0.81**	**0.24**
P3/Fz/Common	0.17	-3.69	1.14	< 0.01
P3/Fz/Rare	**0.04**	**-1.28**	**0.80**	**0.10**

Table 11. The ERP/SITE/CONDITION multiplied by 12 yields the following slopes per year (in ms) for the Common and Rare tones.

COMMON TONE

SITE	N1	P2	N2	P3
Pz	26	27	28	33
Cz	23	29	33	40
Fz	19	38	38	44

RARE TONE

SITE	N1	P2	N2	P3
Pz	5	3	5	10
Cz	0	3	7	12
Fz	7	15	22	15

IV. DISCUSSION

In accord with the exploratory nature of this study, several findings stand out. First, despite considerable ERP variability with young subjects, systematic application of the ERP template effectively measured and identified the N1-P2-N2-P3 waveforms in all subjects, Figures 2, 3 and 4.

Second, the Ignore condition of the 30% oddball paradigm provided consistent evidence that the classic four-wave N1-P2-N2-P3 complex could be elicited in children between three and five years old. The entire N1-P2-N2-P3 complex was evident in all age groups, although the Grand Average plots did not reveal a well-defined N1-P2-N2-P3 complex until age four, Figures 3 and 4. Overall waveform delineation was good at both Cz and Pz. The patterns of presumed development documented in this study did not differ significantly by sex.

Third, the Ignore condition effectively delineated the developmental trajectory of auditory ERPs. As expected from previous lifespan ERP studies (Brown et al., 1983; Polich, 1993), the slope for Rare tone ERPs varied by age. More surprising, however, the overall profile of the N1-P2-N2-P3 complex was most clearly delineated in response to the Common tone. The slopes for all 12 ERPS by AGEMON

for the Common tone were significant,($p < .05$), Table 10. This indicates that the Common tone accounted for the largest share of variance associated with the variation in slope by age. Thus, the Common tone provided an index of age-related change that may reflect neural development, learning, or both.

Fourth, amplitude differences between the Rare/P3 and the Common/P3 tones were not statistically significant despite some accentuation of amplitude associated with the P3/Rare. In some of the 3-year-olds, the Rare/P3 could be identified. By age four years, Rare/P3 amplitude values almost doubled the corresponding values for the Common/P3 at Cz and Pz. Failure to attain statistical significance in relation to the Rare/P3 may seem to support the need for using some kind of task condition, even with young subjects. However, this study did develop and test a replicable measurement system that documented the ontogeny of ERPs in 3-, 4-, and 5-year-olds. The profiles evident in Figures 2, 3, and 4 suggest that the Ignore condition is both an acceptable and revealing starting point for studying the development of ERPs.

Several considerations buttress these findings. First, the sample size was large (N = 48) with fairly even distribution: 16 in Age_Grp3, 18 in Age_Grp4, and 14 in

Age_Grp5. Second, findings are based on three active leads (Fz, Cz and Pz). Third, although not analyzed statistically, EOG data augment the findings by graphically depicting dissociation between the EOG and the Age_Grp3, Age_Grp4, and Age_Grp5 plots (Figures 3 and 4).

The findings support systematic use of template minima (a 40 ms delay and 4 μV amplitude shift) to measure and identify each ERP in the N1-P2-N2-P3 complex. The reliability ratings of .82 for Common and .85 for Rare tones by two independent raters (Table 4) indicate the measurement criteria employed in this study can be used by different raters to identify the N1-P2-N2-P3 complex in young subjects despite inherent subject variability.

As the first ERP in the four-wave-complex, N1 served as the logical starting point for the measurement of the entire four-wave-complex. The decision to focus on N1 as the starting point for waveform measurement was based on evidence that N1 was consistently evident in full term (n = 8) and preterm (n = 8) infants at three, six, and nine months old between 103 and 115 ms (Shucard et al., 1988). Goodin (1986) also noted that N1 and P2 both approximate adult latencies at no later than age five or six years old.

Current findings revealed that N1 latency varied less than any other ERP across each age group (Table 5). Also, N1 occurred in all groups for both tones between 110 and 153 ms. The range of N1 means for 3-year-olds was from 146 to 153 ms. A progressive N1 latency decrease across groups also was evident: 119 to 152 ms in 4-year-olds, and 110 to 140 ms in 5-year-olds. In relation to N1 amplitude, Shucard et al (1988) reported absolute amplitude differences between 4 and 6 μV in 6-to-9-month-old infants. This is consistent with the template amplitude minimum of 4 μV in this study. Finally, it is interesting to note that the mean amplitude for N1 in each age group exceeded 12 μV (Table 6).

These N1 group amplitude means and the consistency of N1's occurrence in the 70-200 ms latency window, corroborate using N1 as the starting point for the measurement of the N1-P2-N2-P3 complex. One other advantage of this approach is the consistent employment of a measurement system that proceeds in a forward direction.

These findings also enhance current understanding about the emergence of the P3. In their review of ERP studies of infants and children, Shibasaki & Miyazaki (1992) point out that the definition of the P300 has not yet been established. Present findings also raise

questions about how early the N1-P2-N2-P3 complex may occur, especially the P3 in the Ignore condition.

The latencies reported in Table 5 are notably earlier than those reported by studies such as Courchesne's (1990). In fact some latencies occur from 100 to 150 ms earlier. Mean P3 latencies (Table 5) in 3-year-olds, ranged from 340 to 396, then decreased progressively in the 4-year-olds, from 334 to 376 ms. The P3 range was smallest in the 5-year-olds, with all means between 317 and 325 ms. The means as reported in Table 5 are also evident in the Grand Average plots, Figures 3 and 4.

Similar latency ranges have also been reported by other investigators. For example, Jirsa and Clontz (1990) reported mean latencies for 18 normal children between nine and 11 years old of 88 ms for N1; 171 ms for P2; and 315 ms for P3. Based on 45 six-to- eight years old, Ivey (1992) reported a mean P3 latency of 335 ms at Cz.

According to Courchesne (1990), however, the task-related auditory P3b hovers around 475 to 500 ms between 4.8 years and 10.9 years old. A recent study of 48 females by Stauder, Molenaar and van de Molen (1993) included 21 kindergartners (mean age 5.5 years) and 27 first graders (mean age 7.5 years). Stauder et al. (1993)

reported a centroparietal positive peak near 600 ms which was interpreted as the P3. However, some of the Grand Average plots in Stauder et al. (1993) included earlier low amplitude ERP positivities which, if identified as the P2, would move the P3 into a much earlier window.

The extent to which the entire N1-P2-N2-P3 complex was evident within the 70 to 600 ms latency window for the both conditions suggests that the Ignore condition is an appropriate starting point for examination and documentation of ERP development. It also raises a vexing possibility in relation to the P300. Distinctions between P3a and P3b (Polich, 1988; Roth, 1973), based on the Attend condition, can not rule out the possibility that the P3 in the present study is different from both P3a and P3b. Roth elicited P3a by altering physical characteristics associated with the stimulus train. Our study did not alter any stimulus parameter within the stimulus train, nor was a time-linked task assigned. One way to distinguish between present latencies and those reported in the extant literature would be to refer to the P300 in this study as the P3/Ignore or **P3i** since it was elicited in a nontask, Ignore paradigm. If subsequent studies did not show P3i to occur consistently earlier than P3a, the distinction could eventually be dropped. In the meantime, its latency window and amplitude compared to P3b merits further attention.

Although this possibility may only partially resolve the extent to which current latencies differ from those reported by other investigators, this study does establish a replicable latency window for N1-P2-N2-P3 and a measurement system that could serve as a basis of comparison for subsequent studies with subjects of similar age. Studies with larger samples of young children are clearly needed to help clarify apparent contradictions between studies and to explore P3i as a distinct ERP with a profile that distinguishes it from P3a and P3b.

The negative slope for the Rare/P3 in this study was 10 ms/yr at Pz, 12 ms/yr at Cz, and 15 ms/yr at Fz (Tables 10 and 11). These values fall about in the mid-range compared to slopes reported for Rare/P3 latencies in other studies of preadolescent subjects. For example, Finley et al. (1985) reported a slope of less than 5 ms/yr; conversely, Goodin et al (1978) and Pearce et al (1989) reported negative P3 slopes between 18 and 20 ms/yr for preadolescent subjects and younger. The slopes reported for the cited studies were based on the Attend condition.

More striking are the negative slopes for P3 in the Common condition of this study. These values all exceeded the corresponding slopes for the P3/Rare tone by a two or threefold margin: 33 ms at Pz, 40 ms at Cz, and 44 ms at

Fz. One study by Jirsa (1990) with subjects between nine and 11 years old did report a slope of 39.5 ms/yr at Cz for the Rare/P3 in the Attend condition. At any rate, the two or threefold differences in slopes as a function of tone probability suggest that the Common stimulus should be looked at more closely in future ERP studies of children. For example, if the slope for Rare tones eventually surpasses the slope for Common tones, at what age does this occur? Does it differ as a function of the task (Attend or Ignore), or is it an age-graded phenomenon?

The consistency of the negative slopes for the Common tone latencies in this study (Tables 10 and 11) reveal notable stability in age-related change. One tentative explanation for the steeper Common slope relates to the process of habituation. The approximate 2-to-1 ratio of the Common versus Rare tone occurrence has a low enough ratio of stimulus presentation that both the Common and Rare tone ERP profiles were evident. In theory, if a Common tone had occurred 90% of the time, the associated ERP would have exhibited smaller amplitudes. However, based on the 70% versus 30% presentation rates used in this study, slightly larger Rare/P3 amplitudes were evident, but the overall delineation of the N1-P2-N2-P3 complex for the Common tone was most stable, better delineated, and therefore yielded significantly steep slopes for the ERPs.

Thus, habituation appears to have operated on a continuum that was reasonably well-delineated by the stimulus train used (p = .7 for Common and p = .3 for the Rare tone). Thompson and Glanzman (1976) recognize the role of habituation in early learning. They also suggest that sensitization may be a critical precursor or concomitant to the role played by habituation in early sensory processing. They also propose that sensitization may play a key role in the formation of a basic substrate that precedes more complex types of associative learning.

Four limitations related to this study need to be recognized. First, the cross-sectional design places some limitations on interpretation of findings, especially in light of the mean age difference between 3- and 4-year-olds (8.6 months) compared to the difference between the 4- and 5-year-olds (12.1 months)(Table 7). Second, children included in this study were drawn from a dozen different preschool sources, including two Head Start sites. However, the apparent interest in a study of this nature by only some parents of young children and the fact that over 90% of the 48 subjects in the primary study were attending preschool suggest rather strongly that the sample is largely composed of middle-class subjects. The extent to which prior experiences related to parenting and/or

preschool experiences may have influenced children's performance in this study is unknown. Third, the signal-to-noise ratio was not as high for the Rare tones as it was for the Common tones. Although this may have limited the overall delineation of the Rare/N1-P2-N2-P3 complex, the fact that the N1-P2-N2-P3 complex can be demonstrated with as few as 20 Rare tones and a 30% probability of occurrence in the nontask condition, augers well with using the Ignore condition with young subjects. A second testing session of each subject within a week or two of initial testing would shed a lot of additional light on these issues. Fourth, the system sensitivity of 500 μV was higher than what is usually used in childhood ERP studies.

Future Directions

A number of issues raised by this study merit consideration in subsequent investigations. First, does the measurement system employed (based on template minima of 40 ms and 4 μV) need to be adjusted for similarly designed studies or for designs based on the Attend condition? Second, will subsequent studies shed further light on the relationship between the Common and Rare slopes for the N1-P2-N2-P3 complex? Third, is it possible to approximate or simulate the Attend condition in an auditory ERP study and to compare such an approach with the

design used in this study? Fourth, developmental ERP studies that examine two or more modalities could help resolve questions related to age-related changes in ERP development that may be unique to a particular modality or non-modality-specific. Finally, is P3i simply a variant of P3a, or can P3i be shown to exhibit an ERP profile distinct from that of P3a and P3b?

Conclusion

The Ignore condition provided consistency of information processing to auditory stimuli. The entire N1-P2-N2-P3 was documented for Common and Rare tones in all age groups. The Rare/P3 was consistently evident in the 4-year-olds and 5-year-olds, but did not differ significantly from the Common/P3. Findings related to the slope of the Common tone ERPs were significant for all ERPs at all sites and suggest stability in age-related change, particularly for the Common tone. Though speculative, it is suggested that habituation may account for the significant slope for the Common tone ERPs. These findings provide an initial and long overdue empirical map of auditory ERP development in young children.

Appendix A: Preliminary Study Parameter Modifications

Modifications in stimulus parameters that were originally specified for the preliminary study were "piloted" on the final four preliminary study subjects, on a 10 year-old female (with three separate runs that varied LBP and system sensitivity settings), and on the project research assistant (RDT). Based on a July 2, 1993 telephone conversation with an investigator who also uses a Nicolet Pathfinder II (John Polich at Scripps Institute in San Diego), the following system defaults were tested: LBP settings of 1 Hz for EOG, .2 Hz for Fz, Cz, and Pz, and a system sensitivity of 200.

Despite the insertion of a mid-train pause and the 30% occurrence of the target stimulus, artifact rejection still approached 80% . Only by setting the sensitivity to 500 and the mid-line (Fz, Cz, & Pz) LBP settings to .5 Hz was the extremely high rejection rate alleviated. Before finalizing these system defaults for the primary phase, the .5 Hz LBP and 500 μV system sensitivity were piloted with the highly compliant 10-year-old subject (above). First, she was tested with LBP settings of .5 Hz and a sensitivity of 200. This run was aborted after 31 Common and 10 Rare tones were all rejected. In a subsequent run with the mid-line LBP settings still at .5 Hz, but the

sensitivity reset to 500, only four Common (4 out of 49) and two Rare (2 of 22) tones were rejected. Thus, 92% of all tones were accepted. By setting the sensitivity back to 200, however, the artifact rejection rate soared to 100% as all 20 Common and 6 Rare tones were rejected. In order to minimize delays in data acquisition and to keep the sensitivity the same for all subjects in the primary study, the system sensitivity was preset at 500 μV.

Appendix B: Subject Attrition due to Offset Spike

One problem that occurred with a random assortment of subjects (n = 9) involved an unaccounted for offset spike between 18 and 32 ms post-stimulus. This spike mostly occurred in the EOG channel for Rare tones. To a lesser extent the offset spike was evident in some mid-line leads, especially Fz. The offset spike occurred at different times of the day (twice in the morning; three times near mid-day; and, four times between 3 and 6 p.m.). The spike artifact could be greatly attenuated by digitally refiltering each channel of each record with band pass settings of 1 Hz (LBP) and 30 Hz (HBP). This approach was not used because of a controversy in published studies about possible attenuation of P3 amplitude when the LBP is set at 1 Hz (cf., Polich, 1993; Goodin, Aminoff, Chernoff & Hollander, 1990). In short, subjects with an early offset spike were dropped from the study unless they met all conditions below:

1. Waveforms returned to a pre-spike level by $\leq$ 50 ms.
2. The entire N1-P2-N2-P3 complex was recognizable for Common and Rare tones.
3. Subject complied with all test session criteria and received no more than one "state rating" of 3 or 4.
4. Subject record included at least 15 accepted Rare tones (75% of complete record).

Appendix C: Summary of Subjects Included in Final Study

A profile of each subject included in the final study lists file name (FILE), sex, Age in Months (AGE), score on hearing test (HTEST), Common and Rare Tones accepted (+)/rejected (-), Per Cent Accepted (%C for Commons; %R for Rares), and subject state ratings for each 3-min interval of data collection. Symbols /- or /-/- in State Column indicate testing session ended early (as soon as 20 Rare tones were accepted).

Age_Grp3 (N=16)

FILE	SEX	AGE	HEAR	COMMON	%C	RARE	%R	STATE
CORM	1	40	6/12*	49+/41-	.54	29+/17-	.53	2/2/2/2
OLIZ	1	47	12/12	55+/36-	.60	20+/18-	.53	3/2/3/-
GEND	0	46	11/12	19+/93-	.17	09+/39-	.19	3/3/3/3
JONY	1	45	11/12	41+/24-	.63	20+/06-	.56	1/1/1/-
ANDS	1	45	12/12	44+/24-	.65	20+/09-	.69	2/2/2/-
SHAI	1	39	11/12	49+/17-	.74	20+/07-	.74	1/1/1/-
DEVN	1	44	12/12	22+/90-	.20	13+/35-	.27	2/2/2/3
SASA	0	44	11/12	36+/76-	.32	15+/33-	.31	3/2/2/2
MIKH	1	47	10/12	38+/74-	.34	15+/33-	.31	3/2/2/2
TAWS	0	46	12/12	54+/43-	.56	20+/22-	.48	2/1/1/1
NATJ	1	41	12/12	51+/25-	.67	20+/11-	.65	1/1/1/1
CHAC	1	47	12/12	35+/77-	.32	08+/40-	.17	2/3/2/3
ALIS	0	45	10/12	45+/21-	.68	20+/07-	.74	1/1/1/-
JULC	0	43	11/12	54+/30-	.64	20+/15-	.57	4/3/3/2
TIAN	0	45	12/12	50+/34-	.60	20+/15-	.57	2/1/1/1
KRIT	0	36	11/12	42+/44-	.49	20+/16-	.56	1/1/2/-

* Subject failed hearing test. Subsequent audiological assessment by pediatrician verified normal hearing.

Age-Grp4 (N=18)

FILE	SEX	AGE	HEAR	COMMON	%C	RARE	%R	STATE
AKEH	0	52	10/12	37+/30-	.55	20+/07-	.74	1/1/1/-
SHAM	0	57	12/12	33+/69-	.32	20+/25-	.44	2/1/1/1
PREG	1	49	12/12	42+/05-	.89	20+/01-	.95	1/2/1/1
KELG	0	49	12/12	68+/29-	.70	20+/22-	.48	1/1/1/1
PATI	1	54	10/12	47+/03-	.94	20+/03-	.87	1/1/-/-
KESC	0	49	10/12	43+/24-	.64	20+/08-	.71	1/2/1/-
NATU	1	55	11/12	39+/73-	.35	16+/32-	.33	1/1/1/1
HELA	0	58	12/12	54+/11-	.83	20+/06-	.77	1/1/-/-
BRIM	0	54	11/12	27+/85-	.24	16+/32-	.33	1/1/2/1
KYLS	1	52	12/12	24+/88-	.21	10+/38-	.21	1/1/1/1
KAPT	0	57	12/12	39+/73-	.34	14+/34-	.29	2/2/2/3
REBF	0	50	11/12	32+/34-	.48	20+/07-	.74	1/1/1/-
LAUP	0	49	12/12	43+/48-	.47	20+/18-	.52	1/1/1/-
JEWH	0	50	11/12	55+/27-	.67	20+/13-	.61	1/1/2/-
TAOL	1	53	10/12	41+/24-	.63	20+/06-	.77	1/1/1/-
OMAM	1	51	12/12	45+/48-	.48	20+/20-	.50	2/1/1/2
KRIH	0	55	10/12	59+/17-	.78	20+/11-	.65	1/1/1/-
JASF	1	50	11/12	47+/37-	.56	20+/15-	.57	2/3/3/3

Age_Grp5 (N=14)

DANM	0	63	12/12	14+/98-	.13	09+/39-	.19	3/3/2/2
LINM	0	63	12/12	45+/67-	.40	17+/31-	.35	3/2/2/2
CHAS	0	60	12/12	52+/34-	.60	20+/16-	.56	2/1/1/1
SKYG	0	63	12/12	53+/14-	.79	20+/08-	.71	1/1/-/-
ELIS	0	67	10/12	43+/56-	.43	20+/23-	.47	3/3/2/1
CHEW	0	66	12/12	39+/73-	.35	12+/36-	.25	1/1/1/-
CHRA	1	66	12/12	36+/14-	.72	20+/03-	.87	1/1/-/-
HOWK	1	60	12/12	52+/16-	.76	20+/09-	.69	1/1/-/-
DANN	1	65	12/12	45+/20-	.69	20+/06-	.77	1/1/1/-
JOHK	1	69	12/12	45+/26-	.63	20+/10-	.67	1/1/1/-
MAIA	0	63	12/12	59+/23-	.72	20+/13-	.61	1/1/1/1
N2CH	1	67	12/12	47+/35-	.57	20+/13-	.61	2/1/1/1
T2CH	1	67	12/12	47+/48-	.49	20+/21-	.49	1/1/1/1
ANGE	0	64	12/12	48+/45-	.52	20+/20-	.50	1/1/1/1

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