

Auditory and visual refractory period effects in children and adults: An ERP study

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Abstract

Objective: This developmental study was designed to investigate event-related potential (ERP) refractory period effects in the auditory and visual modalities in children and adults and to correlate these electrophysiological measures with standard behavioral measures.

Methods: ERPs, accuracy, and reaction time were recorded as school-age children and adults monitored a stream of repetitive standard stimuli and detected occasional targets. Standards were presented at various interstimulus intervals (ISIs) in order to measure refractory period effects on early sensory components.

Results: As has been reported previously in adults, larger components for standards with longer ISIs were observed for an auditory N1 and the visual occipital P1 and P2 in adults. Remarkably similar effects were observed in children. However, only children showed refractory effects on the amplitude of the visual N1 and P2 measured at anterior sites. Across groups, behavioral accuracy and reaction time were correlated with latencies of auditory N1 and visual P2 across ISI conditions.

Conclusions: The results establish a normal course of development for auditory and visual ERP refractory period effects across the 6- to 8-year-old age range and indicate similar refractoriness in the neural systems indexed by ERPs in these paradigms in typically developing children and adults. Further, the results suggest that electrophysiological measures and standard behavioral measures may at least in part index similar processing in the present paradigms.

Significance: These findings provide a foundation for further investigation into atypical development, particularly in those populations for which processing time deficits have been implicated such as children with specific language impairment or dyslexia.

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Keywords: ERP; Refractory period; Visual EP; Auditory EP; Children; Sensory development

1. Introduction

Numerous behavioral, psychometric studies of auditory and visual system development in school-age children have clearly shown that aspects of sensory processing continue to develop across childhood into adolescence (e.g., Allen et al., 1989; Buckingham and Kelly, 1996; Fior, 1972; Hollants-Gilhuijs et al., 1998a,b; Kovács et al., 1999; Lenihan et al., 1971; Maxon and Hochberg, 1982). In consonance, anatomical and MRI data indicate that both the extrastriate

and auditory cortices continue to develop at least until adolescence (e.g., see Garey, 1984; Huttenlocher and Dabholkar, 1997; Moore and Guan, 2001; Sowell et al., 1999; Thompson et al., 2000; Yakovlev and Lecours, 1967). However, relatively little is known about the on-line functional development of basic auditory and visual processing across the school-age years, in part due to the paucity of adequate methodologies useable with children.

The recording of event-related potentials (ERPs) is one non-invasive functional imaging method with exquisite temporal resolution that is amenable to use with children. ERPs are voltage fluctuations in the ongoing electroencephalogram (EEG) in response to controlled stimulus presentations, and have proven sensitive to the cortical activation patterns underlying sensory and perceptual processes

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(e.g., see Rugg and Coles, 1995). Scalp-recorded ERPs reflect the stimulus-locked information processing activities, in terms of net electrical fields, of large assemblies of neurons in different areas of the brain on a timescale of milliseconds (e.g., see Coles and Rugg, 1995). The individual components that constitute the ERP waveform index particular types of information processing, with the early components reflecting activity within sensory systems.

A number of ERP studies have investigated the development of auditory and visual sensory systems and many of the early components of the ERP waveform have been shown to change over time. For example, in the auditory modality, peak latencies of P1, N1, and N2 have been shown to decrease with increasing age from childhood to late adolescence (Borg et al., 1988; Enoki et al., 1993; Fuchigami et al., 1993; Goodin et al., 1978; Oades et al., 1997; Paetau et al., 1995; Rojas et al., 1998; Tonquist-Uhlén et al., 1995). In the visual modality, researchers have similarly reported (non-monotonic) decreases in amplitude of occipital responses to visual stimuli with increasing age (Barnet et al., 1980; Breclj et al., 2002; Buchsbaum et al., 1974; Callaway and Halliday, 1973; Dustman and Beck, 1969), with waveforms to some stimuli still not adult-like at the age of 5 years (Blom et al., 1980; Moscovitz and Sokol, 1983; Sokol and Jones, 1979). Much of the developmental research in the visual modality focuses on infancy rather than childhood (e.g., see Eggermont, 1988).

Recently, there have been a number of reports further investigating the development of the auditory evoked potential, with results confirming and extending earlier findings of change in AEP components into adolescence (e.g., Albrecht et al., 2000; Bruneau et al., 1997; Ponton et al., 2000, 2002). (To our knowledge, no similar recent research has been conducted within the visual domain.) For example, Bruneau et al. (1997) reported differential topography of the N1 in adults (frontocentral maximum) and children (midtemporal maximum), while Ponton et al. (2000) reported gradual latency decreases in P1 and N1(b) and increasing latency in N2 with more step-like amplitude changes from age 5 to 20, dependent on recording location. Further, it appears that maturation rates are not the same throughout the auditory system, such that P2 matures earlier in comparison to N1(b) (Ponton et al., 2000). Dipole source modeling has suggested that the generators contributing to these components may indeed mature at different rates, with, for example, maturation of the generators of the auditory N1(b) and P1 relatively slow in comparison to those for N2 (Ponton et al., 2002; see also Albrecht et al., 2000). It has been suggested (Ponton et al., 2002) that this extended development may be related to the prolonged development of superficial layers of the human auditory cortex (e.g., Moore and Guan, 2001).

Across developmental studies of the auditory evoked potential, there is some controversy regarding waveform morphology. While adult waveforms typically evidence a P50/P1 followed by an N1, children's waveforms

sometimes show a large P1 followed by a negativity at 200–250 ms (termed N1b in some reports and N250 in others, e.g., Albrecht et al., 2000; Bruneau et al., 1997; Ceponiene et al., 1998; Courchesne, 1990; Korpilahti and Lang, 1994; Kurtzberg et al., 1995; Paetau et al., 1995; Ponton et al., 2000; Sharma et al., 1997). The relationship between the child N1b/N250 and the adult N1 is unknown, with some authors suggesting homology (e.g., Korpilahti and Lang, 1994; Kurtzberg et al., 1995) and others claiming two distinct components (e.g., Csépe, 1995; Ponton et al., 2002; Takeshita et al., 2002). Reports of different topography for the first negative peaks in the auditory waveforms of young children and adults (e.g., Bruneau et al., 1997) support the claims of distinct components and indexed neural systems, as do reports of different component structure based on dipole analyses (e.g., Albrecht et al., 2000; Ponton et al., 2002; Takeshita et al., 2002).

Notwithstanding these accumulating findings regarding the normal course of maturation of the human auditory system in terms of ERPs, there is still much to be learned about basic sensory functional development; in particular, little is known about the refractory properties of developing sensory neural networks. It has been shown that ERPs can be used to assess relative refractory periods or recovery cycles for aspects of the auditory and visual systems in paradigms in which a stimulus is presented repeatedly at different interstimulus intervals (ISIs) or pairs of stimuli are presented at different ISIs. In adults, the amplitude of early (100–200 ms) modality-specific ERP components is reduced as stimulus repetition rate is increased. This decrease in responsiveness with decrease in ISI is thought to be a reflection of the lack of excitability of the population of responding cortical neurons, and an index of processing rates within cortical sensory areas (Gastaut et al., 1951). Thus, theoretically, an increase in ERP amplitude to the same stimulus presented with a longer ISI as compared to a shorter ISI is a reflection of the greater physiological recovery over time of the neurons generating the response to that stimulus. It is likely that different populations of neurons have different recovery cycles and that refractoriness of these different networks may have different developmental time courses.

The refractory rate of neuronal populations has been studied in cats and monkeys as well as in humans (e.g., Chang, 1951; Demetrescu and Steriade, 1967; Neville and Foote, 1984; Rosenzweig and Rosenblith, 1950). In the visual modality, studies with adult humans using stimuli with relatively short ISIs have suggested that the recovery cycle extends beyond 200 ms (Bergamasco, 1966; Cigánek, 1964; Floris et al., 1967; Galvin et al., 1976; Musselwhite and Jeffreys, 1983; Riemslog et al., 1985; Skrandies and Raile, 1989). Studies using stimuli with longer ISIs have confirmed a lengthy visual recovery cycle for component amplitude extending beyond 6 s (Lehtonen, 1973). MEG response recovery studies have suggested that occipital

traces, perhaps representing iconic memory, remain for up to 600 ms while later activations in other visual regions extend in duration to 30 s (Uusitalo et al., 1996). Some ERP studies have reported a refractory effect on visual component latency as well (Mitchell, 1983; Neville et al., 1993; Skuse and Burke, 1986).

In the auditory modality, relative amplitude recovery may not be achieved with ISIs shorter than 3 s, and the substantial refractory period may extend to more than 10 s (Bess and Ruhm, 1972; Budd et al., 1998; Davis et al., 1966; Fruhstorfer, 1971; Fruhstorfer et al., 1979; Gjerdingen and Tomsic, 1970; Hari et al., 1982, 1987; Knight et al., 1980; Loveless et al., 1996; Lü et al., 1992; Mäkelä et al., 1993; Nelson and Lassman, 1963; Nelson and Lassman, 1973; Ritter et al., 1968; Roth and Kopell, 1969; Rothman et al., 1970; Sams et al., 1993; Woods et al., 1980). MEG studies of decay of neuronal activation in auditory cortex have suggested that such refractoriness is related to the duration of echoic memory (Lu et al., 1992). ERP latencies of the N1 and P2, particularly at long ISIs, do not typically show refractory period effects (Bourbon et al., 1987; Nelson and Lassman, 1963). The amplitude effect does not appear to be due to habituation, but rather to the refractory periods or recovery cycles of the neurons involved in processing sensory auditory information (Budd et al., 1998).¹

There have been few investigations of the normal developmental course of ERP refractory period effects and little is known about the excitability and refractoriness of developing as compared to mature neural sensory systems. In the auditory modality, MEG studies have shown that the refractory period for M1 (N1) is longer in early childhood (Paetau et al., 1995; Rojas et al., 1998). However, a combined MEG-ERP study reported typical N1 refractory effects in children aged 6–14 with ISIs of 1.6, 3, and 5 s (Takeshita et al., 2002). Another ERP study has shown that the morphology of the auditory waveform varies with ISI in 7- to 9-year-old children (Ceponiene et al., 1998). Using

tones presented at ISIs of 350, 700, and 1400 ms in blocks, Ceponiene et al. reported that the P1 *decreased* in amplitude with increasing ISI but N160 amplitude increased at the longest as compared to the middle ISI, while neither amplitude nor latency of N250 varied reliably with ISI. In the visual modality, the amplitude of early components appears to increase with increasing ISI (of 1, 2, and 4 s) in children and adults (Cohn et al., 1985).

There is also some ERP evidence indicating that refractory periods and the effect of ISI may vary across populations. For example, in adults, neural responses to peripheral visual stimuli are less refractory in the deaf (Neville et al., 1983) and the auditory recovery effect occurs more quickly in the congenitally blind (Röder et al., 1999). Abnormal refractoriness of P1 has been reported in a number of atypical populations, including adults with schizophrenia (e.g., Cullum et al., 1993; Freedman et al., 1987a; Light et al., 2000), autism (e.g., Buchwald et al., 1992), Huntington's disease (e.g., Uc et al., 2003), Alzheimer's disease (e.g., Jessen et al., 2001), traumatic brain injury (e.g., Arciniegas et al., 2000), and post-traumatic stress disorder (e.g., Skinner et al., 1999). Developmentally, in children with Williams Syndrome, auditory refractoriness as measured by ERPs is shorter-lasting than normal, while visual refractoriness appears normal (Neville et al., 1994). In a study of 8- to 10-year-old children with and without specific language impairment (SLI), children with SLI displayed smaller amplitude auditory and visual ERP components, but there were few differences in the effects of ISI between control and SLI children (Neville et al., 1993); others have also reported abnormalities in the AEPs of children with SLI (e.g., Mason and Mellor, 1984). As it has been proposed that fast temporal processing deficits occur in language and reading disorders such that clinical participants evidence impairment at brief presentation rates but not at long presentation rates (e.g., Tallal, 1978, 1998), investigation of the refractoriness of typically developing sensory systems may lead to a better understanding of putative temporal deficits in atypically developing systems. Overall, refractory period effects might be seen as a fundamental measure in the investigation of many neurological and developmental conditions marked by either slowing of processing time or hyperexcitability.

As reviewed above, very few ERP refractory period studies have been conducted with children, particularly young school-age children. In general, there is a dearth of data on normal sensory development in young children, especially electrophysiological data coupled with behavioral data in both the visual and auditory modalities. The current study was designed to investigate refractory period effects in both the auditory and visual modalities in the same 6- to 8-year-old children and adults. Participants were simply asked to monitor a stream of repetitive auditory or visual events (standards) and detect occasional targets. Standards were presented at various ISIs in order to measure

¹ There is some debate in the literature regarding the underlying nature of the decrement in auditory N1 amplitude typically observed with repetition of a stimulus, in particular whether it is the result of habituation or the refractoriness of contributing neural systems. Budd et al. (1998) provide a comprehensive review of the debate and offer ERP evidence that the effect is indeed better characterized as a refractory period or recovery cycle effect. They note that the 'assumption central to this view of the N1 response decrement is that polysynaptic neural systems or neural networks generating the N1 show a phenomenon similar to the excitability cycle of single cells. It is generally argued that the recovery period reflects the dissipation of a state of temporal excitability in the N1 generators following their activation by a stimulus. Although the nature of the gross neural mechanisms or networks underlying these refractory effects is not well understood, it is generally maintained that decrements are observed because of the temporal limitations inherent in the physiochemical mechanisms underlying N1 generation' (Budd et al., 1998, p. 52). As the precise neural mechanisms underlying the effect remain unknown, a more neutral term such as 'adaptation' may be more appropriate to describe the effect at this time. However, as the relevant extant literature typically uses the terms 'recovery cycles' and 'refractory effects,' we use these terms here.

refractory period effects. In most of the auditory studies reviewed, stimuli were presented to one ear at a constant rate and participants were instructed to ignore stimulus presentations (e.g., Albrecht et al., 2000; Ponton et al., 2000, 2002; Tonnquist-Uhlén et al., 2003). In contrast to these previous reports, the present experiment used a more ecologically valid design with binaural, free-field auditory stimuli; required attention and active processing of the stimuli; manipulated stimulus presentation rate in an intermixed design; and explored auditory and visual processing in one group of participants, with the goal of furthering understanding of functional sensory system development across modalities as indexed by both electrophysiological and behavioral measures.

Given the extant behavioral, electrophysiological, and neuroanatomical data as reviewed above, we expected later and larger early sensory components in children as compared to adults. Moreover, we expected longer recovery cycles for amplitude and perhaps latency of the early sensory components at shorter ISIs for both children and adults. That is, we predicted smaller amplitude and perhaps longer latency components to shorter ISI standards across age groups. Based on the recent findings of Ponton and colleagues (Ponton et al., 2000, 2002), we might predict in children less adult-like refractory effects for the more slowly maturing auditory N1(b) and P1 than for the more quickly maturing P2; however, Ceponiene et al. (1998) reported refractory effects for both P1 and N160 in children aged 7–9 years. We also expected topographical differences for N1 effects in children and adults (Bruneau et al., 1997; Tonnquist-Uhlén et al., 1995). In the visual modality, we predicted similar refractory effects for adults and children on the P1, N1, and P2, as previously reported with longer ISIs (Cohn et al., 1985). Behaviorally, we predicted improvements in accuracy and reaction time over developmental time. Across modalities, we hypothesized relationships between behavioral measures of reaction time and latency of ERP components.

2. Methods

2.1. Subjects

Participants were right-handed (Oldfield, 1971), monolingual English speakers with no history of neurological, language, speech, or articulatory disorders. All were volunteers paid for their participation. Socioeconomic status of children's families ranged from lower middle to upper class on the Hollingshead Index of Social Position, with a middle class average. Adults reported normal hearing and normal or corrected-to-normal vision and all children passed a standard hearing screening (1, 2, and 4 kHz under headphones) and visual screenings for acuity (Kindergarten Snellen chart) and color (Matsubura tests, a children's version of Ishihara tests). Participants included

15 adults (9 female), average age 23;8 (SD 4;1); 20 8-year-olds (10 female), average 8;5 (SD 0;4); 23 7-year-olds (10 female), average 7;5 (SD 0;3); and 20 6-year-olds (9 female), average 6;6 (SD 0;3).

2.2. Stimuli

2.2.1. Auditory

Auditory stimuli consisted of a standard 2000 Hz tone and 33 different target sounds (8 bits, 22 kHz). Target sounds were created by modifying digitized sound files of animal noises (meow, roar); they were not identifiable as animal noises, but were clearly distinguishable from the standard tone. Each target sound was heard twice, once in the first half of the list and again in the second half. Each auditory stimulus was 50 ms in duration and was presented over a central speaker located 57 in. directly in front of the participant at a comfortable listening level (65 dB SPL (A-weighted)). Auditory stimuli were presented at one of three interstimulus intervals: 200, 500, or 1000 ms. ISIs were chosen in accordance with the literature which indicates that brief stimuli (<500 ms) are particularly problematic for children with language impairments (e.g., Tallal et al., 1995). A total of 736 stimuli were presented; 600 standard tones (200 at each ISI) and 66 target sounds (22 at each ISI) were analyzed. All stimuli were presented pseudorandomly intermixed, with the exceptions that all targets were followed by a 1000 ms ISI standard (these stimuli were not included in analyses), each half of the list began with two 1000 ms standards (these stimuli were not included in analyses), and no more than four of any given ISI-stimulus were presented in a row (in order to reduce possible effects of repetition priming or habituation). The random presentation of target sounds attempted to insure attention throughout the paradigm.

2.2.2. Visual

Visual stimuli consisted of a standard red square (23 mm per side; $\sim 1^{\circ 2}$ visual angle) and 33 different target animal pictures (maximum 335 mm wide, 300 mm high; $\sim 10^{\circ 2}$ visual angle) displayed on a monitor located 57 in. in front of the participant. Each animal picture target was presented twice, once in the first half of the list and again in the second half. Each visual stimulus was presented for 50 ms, with one of three preceding ISIs: 200, 400, or 600 ms. A total of 736 stimuli were presented; 600 standard squares (200 at each ISI) and 66 target animal pictures (22 at each ISI) were analyzed. All stimuli were presented pseudorandomly intermixed, with the exceptions that all targets were followed by a 600 ms ISI standard (these stimuli were not included in analyses), that each half of the list began with two 600 ms standards (these stimuli were not included in analyses), and no more than four of any given ISI-stimulus appeared in a row (in order to reduce possible effects of repetition priming or habituation). The random presentation

of target pictures attempted to insure attention throughout the paradigm.

2.2.3. Procedure

Adult participants and children and their parents were given a brief tour of the laboratory, the experiments were explained, and any questions were addressed; adults signed a consent form and children signed an assent form. Following electrode cap placement, participants were seated in a comfortable chair in a sound attenuating, electrically shielded booth. In the auditory condition, participants were instructed not to move their eyes from a fixation cross at the center of a monitor located 57 in. directly in front of them. For children, gaze direction was monitored by an experimenter sitting next to the participant and via a remote closed circuit television system, as well as by electrodes placed near the eyes recording electro-oculogram (EOG); for adults, only the latter two applied. The experimenter monitoring the closed-circuit television and the traces from the electrodes near the eyes on-line conveyed any eye movement information to the experimenter seated with the child (through an in-ear microphone inaudible to the child), who reminded the child to fixate; adults who showed evidence of eye movements on-line were reminded to fixate through an intercom system. Participants were further instructed to monitor the auditory stream for occasional target events and press a button on a response box in their laps as quickly as possible when they heard a target event. Instructions were: *keep your eyes at the center of the screen on the plus sign; you will hear the same tone a lot, over and over again; when you hear anything different—like a squeak or squawk—press the [left or right] button*. Response hand was counterbalanced across the first and second halves of the list within participants. Thirty-three practice trials preceded the actual test session (including three target sounds) and a break was given halfway through the stimulus list (after about 4 min), at which time participants were instructed to switch response hand.

In the visual condition, participants were instructed not to move their eyes from the center of a monitor located 57 in. directly in front of them. For children, gaze direction was again monitored by an experimenter sitting next to the participant, via a remote closed circuit television system, and by on-line recordings of EOG; for adults, only the latter two applied. Participants were further instructed to monitor the visual stream for occasional target events and press a button on a response box in their laps as quickly as possible when they saw anything other than the red square; response hand was counterbalanced across the first and second halves of the list within participants. Instructions were: *keep your eyes at the center of the screen; you will see a red square a lot, over and over again; when you see anything else—like a picture of an animal—press the [left or right] button*. As in the auditory condition, 33 practice trials preceded the actual test session (including three target animal pictures) and a break was given halfway through the stimulus list

(after about 4 min), at which time participants were instructed to switch response hand.

Core subtests of the Comprehensive Test of Phonological Processing (Wagner et al., 1999) were administered to all child participants (with the exception of one 7-year-old girl). Scores on the digit span subtest and the Phonological Memory composite were considered in analyses.

Auditory and visual sessions were administered on different days, with order of conditions and order of response hand counterbalanced between visits and participants; behavioral testing was conducted separately at a third visit. No more than 35 days elapsed across visits.

2.2.4. EEG/ERP recording and analysis

Electroencephalogram (EEG) was recorded from 29 tin electrodes mounted in an elastic cap (Electro-Cap International). These included three midline sites (Fz, Cz, and Pz) and 13 pairs of lateral sites (FP1/2, F7/8, FT7/8, F3/4, FC5/6, C3/4, C5/6, T3/4, CT5/6, P3/4, T5/6, TO1/2, and O1/2; refer to Fig. 1). Electrodes were also placed beneath

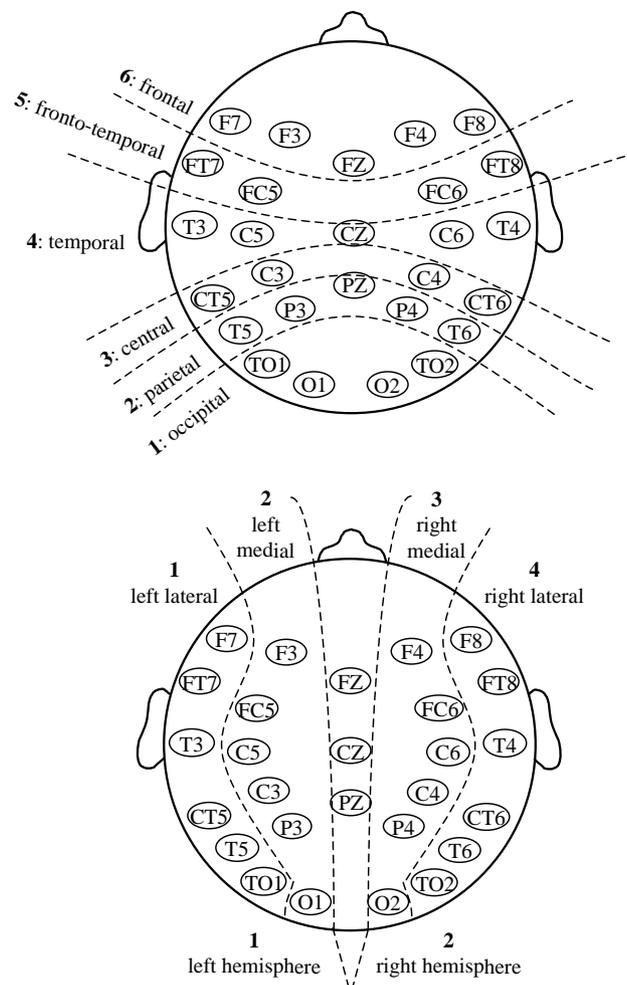


Fig. 1. Schematic representation of the electrode montage and the factors used in analyses. At the top, six levels of the anterior/posterior factor are illustrated. At the bottom, two levels of the lateral/medial factor and two levels of the hemisphere factor are indicated.

the lower right eye and at the outer canthi of the left and right eyes in order to monitor eye movements (EOG); in addition, recordings from FP1/2 were used to reject trials that were contaminated by eyeblink artifacts. Activity at the right mastoid was recorded during the experiment, but all on-line recordings were referenced to the left mastoid; recordings were re-referenced to averaged mastoids in the final data averaging. Eye electrode impedances were maintained below 10 K Ω , mastoid electrodes below 2 K Ω , and scalp electrodes below 3 K Ω .

The EEG was amplified with Grass 7P511 amplifiers (–3 dB cutoff, bandpass 0.01–100 Hz) and digitized on-line (sampling rate 4 ms). Off-line, separate ERPs to standards with the three different ISIs in each modality were averaged for each subject at each electrode site over a 500 ms epoch, using a 100 ms pre-stimulus-onset baseline. Data for targets are not reported due to the relatively small number of trials and to contamination of the majority of those trials by movement artifact due to vigorous button-pressing by the children. Data were subject to post-hoc filtering only at 60 Hz. Trials contaminated by eye movements or blinks (determined by inspection of data recorded at the outer canthus of each eye and by comparison of data recorded at FP1 and below the eye, respectively), muscular activity, or electrical noise were not included in analyses. Standard artifact rejection parameters were initially employed by computer routine, and data were subsequently analyzed on an individual basis for further artifact rejection. A minimum of 30 artifact-free trials in each condition was imposed, and for most subjects the average number of useable trials was substantially larger than 30 (the average number of useable trials for each age group for each condition in each modality was greater than 100).

Peak amplitude and latency were measured for each component of interest in the ERP waveforms. In the auditory modality, the morphology of the waveforms appeared to differ in children and adults (see Fig. 2). As discussed in the Introduction, other researchers have reported a similar pattern, which may be due to true morphological differences or to longer-latency components in children; there is even some suggestion that the N1 may be absent in children particularly when stimuli are presented at short ISIs (Ceponiene et al., 1998; Paetau et al., 1995; Rojas et al., 1998). While recognizing the possibility of non-homology, we identified a P1-N1-P2 sequence in the auditory ERP waveforms for each age group; this nomenclature was employed simply to indicate the first positive, first negative, and second positive peak in the waveforms, respectively. As this experiment was not specifically designed to address the issues of homology or differential componentry in children and adults (rather, the focus was on refractory effects), we attempted to remain agnostic in our choice of labels for the early auditory components; we note the possibility of non-homology between groups by placing an asterisk after auditory

component labels to indicate that the labels are position holders and are not intended to indicate, necessarily, correspondence between child and adult peaks. As no similar debate is ongoing in the visual literature, to our knowledge, we label these peaks in the traditional manner.

In the auditory modality, adults showed an early P1* (measured within the 0–100 ms window) while children showed a delayed P1* (50–250 ms). Subsequently, adults evidenced an N1* (80–180 ms) followed by a P2* (150–300 ms) and children evidenced an N1* (150–350 ms) followed by a P2* (350–450 ms). In the visual modality, the morphology of the waveforms and timing of componentry was more similar in children and adults (see Fig. 3). Along the most posterior row (refer to Fig. 1), children showed a P1 (80–180 ms) followed by an N1 (100–300 ms) and a P2 (200–420 ms) and adults also showed a P1 (80–180 ms) followed by an N1 (120–220 ms) and a P2 (180–320 ms). At sites anterior to this row, children evidenced an N1 (100–200 ms) and P2 (150–320 ms) while adults showed only an N1 (80–200 ms).

To control for the typical overall larger amplitude waves in children, peak amplitude data were normalized based on the formula (score-mean/SD) where score was an ERP average amplitude value (one for each condition and each scalp site for each subject), mean was the mean amplitude across all subjects in each age group for that condition and site, and SD was the standard deviation of the mean amplitude. As this type of normalization eliminates the main effect of group but not interactions among group and other variables (Holcomb et al., 1992), analyses with non-normalized data were run to investigate the main effect of group; in every case, this effect was significant, confirming our predictions and reflecting the fact that ERPs from children were typically larger than those from adults. Therefore, all subsequent amplitude analyses reported below were conducted with normalized data.

In addition to ERP measures, behavioral measures included accuracy of target detection and reaction time to detect targets. Any reaction times (RTs) less than 100 ms or greater than 1000 ms were removed from analyses; in the auditory paradigm, this constituted 5.7% of the RT data for 6-year-olds, 5.1% of the RT data for 7-year-olds, 1.7% of the RT data for 8-year-olds, and 0.1% of the RT data for adults. In the visual paradigm, this constituted 1.5% of the RT data for 6-year-olds, 1.5% of the RT data for 7-year-olds, 0.5% of the RT data for 8-year-olds, and 0% of the RT data for adults. Scores for children on the CTOPP were all within normal limits.

In a standard approach, omnibus mixed-design analyses of variance (ANOVAs) were performed on the ERP and behavioral data from the auditory and visual paradigms separately. The between-subjects factor was age group [four possible levels: 6, 7, 8, adult] and within-subject factors included ISI condition [three possible levels], anterior/posterior [six possible levels: frontal, fronto-temporal,

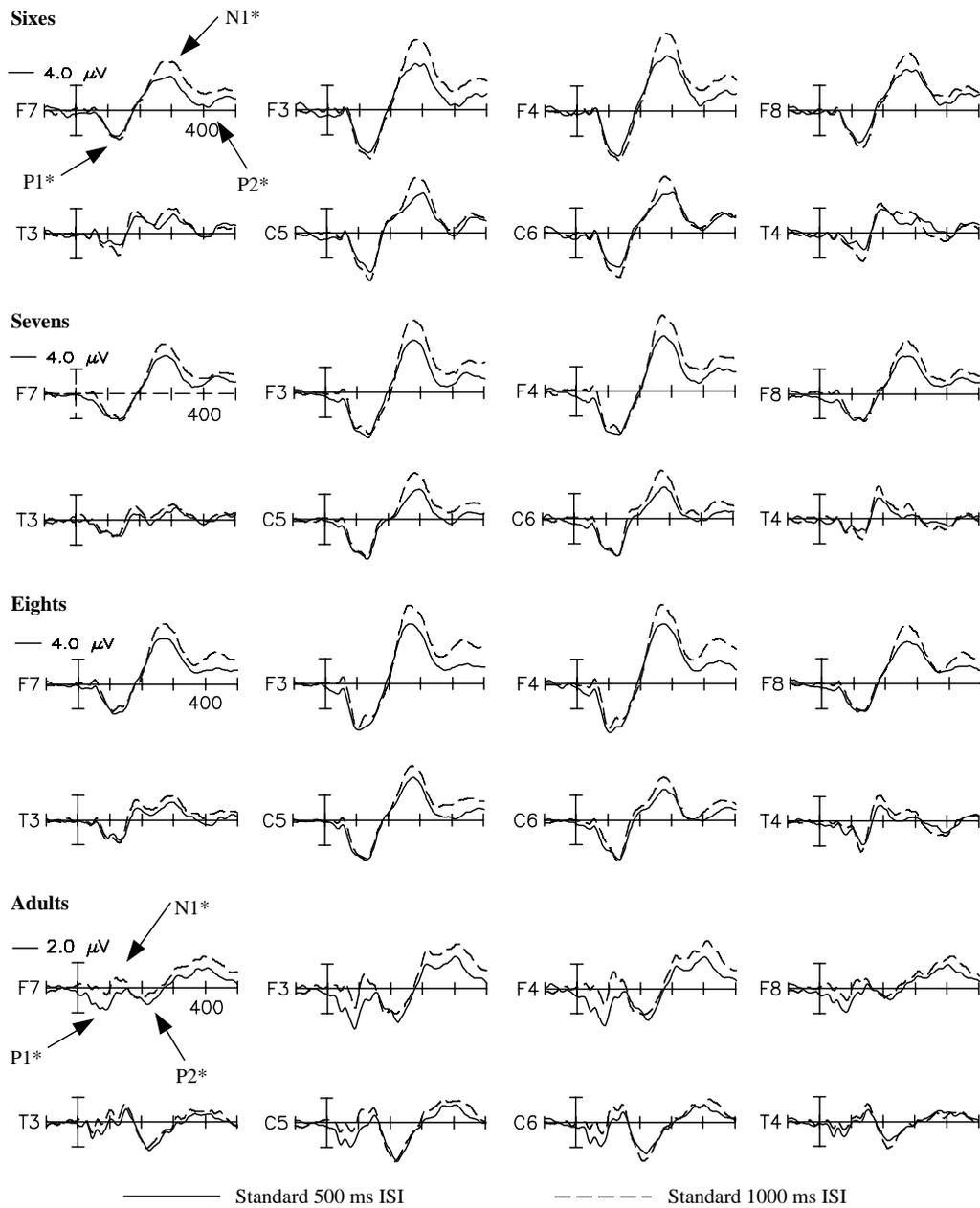


Fig. 2. Grand average ERP waveforms at frontal (F) and temporal (T, C) sites for 6-year-olds, 7-year-olds, 8-year-olds, and adults in the auditory refractory period paradigm. The first positive, first negative, and second positive peak are identified in the 6-year-old and adult grand averages as P1*, N1*, and P2* to indicate that these labels are placeholders and thus that the peaks may not be equivalent across age groups. Left hemisphere sites are on the left, right hemisphere sites are on the right, medial sites are in the middle, the vertical calibration bar indicates onset, and negative is plotted up. Note that the adult waveforms are plotted at half the scale of childrens'.

temporal, central, parietal, occipital], lateral/medial [two possible levels], and hemisphere [two possible levels] (refer to Fig. 1). The Greenhouse-Geisser correction was applied to all within-subjects measures with more than two levels and follow-up comparisons by group were corrected by the number of comparisons conducted (Bonferroni correction). Further, in order to investigate relations between the behavioral and ERP measures, Pearson correlation analyses were conducted with reaction time, accuracy, CTOPP, and latency data. All results are significant at the .05 level unless otherwise noted.

3. Results

3.1. Behavioral results

Accuracy of target detection was high in both the auditory and visual modalities (see Fig. 4), suggesting the possibility of ceiling effects; however, there was some variance in the data and there were significant differences between groups. In the auditory modality, accuracy tended to be higher for the longest ISI targets (condition, $P = .06$) across groups (group \times condition, $P = .78$). However,

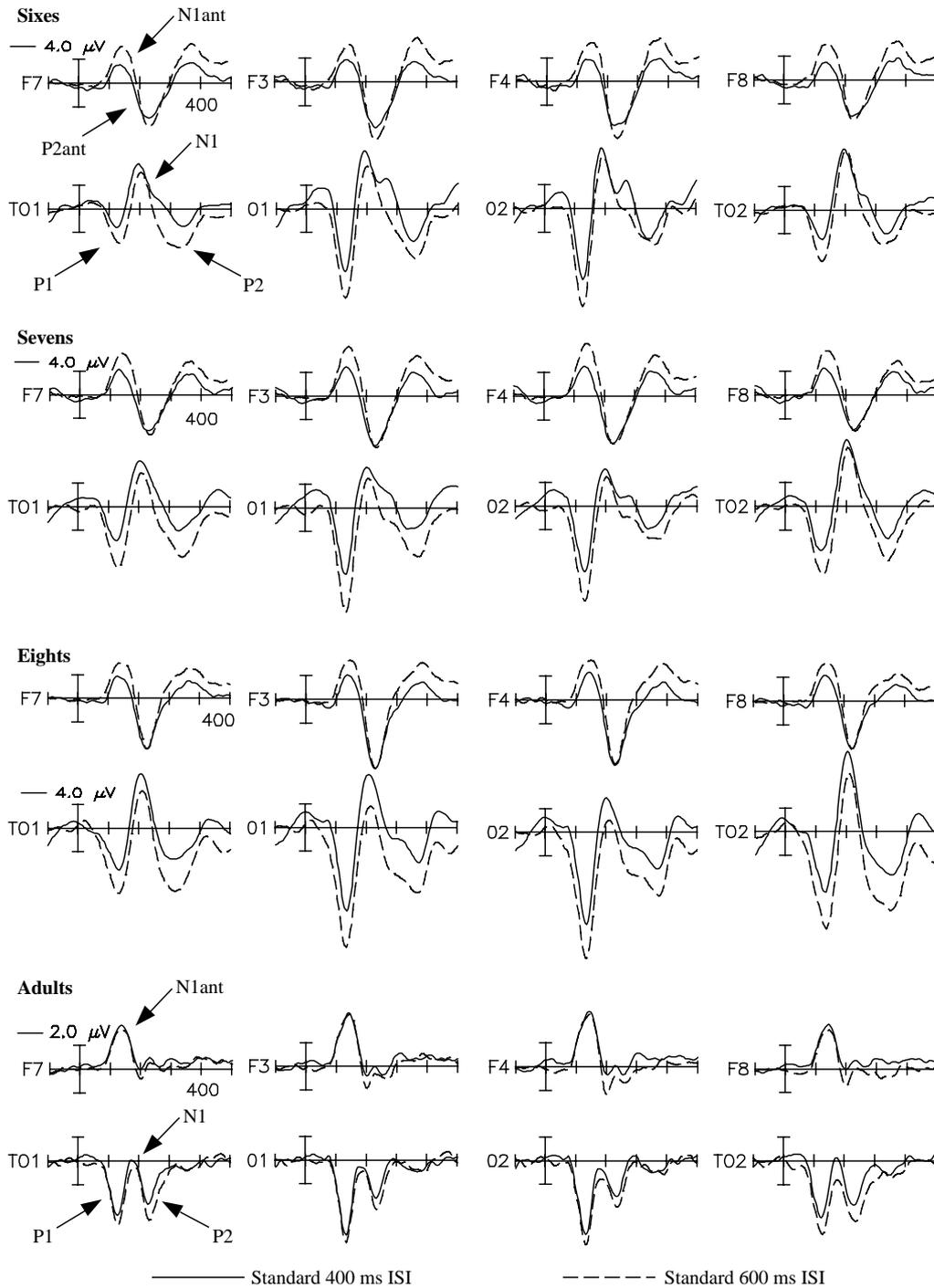


Fig. 3. Grand average ERP waveforms at frontal (F) and occipital (TO, O) sites for 6-year-olds, 7-year-olds, 8-year-olds, and adults in the visual refractory period paradigm. The posterior P1, N1, and P2 and the anterior N1 and P2 are identified. All else as in Fig. 2.

accuracy varied by group (group, $F(3, 74) = 30.6, P < .01$); in planned follow-up comparisons by group, there were no significant differences in accuracy (at the corrected P level of .017) between the 6- and 7-year-old groups, 7- and 8-year-old groups, or 8-year-olds and adults. Similarly, in the visual modality, accuracy was higher for longer ISI targets (condition, $F(2, 148) = 4.2, P < .05$) across groups (group \times condition, $P = .80$). However, the groups differed

(group, $F(3, 74) = 11.7, P < .001$); in follow-up comparisons by group, there were no differences in accuracy of responses between 6- and 7-year-olds or 8-year-olds and adults, but 8-year-olds were more accurate than 7-year-olds ($F(1, 41) = 8.6, P < .01$).

Reaction time (RT) data are presented in Fig. 5. For the auditory stimuli, RT was faster for targets preceded by longer ISIs (condition, $F(2, 148) = 9.0, P < .001$) across

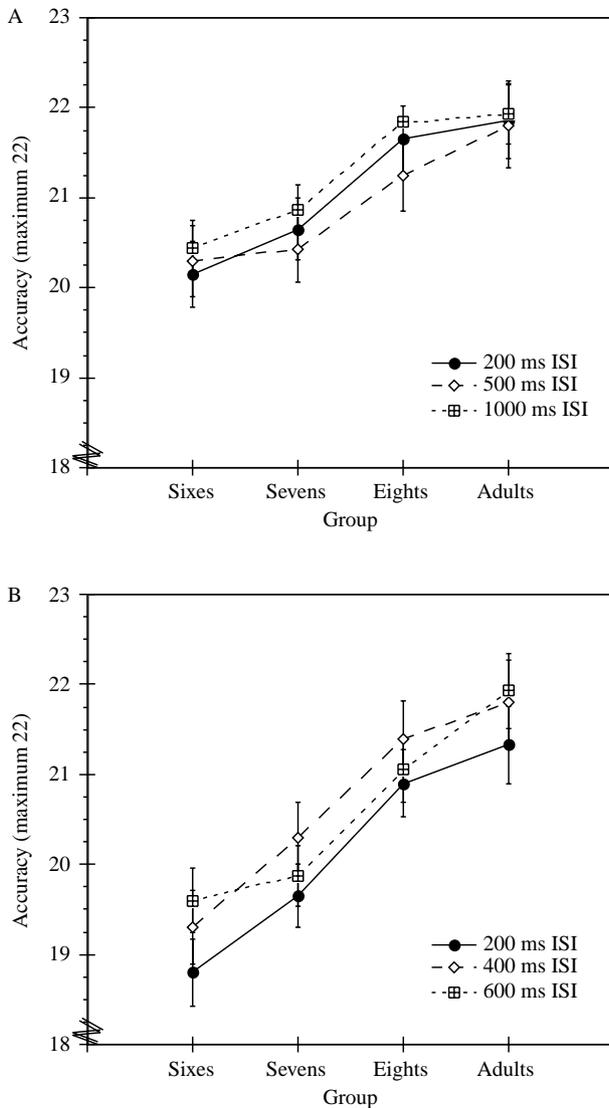


Fig. 4. Accuracy of response to targets presented at three ISIs in the auditory (A) and visual (B) paradigms for the four age groups. Note the scale and the high accuracy of most participants.

groups (group \times condition, $P=.08$). RT varied by group (group, $F(3, 74)=35.6$, $P<.001$); in follow-up comparisons, RT was similar in 6- and 7-year-olds and in 7- and 8-year-olds but faster in adults as compared to 8-year-olds ($F(1, 33)=76.0$, $P<.001$). For the visual stimuli, RT was also faster for targets preceded by longer ISIs (condition, $F(2, 148)=5.5$, $P<.01$) across groups (group \times condition, $P=.10$) and also varied by group (group, $F(3, 74)=74.5$, $P<.01$). In follow-up comparisons by group, RT was similar in 6- and 7-year-olds and in 7- and 8-year-olds but faster in adults compared to 8-year-olds ($F(1, 33)=146.8$, $P<.001$).

In summary, accuracy tended to be higher and reaction times were faster for longer ISI targets. In the auditory modality, accuracy was similar between the age groups compared sequentially, while RT was similar across the

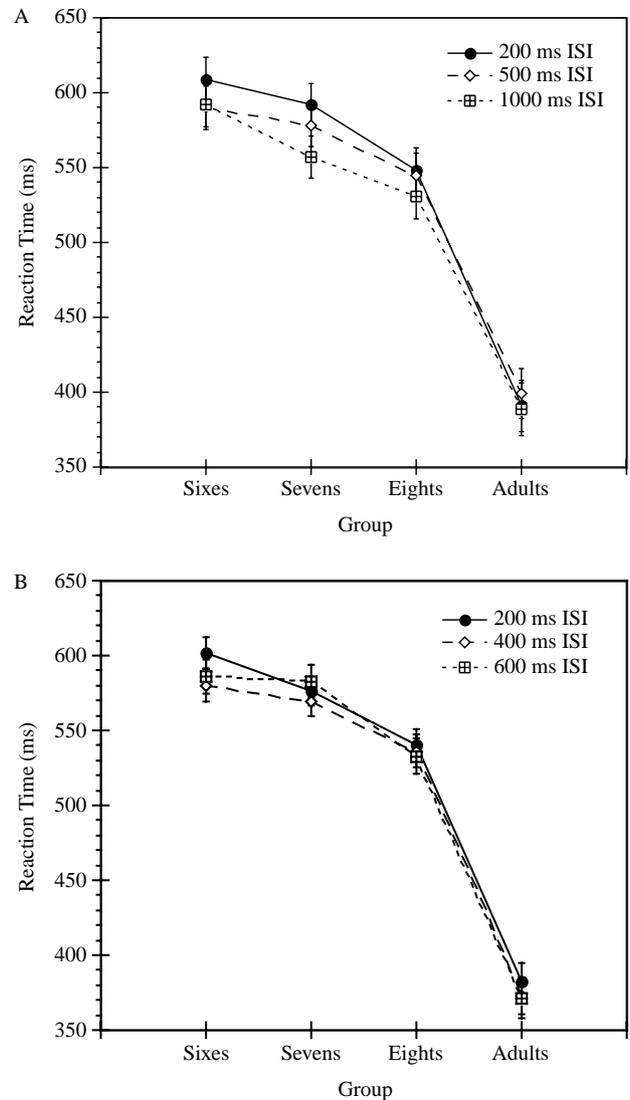


Fig. 5. Reaction time to targets presented at three ISIs in the auditory (A) and visual (B) paradigms for the four age groups.

three groups of children and longer than that in adults. In the visual modality, 8-year-olds were more accurate than 7-year-olds but slower to respond than adults.

3.2.. Auditory ERP results

While at first glance the morphology of the waveforms appeared to differ greatly in children and adults (refer to Fig. 2), as has been reported previously (e.g., Albrecht et al., 2000; Bruneau et al., 1997; Courchesne, 1990; Korpilahti and Lang, 1994; Kurtzberg et al., 1995; Ponton et al., 2000; Sharma et al., 1997), a positivity–negativity–positivity sequence (labeled P1*-N1*-P2* as placeholders, as noted above) was apparent in the waveforms for all age groups, although delayed in children (e.g., Korpilahti and Lang, 1994; Kurtzberg et al., 1995). Also in each age group, ERPs elicited by standards preceded by just 200 ms of silence

(the shortest ISI) did not return to baseline, confirming that ERPs are sensitive to the lower limits of the auditory refractory period but also making measurement problematic. While most previous studies have not employed such short ISI stimuli, there are reports in the literature of short ISI stimuli (<500 ms) resulting in changes to the shape of the early sensory components (Davis et al., 1966), including reports of distorted waveforms obscured by noise (Gjerdingen and Tomsic, 1970). Given this, analyses in the present study were conducted with the 500 and 1000 ms ISI standards only.

3.2.1. P1* (children and adults)

We found no effects of ISI in children and a paradoxically larger P1* to the short 500 ms ISI standards as compared to the long 1000 ms ISI standards in adults (condition \times group, $F(3, 74)=4.5, P<.01$). Ceponiene et al. (1998) reported a similar P1 effect (decrease in amplitude with ISI prolongation); this pattern may be due to overlap of the P1 and N1: as ISI increases, N1 amplitude increases (see below), effecting an apparent decrease in P1 amplitude.²

More consonant with expectations, latency of the P1* was longer to the 1000 ms ISI standards (condition, $F(1, 74)=6.2, P<.05$), and was longer for children as compared to adults (group, $F(3, 74)=94.8, P<.001$). However, these effects interacted (condition \times group, $F(3, 74)=3.7, P<.05$) such that the effect of ISI held only for 6-year-olds.

3.2.2. N1* (children and adults)

Consistent with previous reports of refractory period effects on N1 in adults, the amplitude of the N1* was larger to the longer ISI stimuli across groups (condition, $F(1, 74)=3.15, P<.001$). The distribution of this effect, largest at right hemisphere and anterior medial sites, was similar across groups (condition \times anterior/posterior, $F(5, 370)=16.6, P<.001$; condition \times lateral/medial, $F(1, 74)=7.9, P<.01$; condition \times hemisphere \times lateral/medial, $F(1, 74)=4.3, P<.05$; condition \times anterior/posterior \times lateral/medial, $F(5, 370)=5.9, P<.001$).

As predicted, the latency of the N1* was longer in children than in adults (group, $F(1, 74)=237.9, P<.001$). N1* latency was longer at lateral sites but shorter at medial sites to the 1000 ms ISI standards across groups (condition \times lateral/medial, $F(1, 74)=5.6, P<.05$).

3.2.3. P2* (children and adults)

Refractory period effects on the P2 have been reported, but are less frequently reported than the substantial effects of ISI on N1, perhaps because the effects on N1 extend into the P2 epoch. Indeed, in the present study P2* was greater to the shorter 500 ms ISI standards over medial, anterior, and left hemisphere sites across groups (condition \times

lateral/medial, $F(1, 74)=6.8, P<.05$; condition \times anterior/posterior, $F(5, 370)=4.3, P<.01$; condition \times hemisphere, $F(1, 74)=5.2, P<.05$). Averaged across ISI conditions and measured at site FC5 (medial, anterior, left), P2* amplitude was moderately correlated with N1* amplitude ($r=.46, P<.001$), consistent with the suggestion that N1* effects may have influenced the observed P2* effects.

The P2* was longer in latency for children as compared to adults (group, $F(3, 74)=1044.9, P<.001$) and was longer to 500 ms ISI standards across groups (condition, $F(1, 74)=9.8, P<.01$).

3.2.4. Summary of auditory P1*-N1*-P2* results

Refractory effects on P1*, N1*, and P2* normalized peak amplitude, averaged across subjects and measured at site C3, are shown in Fig. 6. For both children and adults, auditory N1* amplitude showed a typical refractory effect, being larger to the longer 1000 ms ISI standards. The distribution of this effect was similar across groups. P1* and P2* amplitudes did not show typical refractory effects, likely due to the influence of the N1* component. Latency measures did not show consistent effects of ISI. As expected, for each of the early AEP components, amplitude was larger and latency was longer in children as compared to adults.

3.2.5. Correlations among behavioral and electrophysiological measures

Across groups, correlation analyses indicated that reaction times for the 200, 500, and 1000 ms ISI target stimuli were strongly positively related to N1* latency to the 500 and 1000 ms ISI standard stimuli (r 's ranged from .69 to

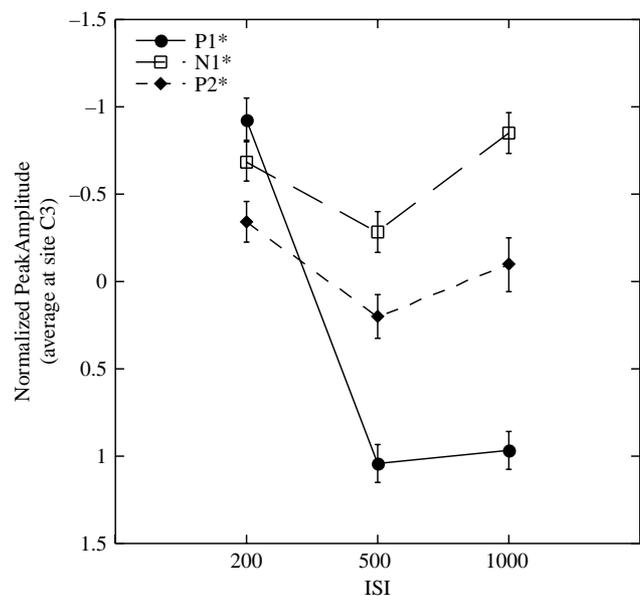


Fig. 6. Summary illustration of refractory effects on auditory P1*, N1*, and P2* normalized peak amplitude measured at site C3 and averaged across participants. N1* showed a typical refractory effect; see text for details.

² We are thankful to a reviewer for pointing out this interpretation of this result.

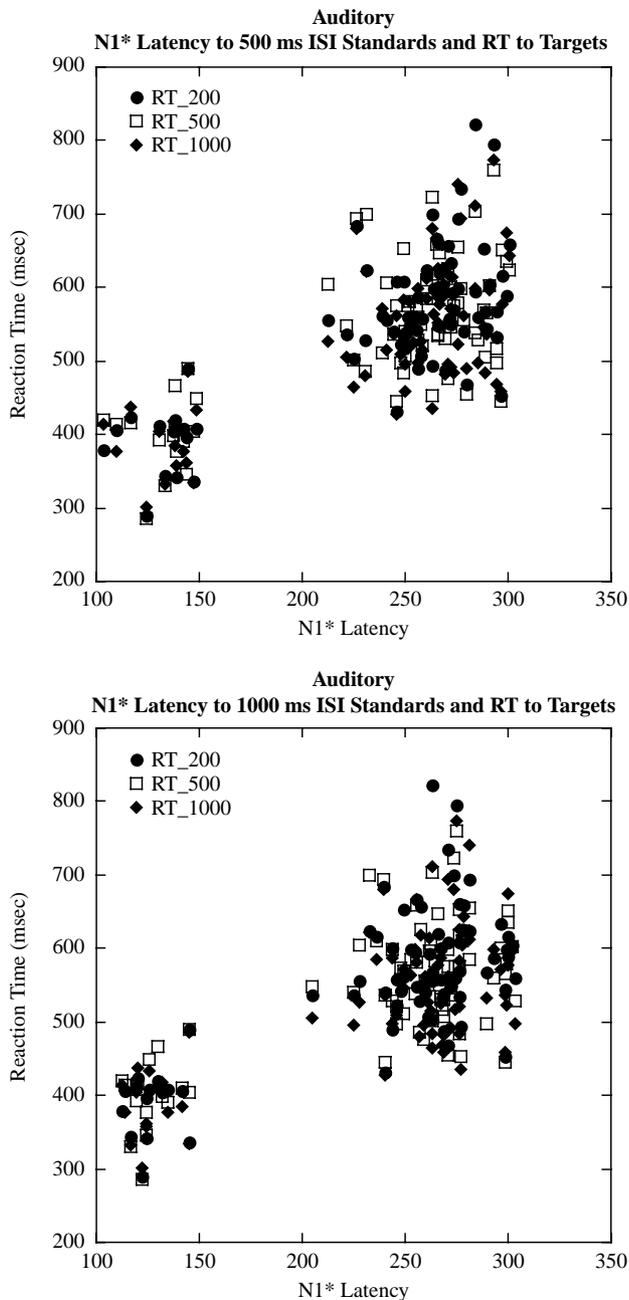


Fig. 7. In the auditory paradigm, reaction times for the 200, 500, and 1000 ms targets were correlated with N1* latency to the 500 and 1000 ms ISI standards across groups. Further analyses within the group of children and the group of adults yielded no significant correlations among reaction times to targets and N1* latency to standards.

.75, all P 's < .001; see Fig. 7).³ Accuracy for 200, 500, and 1000 ms ISI target stimuli was weakly negatively correlated with N1* latency to 500 and 1000 ms ISI standards (r 's ranged from $-.30$ to $-.25$, all P 's < .05).

³ The vigorous button-pressing activity of the children, creating motion artifacts, and the relatively small number of target trials precluded analysis of the electrophysiological responses to targets. Thus, we investigated correlations between N1 latency to standards and RT to targets.

Fig. 7 clearly shows the difference in N1* peak latency between adults and children evident in the ERP waveforms (refer to Fig. 2), with adults clustering at faster latencies and children clustering at slower latencies. Recognizing the possibility that the first negative peaks in the waveforms of adults and children might not be homologous, further correlation analyses were conducted within the two groups. In these follow-up analyses, there were no significant correlations among N1* latency to 500 or 1000 ms ISI standards and reaction times for 200, 500, or 1000 ms ISI target stimuli for children (all P 's > .05) or adults (all P 's > .10).

Finally, in children, there was no correlation between scores on the digit span subtest or the Phonological Memory composite of the CTOPP (Wagner et al., 1999) and electrophysiological measures of N1* amplitude or latency at any ISI, including a difference measure of amplitude for 1000 and 500 ms ISI standards (all P 's > .24).

3.3. Visual ERP results

The overall morphology of the visual ERP waveforms was more similar in children and adults than was the morphology of the auditory waveforms (refer to Fig. 3). However, as in the auditory modality, it was clear that the ERPs in the shortest ISI condition (200 ms) did not return to baseline for any of the groups, confirming that ERPs are sensitive to the lower limits of the visual refractory period as well. Indeed, the absolute visual refractory period (window within which two visual stimuli are perceived and processed as one) has been reported to be about 40 ms in ERP studies (Cigánek, 1964; Musselwhite and Jeffreys, 1983; Riemsdag et al., 1985). There is at least one report indicating that recovery of the original waveform does not occur unless paired stimuli are separated by 100 ms or more, and even then may not be complete (Schwartz and Shagass, 1964), consistent with the response to the shortest ISI stimuli observed here. In consonance with the auditory paradigm, analyses were conducted with the 400 and 600 ms ISI standards only.

3.3.1. Posterior P1 (children and adults)

Measured along the occipital row, as expected, the P1 was larger to the longer 600 ms ISI standards than to the shorter 400 ms ISI standards overall (condition, $F(1, 74) = 51.6$, $P < .001$); this held at both lateral and medial sites for children but only at lateral sites for adults (condition \times lateral/medial \times group, $F(3, 74) = 3.3$, $P < .05$).

Also as expected, P1 latency was shorter in adults than in children (group, $F(3, 74) = 3.0$, $P < .05$), but there were no significant effects of ISI on P1 latency.

3.3.2. Posterior N1 (children and adults)

Measured along the occipital row, N1 was unexpectedly larger to the shorter 400 ms ISI standards than to the longer 600 ms ISI standards (condition, $F(1, 74) = 15.3$, $P < .001$).

overall. Averaged across ISI conditions and measured at site O1, N1 amplitude was correlated with P1 amplitude ($r = -.46, P < .001$), consistent with the idea that refractory effects on the P1 may have extended into the N1 window and obscured effects on the N1.

As predicted, N1 latency was longer in children than adults (group, $F(3, 74) = 11.5, P < .001$), but N1 was later to the 600 ms ISI stimuli than to the 400 ms ISI stimuli across groups (condition, $F(1, 74) = 4.8, P < .05$).

3.3.3. Posterior P2 (children and adults)

Measured along the occipital row, P2 was larger to 600 ms ISI standards than to 400 ms ISI standards across groups (condition, $F(1, 74) = 81.7, P < .001$). This held particularly over left hemisphere and lateral sites, also across groups (condition \times hemisphere, $F(1, 74) = 5.9, P < .05$; condition \times lateral/medial, $F(1, 74) = 5.1, P < .05$).

P2 latency was shorter in adults than in children (group, $F(3, 74) = 36.7, P < .001$), but there were no significant effects of ISI on P2 latency.

3.3.4. Anterior N1 (children and adults)

Visual responses were expected to be maximal at occipital sites and were measured at those sites in primary analyses. However, clear peaks were also evident at more anterior sites; these were measured separately. It is possible that these peaks represent activity within the same dipole source as indexed by the occipital peaks. However, this seems unlikely as there was no evidence of reversal of polarity, but may be dependent on the orientation of the generator(s).

Measured at sites anterior to the occipitals, the N1 was larger to the longer 600 ms ISI stimuli than to the shorter 400 ms ISI stimuli (condition, $F(1, 74) = 56.6, P < .001$). However, this effect interacted with group such that it

held only for children (see Fig. 8; condition \times group, $F(3, 74) = 7.0, P < .001$). This effect of ISI was greatest at medial anterior sites (condition \times anterior/posterior \times lateral/medial, $F(3, 222) = 10.9, P < .001$).

Averaged across ISI conditions and groups, amplitude of the posterior N1 measured at site O1 was not correlated with amplitude of the anterior N1 measured at site FC5 ($r = .19, P = .10$), inconsistent with interpretation of the two effects as reflecting activity of the same dipole generator.

Also unlike the posterior N1, the anterior N1 had a similar latency in children and adults (group, $P = .85$) and was earlier to the 600 ms ISI standards at left frontal sites across groups (condition \times hemisphere \times anterior/posterior, $F(3, 222) = 5.1, P < .01$).

3.3.5. Anterior P2 (children only)

Measured at sites anterior to the occipitals in children only, the P2 was larger for 600 ms ISI standards than for 400 ms ISI standards, particularly at anterior and medial sites (condition \times anterior/posterior \times lateral/medial, $F(3, 180) = 3.5, P < .05$). Averaged across ISI conditions, amplitude of the posterior P2 measured at O1 and amplitude of the anterior P2 measured at FC5 were weakly correlated ($r = .32, P < .01$), consistent with an interpretation of these effects as reflecting, at least in part, activity of the same generator(s).

The peak latency of the anterior P2 did not vary as a function of ISI.

3.3.6. Summary of visual P1-N1-P2 results

Refractory effects on P1, N1, and P2 normalized peak amplitude, averaged across subjects and measured at site

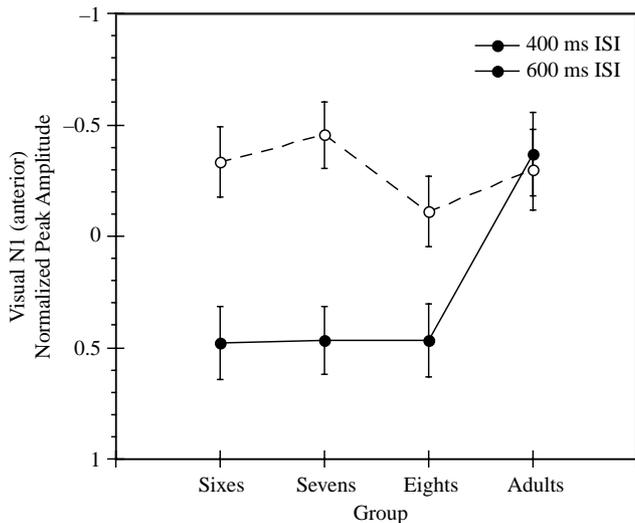


Fig. 8. Illustration of the interaction between group and ISI for normalized peak amplitude of the visual N1 measured at anterior sites in children and adults. Only children showed an effect of ISI.

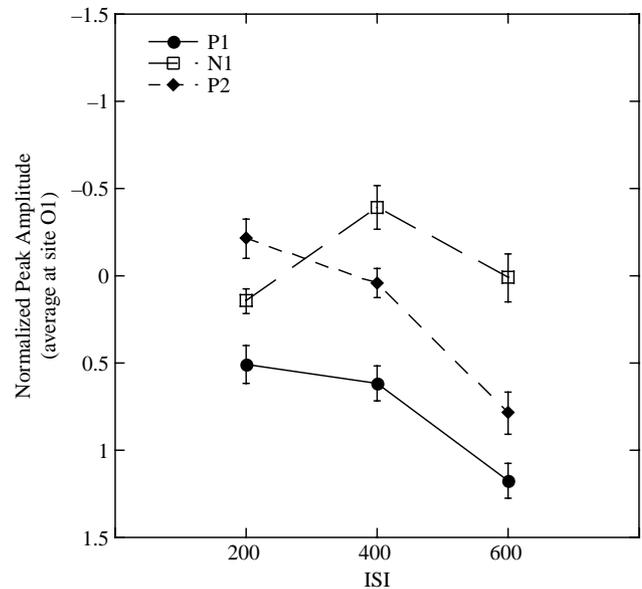


Fig. 9. Summary illustration of refractory effects on visual P1, N1, and P2 normalized peak amplitude measured at site O1 and averaged across participants. P1 and P2 showed typical refractory effects; see text for details.

O1, are shown in Fig. 9. For both children and adults, visual P1 and P2 amplitude measured at posterior sites showed a typical refractory effect, being larger to the longer 600 ms ISI standards. These effects were similarly distributed for children and adults, with some evidence of a more widespread effect in children for the P1. Amplitude of an N1 and P2 measured at sites anterior to the occipitals also showed typical refractory effects, but only for children; the anterior N1 appeared to be unrelated to the posterior N1, while there was some evidence for a relation between the anterior and posterior P2s. Overall, latency measures did not show consistent ISI effects. As expected, for each of the early posterior VEP components, amplitude was larger and latency was longer in children as compared to adults.

3.3.7. Correlations among behavioral and electrophysiological measures

Across groups, correlation analyses indicated no relation between reaction time to 200, 400, or 600 ms ISI targets and P1 latency to 400 and 600 ms ISI targets averaged across occipital sites. Accuracy for 200 ms ISI targets was related to P1 latency for 600 ms ISI standards ($r = .23$, $P < .05$) and accuracy for 400 ms ISI targets was related to P1 latency for 400 and 600 ms ISI standards ($r = .25$ and $.23$, respectively, all P 's $< .05$).

Further analyses indicated weak negative relations among P2 latency to 400 and 600 ms ISI targets averaged across occipital sites and accuracy for 200, 400, and 600 ms ISI targets (r 's ranged from $-.24$ to $-.32$, all P 's $< .05$) but stronger positive correlations among reaction times to 200, 400, and 600 ms ISI targets and posterior P2 latency to 400 and 600 ms ISI standards (r 's ranged from $.59$ to $.65$, all P 's $< .001$; see Fig. 10).

Follow-up correlation analyses within the group of children and the group of adults, consistent with the analysis of the auditory data, indicated no relation between reaction times to 200, 400, or 600 ms ISI targets and P2 latency to 400 or 600 ms ISI standards in children (all P 's $> .72$) or adults (all P 's $> .17$).

4. Discussion

In an investigation of event-related potential (ERP) refractory period effects in the auditory and visual modalities, the effects of ISI were quite similar in school-age children and adults although children evidenced typically larger and longer-latency sensory components. In the auditory modality, adults showed expected refractory period effects for N1* amplitude, as did children. In the visual modality, adults showed expected refractory period effects for occipital P1 and P2 amplitude, as did children; however, only children showed refractory effects on the amplitude of N1 and P2 measured at anterior sites. While amplitude of early components evidenced refractory effects, latency was not consistently sensitive to ISI across

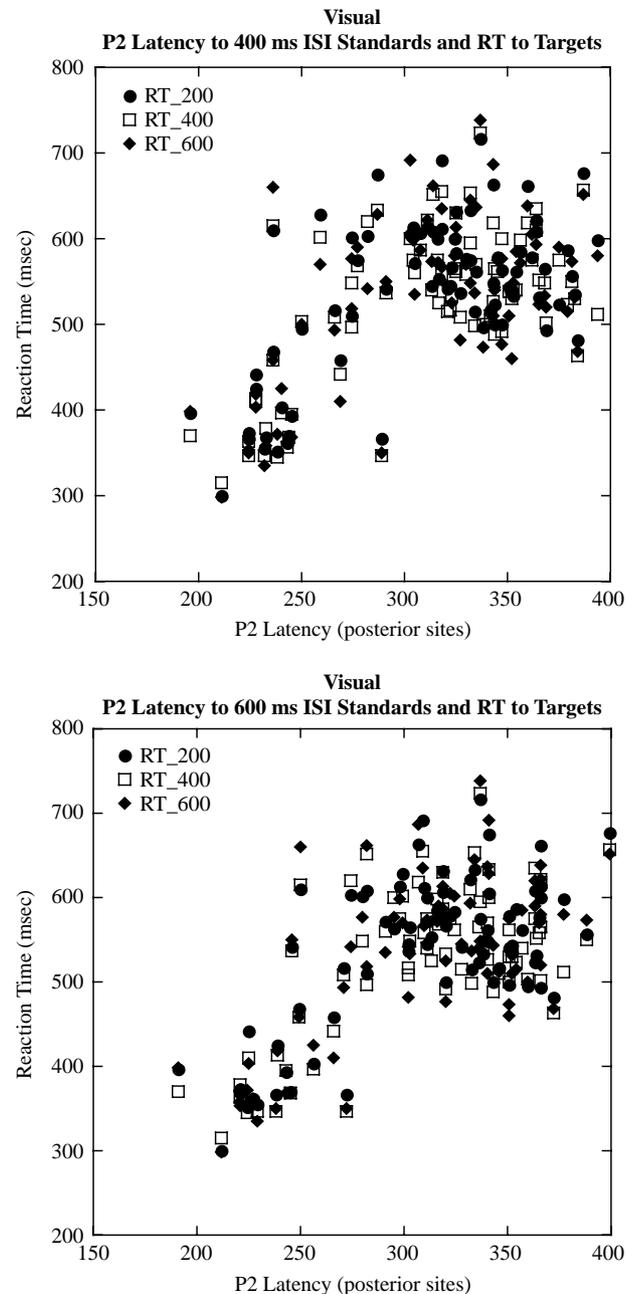


Fig. 10. In the visual paradigm, reaction times for the 200, 400, and 600 ms targets were correlated with P2 latency (measured at posterior sites) to the 400 and 600 ms ISI standards across groups. Further analyses within the group of children and the group of adults yielded no significant correlations among reactions times to targets and P2 latency to standards.

modalities. Behaviorally, accuracy increased and RT decreased with age; the effects of ISI were similar across age groups and modalities such that accuracy tended to be higher and RT was faster for longer ISI targets. In the auditory modality, RT was positively correlated and accuracy was negatively correlated with N1* latency across groups; a similar pattern of results was found for the posterior P2 and behavioral measures in the visual modality across groups. In addition to revealing these brain-behavior

relationships, the present findings establish a normal course of development for auditory and visual refractory period effects to relatively short ISI stimuli as indexed by ERPs across the 6- to 8-year-old age range.

4.1. Auditory modality

Upon first glance, the morphology of the ERP waveforms elicited in the auditory paradigm appeared to differ greatly in children and adults. However, a P1*-N1*-P2* sequence was apparent in both adults and children, but at a typically longer latency in children (e.g., Davis and Onishi, 1969; Goodin et al., 1978; Oades et al., 1997; Tonquist-Uhlén et al., 1995). Other auditory ERP studies have reported a positivity peaking around 100 ms followed by a negativity peaking around 220 ms in children (e.g., Ceponiene et al., 1998; Courchesne, 1990; Korpilahti and Lang, 1994) similar to the componentry observed in the present study.

As reported previously in adults (e.g., Budd et al., 1998; Davis et al., 1966; Fruhstorfer, 1971; Fruhstorfer et al., 1979; Knight et al., 1980; Ritter et al., 1968; Rothman et al., 1970; Woods et al., 1980) and older children (Ceponiene et al., 1998; Karhu et al., 1997; Neville et al., 1993), clear refractory period effects were observed on N1* amplitude in adults as well as in children in the present study.⁴ Across groups, N1* was larger to the longer 1000 ms ISI standards as compared to the 500 ms ISI standards. Moreover, the distribution of this effect—largest over the right hemisphere and at anterior medial sites—did not vary by group (cf. Bruneau et al., 1997, who reported topographical differences in N1 in children and adults, but did not investigate refractory effects). This consistent pattern suggests that the refractoriness of neuronal networks indexed by N1* in this paradigm is relatively adult-like by the age of 6 (see also Takeshita et al., 2002), which might be seen to contrast with behavioral and anatomical data indicating that many aspects of the auditory system continue to develop across childhood (e.g., Allen and Wightman, 1994; Fior, 1972; Huttenlocher and Dabholkar, 1997; Maxon and Hochberg, 1982; Moore and Guan, 2001). It has been reported that N1 likely has multiple generators, including ones in primary and association auditory cortical areas (Näätänen and Picton, 1987) and the planum temporale (Liégeois-Chauvel et al., 1994). Others have reported that the orientations of the AEP generators are essentially adult-like by age 5 (Ponton et al., 2002, p. 417); our results are consistent with this in suggesting that the refractory properties of at least some subset of these auditory cortical networks are similar in

school-age children and adults, and therefore, represent an aspect of auditory processing that matures quite early.

Indeed, this pattern might also be seen to contrast with the developmental improvements in behavioral measures of accuracy and reaction time taken in the present paradigm. Nonetheless, there were strong positive correlations (ranging from .65 to .75) between N1* latency to standards and reaction time to targets across ISI conditions across groups. Both N1* latency at medial sites and RT were faster for stimuli with longer ISIs. To our knowledge, this is one of the first reports of such a brain-behavior relationship in a simple sensory refractory paradigm. It implies that standard RT and N1* latency can serve, at least in part and in the context of the present paradigm, as similar measures of processing time across child and adult populations; both of these measures may reflect, for example, efficiency of contributing neural systems in terms of degree of myelination.

Interestingly, the significant correlations among RTs to targets and N1* latencies to standards disappeared when analyses were restricted within the group of children and the group of adults. This pattern is consistent with the RT results, indicating similar performance in 6-, 7- and 8-year-olds and relatively better performance in adults. It may be the case that there is simply not enough developmental variance within the 6- to 8-year-old age range to support correlations within the present paradigm; only by widening the developmental timeframe are relationships revealed. As with the central auditory refractory effect findings, the similar pattern of results in children and adults is striking—particularly when the possible non-homology of the first negative peaks in the auditory waveforms of children and adults is considered. That is, even if the first negative peaks are indexing different neural systems in children and adults, as recent reports have suggested (e.g., Albrecht et al., 2000; Ponton et al., 2002; Takeshita et al., 2002), the characteristics of those systems in terms of refractoriness and correlation with RT appear to be similar. Nevertheless, the general pattern of few differences among the three groups of children emphasizes the importance of considering maturation of sensory systems across an extended age range in order to chart developmental change.

MEG studies have suggested that magnetic measures of refractoriness in primary auditory cortex are related to the duration of echoic memory (Lu et al., 1992). We found no evidence of a relation between digit span and N1* amplitude or latency in children, although digit span may be a poor proxy for echoic memory duration; however, we also found no correlations among a composite score of phonological memory on the CTOPP and N1* amplitude or latency. Accuracy of target detection was weakly negatively correlated (ranging from $-.30$ to $-.21$) with N1* latency to standards across ISI conditions across groups, reflecting another link between behavioral performance and component latency. As with the RT data, there are many possible explanations as to why an earlier N1* might be related to better accuracy, including, for example,

⁴ This study was not designed to address the issue of whether the earlier negative peak observed in adults (N100) and the later negative peak observed in children (N250) are homologous. Our results simply show that the first negative peaks in the ERP waveforms of both children and adults evidence similar refractory period effects in the present paradigm.

myelination and maturation of contributing neural systems. Unfortunately, the correlational nature of our data does not permit a definitive interpretation of these results.

Other authors have reported refractory period effects on auditory P2 in adults (Davis et al., 1966; Fruhstorfer, 1971; Fruhstorfer et al., 1979; Knight et al., 1980; Woods et al., 1980). Here, we found a larger and later P2* to the shorter 500 ms ISI stimuli as compared to the long 1000 ms ISI stimuli across groups. Given the moderate correlation between N1* and P2* amplitudes (.46), it is possible that this pattern is due to the prolongation of the substantial effect of ISI on N1* into the P2* epoch. Regardless, the effect was consistent across children and adults.

A similar effect, previously reported and also likely due to overlap with N1 (Ceponiene et al., 1998), was seen for P1* amplitude; however, this effect was observed only in adults—children showed no effects of ISI on P1* amplitude. Ceponiene et al. (1998) reported a decrease in P1 amplitude with increasing ISI for 700 and 1400 ms ISI stimuli in both adults and 7- to 9-year-old children. Stimuli in that study were presented in blocks under conditions of inattention, which, along with the longer ISIs, might have influenced the observed difference in results. Previous studies have reported that the generators of the P1 may be thalamocortical (Erwin and Buchwald, 1986) or overlapping sources in primary auditory cortex (Liégeois-Chauvel et al., 1994; Onitsuka et al., 2000). Studies of very young children with cochlear implants have employed the P1 as an index of remarkably rapid development and plasticity of the auditory system (e.g., Sharma et al., 2002). Overall, P1 is thought to reflect early auditory sensory gating; in paired-click paradigms with adults, this component is suppressed at shorter ISIs (e.g., Cardenas et al., 1997; Dolu et al., 2001; Müller et al., 2001) and shows abnormal suppression in a number of atypical populations (e.g., Arciniegas et al., 2000; Buchwald et al., 1992; Cullum et al., 1993; Freedman et al., 1987; Light et al., 2000; Skinner et al., 1999). Similar paired-click studies with typically developing children have reported that suppression of the P1 increases with age, reaching normal adult levels in early to mid adolescence (Freedman et al., 1987b; Marshall et al., 2004; Myles-Worsley et al., 1996), perhaps related to late maturation of contributing frontal generators (see Marshall et al., 2004; Weisser et al., 2001). Our lack of P1* suppression in children (i.e., a lack of an effect of ISI) may be related to these developmental findings; however, stimuli in double-click studies are typically presented in pairs with a 500 ms ISI and 10 s inter-pair interval and our constant sequence of randomly varying ISIs may not be comparable. These sorts of design manipulations will be important for future studies, in regard to charting P1* refractory effects in both normal development and children at risk.

4.2. Visual modality

The morphology of the ERP waveforms elicited by visual stimuli was similar in children and adults, evidencing

the typically expected larger and later yet homologous components in children as compared to adults. At occipital sites, both children and adults showed the previously-reported P1-N1-P2 pattern. At anterior sites, both children and adults showed an N1 while only children evidenced a substantial subsequent positivity (P2).

Previous reports have found refractory effects for early visual components P1, N1, and P2 in adults (e.g., Cigánek, 1964; Floris et al., 1967; Lehtonen, 1973; Musselwhite and Jeffreys, 1983; Neville et al., 1983; Skrandies and Raile, 1989). In the present study, amplitude of the occipital P1 showed the expected refractory effect for adults as well as for children: P1 was larger to the long 600 ms ISI standards than to the shorter 400 ms ISI standards. The distribution of this effect was more lateralized in adults than in children, implying a more widespread effect in children. However, as analyses were conducted only along the most posterior occipital row of electrode sites, interpretation of this distributional difference is limited. Previous studies have indicated that P1 generators include both dorsal and ventral extrastriate sources (Di Russo et al., 2001); the modest distributional difference observed here may be related to different developmental time courses for the dorsal and ventral visual streams (Crewther et al., 1996, 1999).

Amplitude of P2 measured at occipital sites showed a similar refractory effect, being larger to the longer ISI stimuli across groups. However, the left hemisphere, lateral distribution of the P2 effect was similar across children and adults. These findings are consistent with an hypothesis of homology between the child and adult visual posterior P2 and a similar orientation of the P2 generator. Neither the latency of P1 nor P2 was sensitive to the ISI manipulation, although longer latency components with shorter ISI stimuli have been reported previously in the visual modality (e.g., Neville et al., 1993). Overall, these findings are consistent with previous reports of similar visual refractory effects in adults and older children (Cohn et al., 1985).

Across groups, the amplitude of the occipital N1 was also modulated by ISI. However, N1 was larger to the shorter 400 ms ISI standards than to the long 600 ms ISI standards. Again, it is possible that this pattern is due to the prolongation of the substantial effects of ISI on the preceding P1, which may have extended into the N1 epoch; a correlation between N1 and P1 amplitude (.46) is consistent with this interpretation. The possibility of partial overlap in generators is also consistent with this interpretation. In adults, evidence suggests that the occipital P1 is generated in ventral and dorsal lateral occipital cortex while occipital N1 is generated by a distributed array of ventral occipital generators (Clark and Hillyard, 1996; Di Russo et al., 2001). Overall, the present results from posterior analyses suggest that the refractoriness of occipital networks involved in early visual processing and indexed by ERPs is relatively similar in adults and young school-age children.

As in the auditory modality, this electrophysiological pattern of essentially adult-like refractory effects contrasts

with improvements in accuracy and reaction time with age. This discontinuity in the brain and behavioral data is reconciled in correlation analyses indicating a strong positive relationship (.59–.65) between reaction times to targets at all ISIs and posterior P2 latency to standards at all ISIs across groups. As in the auditory modality, it appears that RT and component latency are indexing, at least in part and perhaps limited to the present design, similar processes. Also as in the auditory modality, these relationships did not hold in within-group (children and adults) analyses, consistent with the pattern of RT findings indicating similarity across the groups of children as compared to better performance in adults; only within a wider developmental timeframe does the brain-behavior relationship emerge. That there were no significant correlations between RT to 200, 400, or 600 ms ISI targets and P1 latency to standards indicates that this relationship is component-specific, and may reflect different maturational time courses for different components outside of refractoriness. Accuracy was weakly negatively correlated with posterior P2 latency across ISI conditions ($-.24$ to $-.32$) in a pattern similar to that observed in the auditory modality.

A previous study with older children has reported an N1 and P2 at anterior sites both sensitive to manipulations of ISI (Neville et al., 1993). Here, we replicate this finding in younger children. N1 amplitude measured at sites anterior to the occipitals was larger to 600 ms ISI standards than to 400 ms ISI standards—but only in children, not in adults. This is consistent with the suggestion of more widespread visual refractory period effects in children. It is possible that the observed anterior peak is simply a reflection of the opposite end of the posterior N1 generating dipole, suggesting a different orientation of the dipole or a different neural generator in children as compared to adults (cf. Ossenblok et al., 1992). It is also possible that the posterior and anterior N1 observed in children are separate components with different dipole sources (extrastriate and centro-parietal, respectively), as has been reported in adults (Di Russo et al., 2001). The latter possibility seems a more consistent explanation of the present data for a number of reasons: no anterior–posterior reversal of polarity was observed within the N1 window; there was no evidence of a correlation between measures of posterior and anterior N1 amplitudes; latency of the anterior N1 was similar in children and adults but latency of the posterior N1 was longer in children; and anterior and posterior N1 latencies showed different refractory effects (posterior N1 was later to 600 ms ISI stimuli while anterior N1 was earlier to 600 ms ISI stimuli). If these are two separate components, the present pattern of results implies more extensive visual processing networks sensitive to manipulations of ISI in children.

This conclusion is supported by the findings regarding P2 measured at sites anterior to the occipitals. While the anterior P2 was not identifiable in adult waveforms, the clear anterior P2 in children showed typical refractory

effects, being larger to 600 ms ISI standards than to 400 ms ISI standards. However, there was some evidence that the amplitudes of P2 measured at anterior and posterior sites were correlated (.32), suggesting that these effects might have been partially indexing the refractoriness of the same generating network despite a lack of reversal of polarity across the anterior–posterior axis.

5. Summary and conclusion

The same children and adults tested in auditory and visual versions of an ERP refractory period paradigm evidenced remarkably similar effects of ISI. Both children and adults showed refractory period effects on auditory N1* and visual occipital P1 and P2. In the visual modality, children showed more widespread refractory effects extending to anterior sites. These refractory findings add to a growing ERP literature on basic development of sensory processing systems, which has tended to focus primarily on changes over time in dipole sources and component amplitude and latency (e.g., Ponton et al., 2000, 2002).

Behavioral studies have indicated that various aspects of auditory and visual sensory processing continue to develop throughout childhood (e.g., Fior, 1972; Hollants-Gilhuijs et al., 1998a; Kovács et al., 1999; Maxon and Hochberg, 1982). Consistent with previous findings and predictions, the present electrophysiological data indicate that the amplitude and latency of early sensory ERP components also show developmental changes throughout childhood. In contrast, the physiological refractoriness of neuronal populations indexed by our simple paradigms appears to be relatively adult-like in school-age children, such that basic refractory properties of sensory networks indexed by ERPs in these paradigms appear mature by the age of 6. In the visual modality, the more widely distributed effects in children suggest that functional networks for processing visual information continue to develop at least into late childhood, consistent with behavioral findings. Perhaps for the first time, we report a relationship between our own behavioral measures (reaction time and accuracy) and the latency of ERP components exhibiting refractory period effects across age groups, suggesting that neural and behavioral measures may at least in part index similar processes.

These findings establish a developmental baseline for ERP sensory refractory period effects in the auditory and visual modalities in young school-age children. It is important to chart this developmental course not only to gather basic data, but also because sensory system processing has been implicated in a number of developmental disorders such as SLI and dyslexia (e.g., Lovegrove, 1996; Talcott et al., 1999, 2000; Tallal et al., 1991). In particular, atypical fast temporal processing across modalities has been implicated in language and reading

disorders (Tallal et al., 1995); refractoriness is yet another measure of neural processing speed. With an estimated 7.4% of kindergarten children diagnosable with SLI and an estimated 5–10% of school-age children diagnosable with dyslexia (Dickinson et al., 1989; Tomblin et al., 1997), it is important to understand the normal course of development of multiple aspects of sensory systems, including refractory properties, in order to understand how these systems might be implicated in cases of atypical development (e.g., see Neville et al., 1983, 1994; Röder et al., 1999). Indeed, comparative studies employing versions of the present paradigms are currently under way with children who have been diagnosed with SLI in order to further assess the hypothesis that SLI involves a panmodal deficit in fast temporal processing (Neville et al., 1993; Tallal et al., 1991).

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