

Developmental changes in the theta response system: a single sweep analysis

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Abstract Recently, increased interest has been focused on the EEG frequency responses in the theta (4–7 Hz) range because of their association with stimulus information processing. However, it is not known whether the event-related theta response depends on the development of the spontaneous theta activity and how it varies with age in children. In the present study, a single-sweep analysis was performed to assess the developmental changes in event-related EEG theta activity. Auditory passive, oddball target, and standard event-related potentials (ERPs) were recorded at Fz, Cz, and Pz from 50 children aged 6–11 years and 10 young adults. Theta responses were analyzed in two time windows of the post-stimulus epochs for three single-sweep parameters: amplitude, phase-locking with stimulus, and enhancement relative to prestimulus activity. For all three types of stimuli, adults had theta responses with lower amplitude, higher enhancement, and stronger phase-locking than those of children. Unlike adults, no reliable differences between the early and late theta response were found for children. Significant developmental changes were observed for theta response amplitude, which decreased, and phase-locking of early theta responses, which increased, with advancing age. These findings indicate that the theta component of the auditory ERP differs remarkably between children and adults and undergoes developmental alterations, possibly reflecting specific differences in stimulus information processing.

Introduction

After external stimulation oscillatory electroencephalographic (EEG) responses in different frequency ranges (theta, alpha, gamma, etc.) can be recorded from the brain (Başar & Bullock, 1992). These oscillatory EEG responses have been proposed to originate from the event-related reorganization of the ongoing EEG as reflected by the synchronization, magnitude enhancement or damping, and phase-reordering of the EEG after stimulation (Başar, 1980, 1992; Parvin, Torres, & Johnson, 1980; Sayers, Beagley, & Henshall, 1974). Within this framework, the EEG frequency responses are strongly associated with the background EEG activity. Given the natural changes in the spontaneous EEG in the course of development (Niedermeyer, 1993), as well as the functional relevance of event-related oscillations (Başar, Hari, Lopes da Silva, & Schürmann, 1997; Pantev, Elbert, & Lütkenhöner, 1994), the analysis of the EEG frequency re-

sponses in children might provide a useful physiological approach for studying developmental brain functioning.

Event-related oscillations in the theta frequency range (4–7 Hz) define the theta frequency component of the event-related brain potentials (ERPs) or the EEG theta response. Prominent theta responses have been observed in various experimental conditions in both humans and animals and have been assigned an important role in integrative stimulus processing (Miller, 1991; Schürmann & Başar, 1994). The scalp recorded theta responses have been proposed to reflect the functioning of a diffuse and distributed theta system in the brain (Başar-Eroglu, Başar, Demiralp, & Schürmann, 1992) involving primarily the hippocampus and associative frontal cortex (Başar-Eroglu et al., 1992; Demiralp & Başar, 1992; Klimesch, Schimke, & Schwaiger, 1994; Miller, 1991) and generating both the spontaneous and elicited theta oscillations (Başar, 1992).

The spontaneous EEG theta activity has been found to decrease in absolute and relative band power with progressing age in children (Gasser, Verleger, Bächer, & Sroka, 1988; John et al., 1980; Matoušek & Petersén, 1973; Matthis, Scheffner, Benninger, Lipinski, & Stolzis, 1980). However, the information about theta response development is insufficient although the event-related theta activity may also vary with age in children. First, the evoked potential magnitude is known to be significantly correlated with the power of the background EEG but in many instances EEG and ERP amplitudes have shown relatively independent behavior (e. g., Shagass, 1976). It is an open question whether a decrease in theta activity during stimulus processing accompanies the developmental reduction of the spontaneous EEG theta power. Secondly, increased theta activity in human adults has been consistently associated with higher cognitive processes such as memory, concept learning, attention, etc. (Başar-Eroglu et al., 1992; Inouye, Shinosaki, Iyama, Matsumoto, & Toi, 1994; Klimesch et al., 1994; Klimesch, Doppelmayr, Russeger, & Pachinger, 1996; Lang, Lang, Diekmann, & Kornhuber, 1989; Mizuki, Takii, Nishijima, & Inanaga, 1983). Given these correlations, it is striking that although the spontaneous EEG theta power decreases with age in children and is relatively small in adults, the efficiency of cognitive functioning improves in the course of development (Piaget, 1969). This implies that changes in theta system involvement during event processing as reflected by the theta response should occur with brain development. Finally, theta responses of young (3-year-old) children were demonstrated to be larger, delayed, and more variable than those of adults (Başar, 1982; Başar-Eroglu, Kolev, Ritter, Aksu, & Başar, 1994; Kolev, Başar-Eroglu, Aksu, & Başar, 1994). Altogether, these findings suggest that the EEG theta response undergoes specific developmental variations but it is unknown how and which response characteristics change as children mature. Therefore, the present study aimed to assess age-dependent alterations of EEG theta responses in 6 to 10-year-old children. Healthy young adults were also studied to evaluate the mature theta response.

As mentioned above, the EEG frequency responses are proposed to originate from the re-

organization of the spontaneous EEG. Therefore, theta response characteristics reflecting the stimulus-related changes in the ongoing EEG should be regarded as relevant for analysis. Such characteristics are the response phase-coupling to stimulus and amplitude enhancement or suppression in the post-stimulus epoch (Kalcher & Pfurtscheller, 1995; Sayers, Beagley, & Riha, 1979). In the averaged ERPs, however, amplitude and phase-locking effects are confounded and cannot be analyzed separately (e. g., Ruchkin, 1988). To quantify theta response phase-locking independently of amplitude effects, an original method for single-sweep analysis was applied (Kolev & Daskalova, 1990; Kolev & Yordanova, 1997; Yordanova & Kolev, 1996a, in press). Thus, the major questions addressed in this research were how single theta response amplitude, phase-locking, and enhancement relative to prestimulus activity vary with age in children and whether their developmental changes depend on the background EEG theta activity?

Previous studies on adults have shown that event-related theta activity differs between processing conditions (Başar-Eroglu et al., 1992; Demiralp & Başar, 1992; Klimesch et al., 1994; Mecklinger, Kramer, & Strayer, 1992; Yordanova & Kolev, in press). To examine whether the age-related variations in the theta response are restricted to a specific processing condition, passive and task auditory stimuli were used. Since the latency of the maximal theta response in the averaged ERP has been shown to be longer in younger children (Başar-Eroglu et al., 1994; Yordanova & Kolev, 1996b), measurement and evaluation were made for early and late post-stimulus epochs to enable assessment of single theta response dynamics over time after stimulus appearance. The relationship between single theta response parameters and the ongoing (prestimulus) theta band power was also evaluated. Results of the alpha frequency range in the same groups of children are presented in a related paper (Yordanova & Kolev, 1996a).

Methods

Subjects

A total of 50 healthy children from 6 to 10 years of age served as subjects, together with ten adults from 20 to 30 years of age. As indi-

Table 1 Distribution according to age of the subjects studied. Each group contained 10 subjects.

	Children 6 years	7 years	8 years	9 years	10 years	Adults 20–30 years
mean age (years)	6.50	7.60	8.50	9.30	10.60	24.10
(months)	77.90	91.20	102.10	111.50	127.10	289.20
SD (months)	4.65	3.25	4.68	3.03	4.43	44.40

cated in Table 1, the ages of the children ranged between 72 and 132 months, and were divided into 5 age groups consisting of 10 subjects (4–6 females) each. Children were obtained from local schools in Sofia and adult subjects were volunteers, primarily students from the Medical University in Sofia. Children were selected from a large sample after a neurological screening and were free of neurological disturbances. Interviews with teachers and parents of the children revealed no signs of attentional, behavioral, or learning problems. The children were of similar socio-economic status (professional – executive) as assessed by parents' education and occupation, and had normal or higher IQ scores as indicated by Raven's and verbal tests. Subjects were right-handed (Annett, 1985), without any history of neurologic, psychiatric, or hearing problems, and were paid for their participation in the experiment.

Stimuli and procedure

The subjects were assessed in a dimly lit, electrically shielded room and were monitored by means of a closed-circuit TV and intercom system. Children were given enough time before the recording sessions to become acquainted with the environment.

The auditory stimuli were generated by a PC, filtered, amplified, and reproduced by a loudspeaker in a free-sound field. All stimuli were presented with intensity of 60 dB SPL and duration of 50 ms (rise/fall 10 ms). The stimuli were delivered with random interstimulus intervals (3.5–6.5 s) in two different task situations:

- 1) Tone bursts of 800 Hz frequency ($N = 50$) were presented in a passive listening condition, with subjects instructed to relax silently. Before the recording session, they were told that the stimuli would be delivered for testing the technical equipment and would be of no relevance for them.
- 2) Auditory target and nontarget stimuli were

presented in an oddball task. During the task condition, 100 high and low frequency tones (1200 Hz and 800 Hz) were delivered randomly, with probability $P = 0.75$ for the high tones, and $P = 0.25$ for the low tones. Subjects were required to press a button with their dominant hand as quickly and accurately as possible in response to the low tones. In both the passive and oddball conditions the subjects kept their eyes closed.

Data collection and processing

Electrodes

The EEG was recorded with Ag-AgCl disc electrodes placed on midline frontal, central and parietal sites (Fz, Cz, and Pz), with linked mastoids as a reference. The ground electrode was positioned on the forehead. The electrooculogram (EOG) was recorded bipolarly with electrodes placed below and at the outer canthus of the left eye. Electrode impedance did not exceed 10 kOhms.

EEG recording and data storage

EEG was amplified with cutoff frequencies of 0.5 and 70 Hz by means of a Nihon Kohden electroencephalograph (model EEG-4314F). Stop-band filtering (band limits 48–52 Hz) was used for eliminating line frequency interference. The amplified EEG analog signals were digitized with a sampling frequency of 250 Hz (12 bit analog-to-digital converter) and stored for offline processing with epoch length of 1024 ms pre- and 1024 ms post-stimulus. Reaction times (RTs) were recorded automatically.

Artifact rejection

The stored raw single sweeps were inspected visually offline to eliminate EEG segments contaminated with blink, muscular, or any other type of artifact activity, with any EEG or EOG trial exceeding $\pm 50 \mu\text{V}$ for adults and $\pm 90 \mu\text{V}$ for children excluded from further analysis. Thus, the number of artifact-free sweeps

analyzed for each subject in each condition was between 40 and 50 for the passive and nontarget ERPs, and about 20–23 for the target ERPs.

Data analysis

Prestimulus EEG power spectral density

For each artifact-free single sweep, the power spectral density functions were calculated for the prestimulus epochs (–1000, 0 ms) using the Fast Fourier Transform (FFT), and then averaged separately for each stimulus type. For statistical evaluation, the mean absolute band power (X) in the range of 4–7 Hz was log-transformed according to the formula $Y = \log_{10}(X)$ to normalize the power distributions (Gasser, Bächer, & Möcks, 1982; Gasser et al., 1988).

Digital filtering

Averaged and single-sweep ERPs were digitally bandpass filtered in the theta frequency range (4–7 Hz). To provide a zero phase shift, a modified linear bandpass filter was used, whose weights were based on binomial coefficients (Wastell, 1979). The filter bandwidth was adjusted to be 5% from the total analyzed frequency band, which was experimentally proven to minimize filtering artifacts. Although in this study the main emphasis is placed on sin-

gle-sweep parameters, averaged unfiltered and filtered (4–7 Hz) ERPs were also obtained to enable comparison with results from the single-sweep analysis and with literature data.

Single sweep analysis

Three parameters of the single-sweep theta responses were analyzed for two time windows, early (0–300 ms) and late (300–600 ms): (1) maximal amplitude, (2) phase-locking, and (3) amplitude enhancement relative to prestimulus theta activity.

- 1) The maximal peak-to-peak amplitude of the single theta responses was measured in each of the two time windows. The mean value was calculated for each subject, stimulus type, and electrode location.
- 2) For a quantitative evaluation of the phase-locking, a modification of the single sweep wave identification (SSWI) method was applied (Kolev & Daskalova, 1990; Kolev & Yordanova, 1997). The steps of the analysis procedure are described below and are illustrated schematically in Figure 1.

First, extrema (minima and maxima) were identified in the filtered (4–7 Hz) single sweeps. The amplitudes of the identified extrema were coded with +1 for the maxima and with –1 for the minima. Amplitude and latency

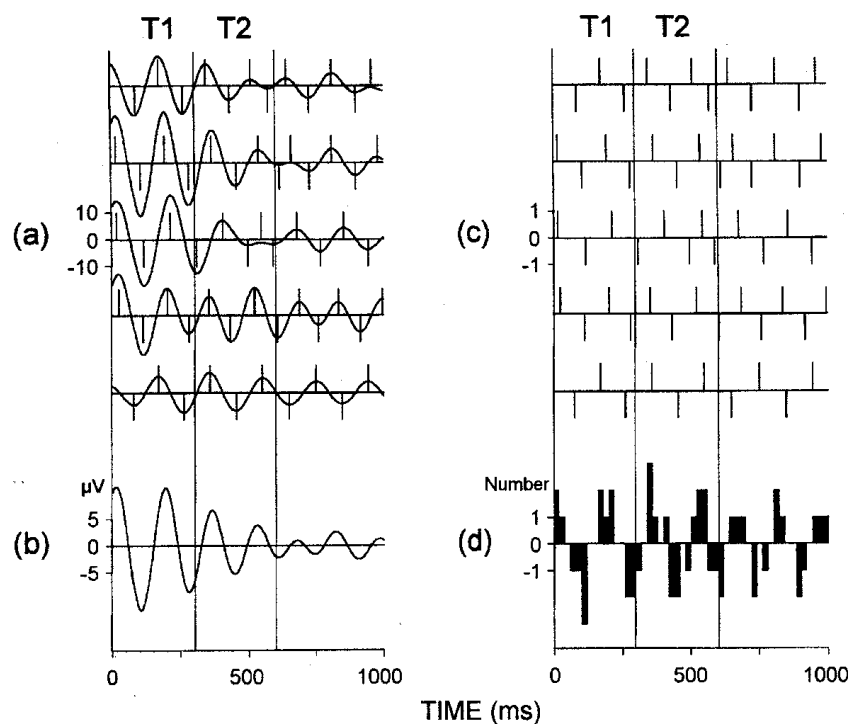


Figure 1 Single sweep wave identification (SSWI) method. The left panel presents (a) five single sweeps filtered in the theta range (4–7 Hz), and (b) their averaged waveform. The wave extrema in the single sweeps are detected according to the local maxima and minima, shown as vertical bars in (a). The same vertical bars (c) are located at the corresponding latency positions without the signals, and (d) the corresponding SSWI histogram is built according to the rule: in consecutive 20 ms time-lags +1 is added to the histogram bar if the detected extremum in the single sweep is maximum, or respectively –1, if the detected extremum is minimum. T1 – time window 0–300 ms, T2 – time window 300–600 ms.

values of the identified extrema were stored. This step is illustrated in Figure 1a where several representative single sweeps are shown. Figure 1c illustrates the detected points with coded amplitudes presented without the signals along the time axis.

Second, a histogram of the number of phase-locked single theta waves (single sweep wave identification histogram, SSWI histogram) was constructed. To perform data reduction, the analysis epoch was divided into time intervals of 20 ms. For each time interval the identified coded extrema were summed across trials. Thus, the number of the phase-locked waves in the consecutive single sweeps for each 20-ms interval was determined, and the obtained value was assigned to the corresponding histogram bar (Fig. 1d). Typical SSWI histograms are shown also in Figure 4c.

Third, quantitative evaluation of single-sweep phase-locking was performed. The SSWI histogram was normalized by dividing the bar values by the number of single sweeps included. The sum of absolute bar values of the normalized SSWI histogram was calculated for the time windows 0–300 and 300–600 ms post-stimulus, thereby giving information about the strength of single-sweep phase-locking in two consecutive post-stimulus periods. The sums were computed for each subject, stimulus type, and electrode site.

- 3) Single-sweep enhancement relative to pre-stimulus activity was analyzed by calculating the enhancement factor EF (Başar, 1982): For each single sweep N , the ratio of the maximal response amplitude R_N to the root mean square value rms_N of the ongoing EEG amplitude prior to the stimulus (in the time window $-500,0$ ms) was calculated according to the formula:

$$EF_N = \frac{R_N}{2\sqrt{2}rms_N}$$

The term $2\sqrt{2}$ gives the relation between the maximal amplitude and rms amplitude in case they are equal. As tested experimentally, the post-stimulus amplitude is enhanced if $EF > 1.5$ (Başar, 1982). EFs were calculated for the early and late time windows. Thereafter, the mean values for each subject, location, and stimulus were obtained.

Statistical analysis

Each of the three parameters of single theta responses (individual means of the maximal peak-to-peak theta amplitudes, integral values of the normalized SSWI histograms, and individual means of enhancement factors) was analyzed separately for the passive, target, and nontarget ERPs. Individual values were subjected to repeated measures analysis of variance with one between subject variable, AGE (6 levels corresponding to each age group, 6, 7, 8, 9, 10 years, and adults), and two within-subjects variables, TIME WINDOW (early vs. late), and ELECTRODE (Fz, Cz, and Pz). The same analysis was performed for the maximal peak-to-peak amplitudes of averaged filtered (4–7 Hz) ERPs. The Greenhouse-Geisser correction was applied to the analyses with repeated measures factor ELECTRODE. The original df and the probability values from the reduced df are reported here. Results from testing simple effects not presented in tables are regarded as significant only if the probability values P were smaller than .05. In order to describe group specific differences, post-hoc univariate F -contrasts were performed. The Bonferroni procedure was used to correct the probability values for the number of comparisons made. The corrected probability values are reported in the results. A two-way ANOVA (AGE \times ELECTRODE) was performed on the log-transformed absolute theta-band power values of the prestimulus EEG of the passive, target, and nontarget ERPs, and one-way ANOVA (AGE) was performed for reaction time and error rate data. To analyze the relationship between prestimulus theta activity and theta response, step-wise multiple regression analyses were carried out for the log-transformed absolute theta-band power and single-response parameters. To evaluate the relationship between RT and event-related theta activity, Pearson correlation coefficients were calculated for single theta response parameters to targets at each lead and RTs.

Results

Behavioral data

As indicated by the significance of the age factor (AGE: $F(5,54) = 14.5$, $P < .001$), children's RTs to targets decreased with increasing age

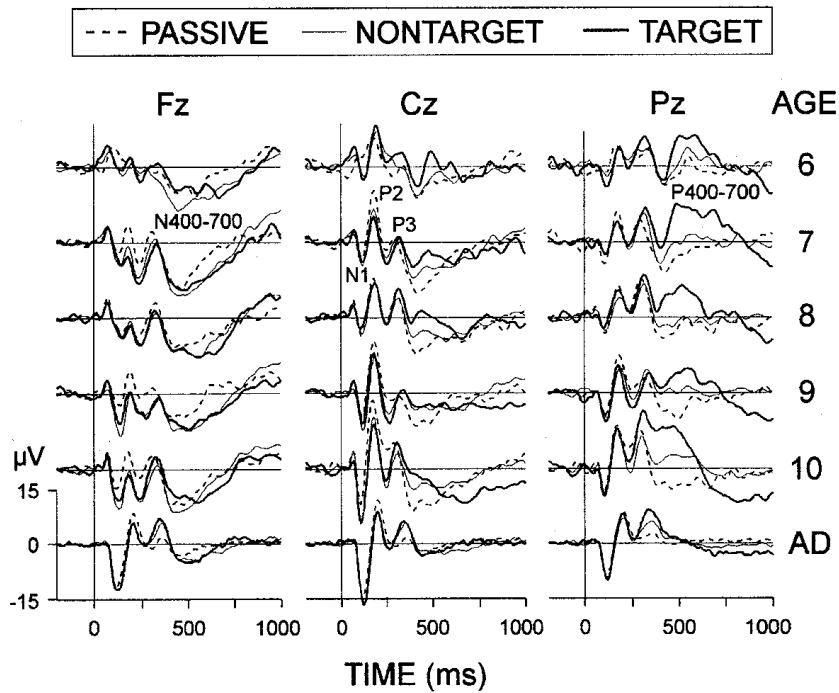


Figure 2 Grand average passive, nontarget, and target ERPs at three electrode locations (Fz, Cz, Pz) from different age groups: 6-year-olds, 7-year-olds, 8-year-olds, 9-year-olds, 10-year-olds, AD – adults. Each age group consists of 10 subjects. Stimulus presentation is at 0 ms.

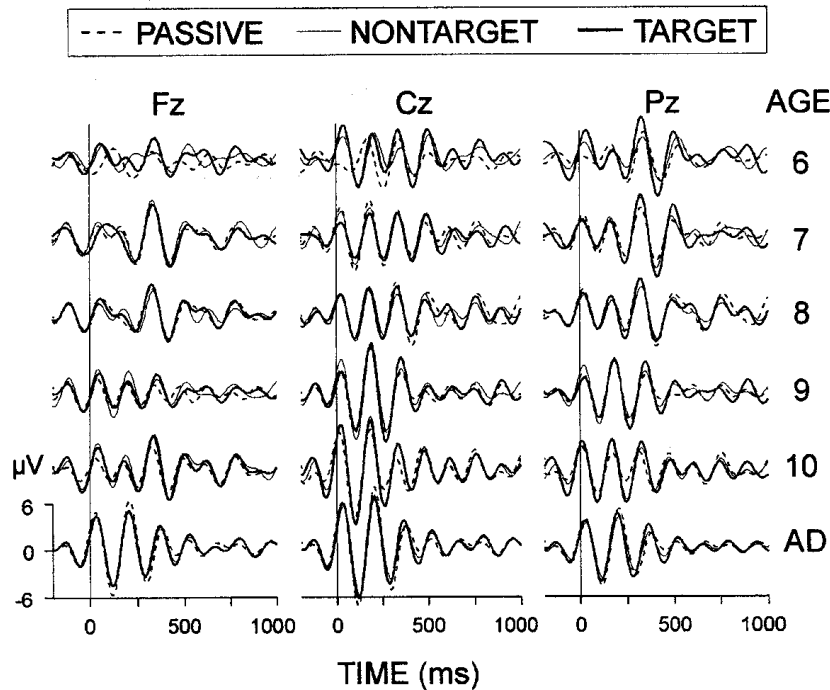


Figure 3 Grand average passive, nontarget, and target ERPs at three electrode locations (Fz, Cz, Pz) filtered in the theta (4–7 Hz) range. The age groups are as designated in Figure 2.

(group means of 6-, 7-, 8-, 9-, and 10-year-old children: 716, 702, 675, 602, 472 ms respectively), but were significantly slower than those of adults (mean 390 ms). RTs did not differ between the groups of 6–8-year-olds, who also manifested significantly slower responses than 9–10-year-old children. Error rate was higher in children relative to adults, but this difference was not significant.

Time domain averaged ERPs

Time domain ERPs are presented to illustrate that the present data are consistent with previous results obtained with the classical ERP method. Figure 2 shows that the ERPs of both children and adults were characterized by N1, P2, N2, and P3 (P300) components. Children additionally displayed a frontal late negative wave N400–700, and a parietal late positive

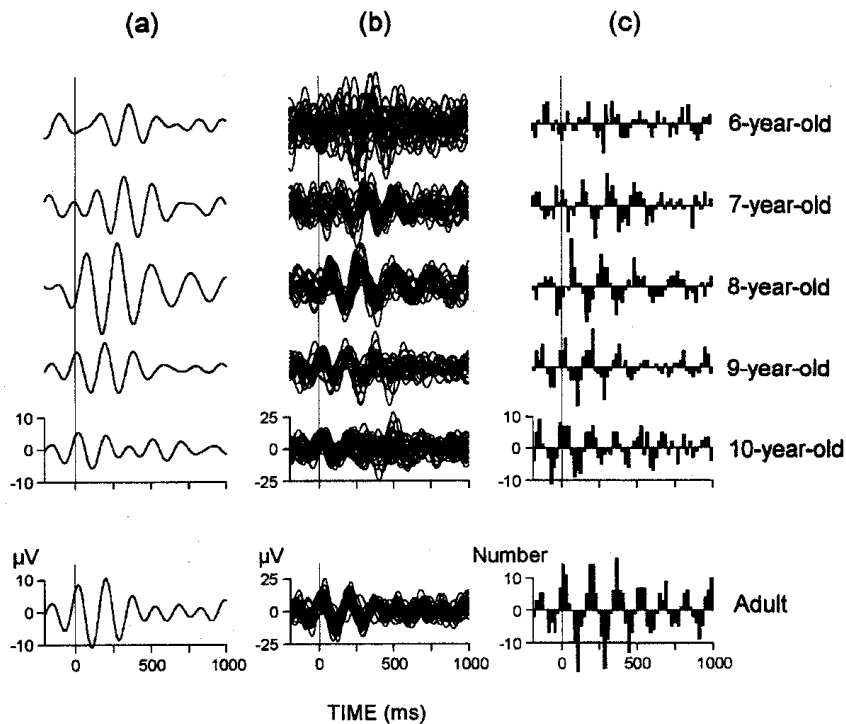


Figure 4 (a) Averaged ERPs filtered in the theta (4–7 Hz) range, (b) superimposed single sweeps filtered in the same (4–7 Hz) range, and (c) the corresponding SSWI histograms for six representative subjects at 6, 7, 8, 9, and 10 years of age, and an adult. Children had larger single theta responses than adults, especially in the late time window (300–600 ms). As reflected in the SSWI histograms, children also displayed a weaker phase-locking in both the early and late time windows than adults. All recordings are from the passive listening condition at Cz. Along the Y-axes – amplitude (μV) for (a) and (b), and number of synchronized single waves for (c).

wave P400–700 that occurred primarily in response to the targets and decreased in latency with advancing age in children. A detailed analysis of the time-domain ERP components has been reported elsewhere (Yordanova, Angelov, Silyamova, & Kolev, 1992).

Theta activity analysis

Prestimulus theta power

The values of the absolute theta power of the EEG preceding the passive, target, and nontarget ERPs were first subjected to AGE \times STIMULUS \times ELECTRODE analysis of variance. No significant main effect or interactions of STIMULUS were obtained. The significant effect of AGE found for each stimulus type resulted from the gradual decrease in theta power between 6 and 10 years, with the lowest values manifested by adults (AGE: $F(5,54) > 48.0, P < .001$). The prestimulus theta power was highest at Cz (ELECTRODE: $F(2,108) > 7.8, P < .001$).

Averaged filtered ERPs

Figure 3 illustrates that the maximal peak-to-peak amplitude in the averaged (4–7 Hz) ERPs did not depend on AGE ($F(5,54) < 0.64, P > .5$). In 6–8-year-old children, the maximal theta response at Pz and Cz occurred later (AGE \times TIME WINDOW: $F(5,54) > 3.37, P < .05$). It is also noticeable that the frontal theta responses of chil-

dren were delayed relative to those of adults. Maximal values were found at Cz (ELECTRODE: $F(2,108) > 6.1, P < .001$).

Single-sweep analyses

Figure 4 displays representative individual data to visualize the specific information reflected by each of the three parameters analyzed. Results from statistical evaluation of single-sweep amplitude, phase-locking, and enhancement factor are summarized in Table 2.

– Maximal peak-to-peak amplitude

As presented in Table 2, the statistical outcomes were similar for the three types of stimuli and will be discussed in terms of the overall patterns for the passive, target, and nontarget ERPs.

Figure 5a illustrates that: (1) adults had significantly lower single-sweep amplitudes than children from each group, with $F(1,54) > 11.7$ and $P < .005$ for each of the univariate F -contrasts between single groups, (2) theta amplitudes declined with age in children, and (3) the developmental time courses differed between the passive and task-related stimuli: For the target and nontarget ERPs, no difference was found among the groups of 6–9-year-olds, and the 10-year-old children produced the lowest amplitudes compared to the rest of the chil-

dren groups ($F(1,54) > 6.94$, $P < .05$ for each contrast). For the passive ERPs, significant decreases were observed for the groups of 7- and 9-year-olds ($F(1,54) > 9.7$, $P < .05$).

The significant main effect of TIME WINDOW was due to the overall higher early than late theta responses. However, a significant AGE \times TIME WINDOW interaction also was found. Figure 5a illustrates that only in adults and 10-year-old children (for targets) were the early theta responses larger than the late ones. As indicated by the significant ELECTRODE \times TIME WINDOW interaction (Table 2), the difference between early and late theta responses was most pronounced at Cz, with a simple TIME WINDOW effect at Cz yielding $P < .001$.

In sum, single theta response amplitudes decreased with age in children and were lowest in adults. For each group, the early theta responses were maximal at the vertex. The difference between early and late response amplitudes was significant only in adults.

– Phase-locking

The statistical results were again similar for the passive, target, and nontarget ERPs (Table 2). Figure 5b demonstrates that the phase-locking was stronger in adults than in children from each group ($F(1,54) > 25.05$, $P < .005$ for each contrast). As indicated by the significant AGE \times TIME WINDOW interaction ($P < .001$), the phase-locking of the early theta responses increased with age in children, whereas no difference between children groups was found for the late theta responses. Also, the early theta responses were more strongly phase-coupled than the late ones (TIME WINDOW: $P < .001$) but the early vs. late difference was significant only for the adult subjects (Fig. 5b). As shown in Figure 6a, the developmental increase in the phase-locking of the early theta responses was expressed mainly at Cz and much less evident at Fz and Pz. These effects were statistically reliable only for the nontarget ERPs (AGE \times TIME WINDOW \times ELECTRODE: $P < .05$). In addition, the early but not the late theta responses were best synchronized at the vertex (ELECTRODE: $P < .001$; ELECTRODE \times TIME WINDOW: $P < .001$).

In total, the phase-locking of theta responses was significantly stronger in adults than in children. A developmental increase was observed for the phase-locking of the early theta responses at the vertex location.

– Enhancement factors

Figure 5c illustrates that the EFs of adults were significantly larger than those of children at each age (AGE: $P < .001$; and for each between-group contrast: $F(1,54) > 32.3$, $P < .005$), with no statistical differences obtained among the groups of children. The effect of the TIME WINDOW originated mainly from the significantly greater early than late EFs in adults (AGE \times TIME WINDOW: $P < .001$). Simple TIME WINDOW effects tested for each age group showed that in contrast to adults, 6-year-old children manifested significantly stronger enhancement for the late than for the early theta responses in the task-related ERPs, with no reliable early vs. late differences found for the rest of the children groups, and for the passive ERPs (Fig. 5c). In addition, unlike adults, all children had greater EFs for the late than for the early theta responses to task-related (target and nontarget) ERPs over the frontal brain area (AGE \times TIME WINDOW \times ELECTRODE: $P < .05$ for the nontarget) – an effect illustrated in Figure 6b. For adults the most pronounced differences between early and late EFs were found at the mid-central location.

Altogether, the enhancement of theta responses relative to prestimulus theta activity was substantially greater in adults than in children. No increase in EFs was observed in children from 6 to 10 years. In contrast to adults, children tended to produce a stronger enhancement of the late theta responses, especially from 6 to 7 years of age, to task-related stimuli and at the frontal site.

– Multiple regression analyses

The results obtained so far demonstrated the presence of developmental variations in the amplitude and phase-locking of the early theta responses. However, the prestimulus theta power also decreased with increasing age, which may be responsible for the observed age-related changes in these two single theta response parameters. To determine to what extent age influenced theta response parameters due to the developmental power reduction of the prestimulus theta activity, step-wise multiple regression analyses were performed for children data from each stimulus type. The dependent variables were single theta response amplitude and phase-locking, and the predic-

tor variables were log-transformed prestimulus theta power and children's age in months. The results obtained were similar for the three stimulus types. At each electrode site, single theta response amplitude was entirely predicted by the prestimulus theta power, since the age variable was removed from the equations ($R^2_{\text{total}} > .46$, $F(1,47) > 39.6$, $P < .001$). In contrast, the stability of phase-locking at Cz depended only on the age factor and was not predicted by variations of the prestimulus theta power ($R^2_{\text{total}} > .17$, $F(1,47) > 3.02$, $P < .005$). No significant correlations were found between children's reaction times and single-sweep parameters of theta responses to odd-ball targets.

Discussion

The present study assessed the event-related theta activity in children and adults at the level of single-sweep analysis. It was hypothesized that the EEG theta responses would differ between children and adults as well as among children groups, which can be evinced by differences in single-sweep parameters. This hypothesis was confirmed and significant age-related variations were found for single theta response amplitude, phase-locking, and enhancement relative to prestimulus activity. Furthermore, these variations were specific for each parameter. A major finding was that although single-sweep amplitudes decreased, the phase-locking increased with age. As described in the results, the averaged filtered ERPs did not manifest significant differences between children and adults. This was because the smaller single-sweep amplitudes of adults were accompanied by a pronounced phase-locking, and the opposite was true for children. Thus, since additional information was obtained that was obscured in the averaged waveforms, the developmental changes in the EEG theta response could be revealed and evaluated precisely at the level of single-sweep analysis.

Single-sweep theta responses in adults

In adults, the theta component of averaged auditory ERPs has been described previously (Başar-Eroglu et al., 1992; Demiralp & Başar, 1992). In the present study, by using single-sweep analysis the following new characteris-

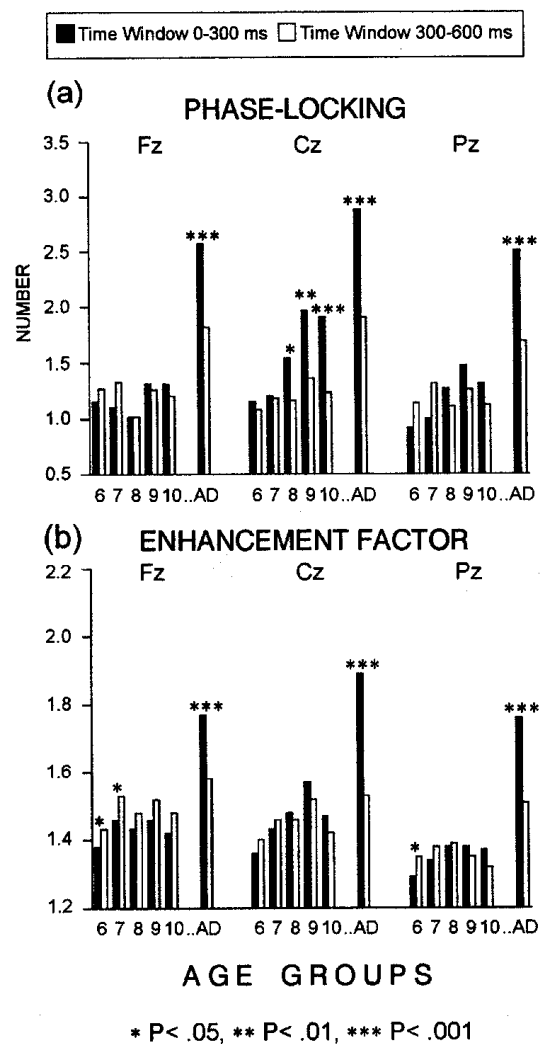


Figure 6 Effects of TIME WINDOW on theta responses to nontarget stimuli from each ELECTRODE and AGE group: (a) number of phase-locked single theta waves, (b) enhancement factor. The age groups are designated in the same manner as in Figure 2.

tics of the event-related theta activity were found: (1) Auditory theta responses display strong phase-locking and amplitude enhancement in the post-stimulus epoch, which verifies the stimulus-related reorganization of the ongoing theta activity in adults; (2) The early theta responses (0–300 ms) are higher in magnitude and enhancement, and stronger in phase-locking than the late ones (300–600 ms), with the differences between early and late components being most pronounced at the mid-central location. These observations were true for passive, target, and nontarget ERPs, which shows that the early and late theta responses may reflect mechanisms activated during both passive and task stimulus processing. Previous

reports on adults have found that enhanced (synchronized) event-related theta activity accompanies short-term memory activation (Klimesch et al., 1994; Mecklinger et al., 1992) and increased focused attention (Başar-Eroglu et al., 1992). These memory- and attention-related effects were observed for the post-stimulus epochs later than 250–300 ms. In addition, the late (300–600 ms) fronto-parietal theta responses to target oddball tones have been reported to be more enhanced and more strongly phase-locked than the late responses to passive stimuli, whereas the early theta components did not differ between target and passive stimulus processing (Yordanova & Kolev, in press). Stimulus type effect was not tested in the present study because only the developmental changes in theta activity were focused on. However, the reports mentioned above suggest that the early and late responses of adults as observed here may relate to different processing mechanisms.

Differences in theta responses of children and adults

The organization of the auditory theta response was specific for children. This was evidenced by the significant differences between the single-sweep parameters of 6–10-year-old children and adults: (1) Single theta responses of children were larger but not enhanced against prestimulus theta activity, and also less synchronized than those of adults; (2) In adults, the early theta oscillations showed higher responsiveness than the late ones, whereas in children the late responses were either more enhanced than the early ones or no reliable differences were observed between the early and late theta activity. It is noteworthy that the age-related variations were similar for the three stimulus types. These findings generally indicate that during auditory stimulus processing the theta response system in adults operates in a manner different from that in 6–10-year-old children. Since the passive and task-related stimuli produced similar age-related differences, it may be further suggested that the specific organization of the theta response in children reflects developmental variations of basic stimulus-processing mechanisms common for the different processing conditions. Such a proposal is supported by the observation that single

theta response parameters do not correlate with response speed.

Theta response system development

Single theta responses in children not only differed from those in adults, but also changed with advancing age from 6 to 10 years: A decrease in single-response amplitudes occurred at 10 years for the task stimuli and at 7 and 9 years for the passive stimuli, with the values of the mature theta response not achieved even by oldest (10-year-old) children. The developmental alterations in amplitude are not likely to result from differences in cranial parameters such as thickness of the scalp or head circumference (Gasser et al., 1988; Polich, Ladish, & Burns, 1990) – a conclusion supported also by the different time courses of single theta amplitudes for the passive and task stimuli. As revealed by the multiple regression analysis results, these age-related amplitude effects resulted exclusively from the developmental decrease in the power of the ongoing EEG theta activity. Furthermore, the early theta responses displayed a maximum at Cz as did the prestimulus theta power. The observation of the strong relationship between the pre- and post-stimulus theta amplitudes may be regarded as supporting the concept of the diffuse and distributed theta system in the brain generating both the spontaneous and stimulus-related 4–7 Hz activity (Başar, 1992). Hence, the developmental reduction of EEG theta activity may indicate a decrease in the number and/or intensity of the neuronal elements that determine operative theta states of the brain.

The present results demonstrate, however, that single theta responses of children are large but do not change relative to the prestimulus theta activity after stimulation. Also, the ability to enhance the magnitude of the evoked theta component does not improve from 6 to 10 years.

In parallel to the decrease in amplitude, an increase in the phase-locking of early theta responses took place at about 9 years of age. However, for all three types of ERPs adults had remarkably stronger phase-locking than any of the children groups. Hence, it may be concluded that the capability to produce stable (congruent) theta responses to auditory stimulation improves with development but appears related

to brain mechanisms that reach maturity at developmental stages later than 10 years.

The phase-locking in children did not depend on the power of the prestimulus EEG theta activity. Instead, subject age was the determinant of the developmental increase in phase-synchronization. This result demonstrates that theta response phase-locking reflects processes specifically activated after stimulus presentation. It is to be noted that the developmental increase in phase-locking was found only for the early theta responses and at the central site where the early theta responses of adults were mostly expressed (Fig. 6a). Although the phase-locking of late responses was also significantly stronger in adults than in children, no increase of late theta response phase-locking was observed for children groups. These differential time courses support the assumption that the early and late responses may have different functional roles.

In addition, major developmental differences were revealed for the time structure of all single-sweep parameters: Adults manifested pronounced differences between the early and late theta responses, but in children younger than 9–10 years the magnitude and phase-locking of the early theta responses were similar to those of the late responses. Furthermore, younger (6–7-year-old) children had a greater enhancement for the late compared to the early theta responses (Fig. 5c) and all children groups tended to enhance the frontal late theta responses more than the early ones (Fig. 5b). Given the previous results of adults outlined above, it cannot be ruled out that the relation between early and late theta responses varies as a function of the specific task conditions. Whether the reverse pattern in children reflects a response delay, a different way of involvement of processes functionally specific to the early and late responses in adults, or a qualitatively different mode of organization of the event-related theta activity, is an open question. The precise functional significance of the event-related theta activity in both adults and children requires further investigation, especially with respect to the meaning of single-sweep parameters. Nevertheless, the present findings suggest that single theta response parameters and their timing may provide a sensitive indicator of stimulus- and task-related information processing in children.

Altogether, the single-sweep analysis results demonstrate that the theta response system is not completely developed at the age of 10 years. The age at which the adult values of single theta response parameters are reached is not clear from the results but the processes related to theta response system functioning obviously reach maturation at later stages of development. It should be emphasized that at the age of 10 years the frontal lobes, unlike other brain structures, are reported not to have reached functional maturity with respect to their anatomical structure and input-output connections (Rothenberger, 1990). Miller (1991) has raised the hypothesis that the EEG theta rhythm reflects the fronto-hippocampal interplay during context processing. The present findings of the incomplete development of theta responses at 10 years of age as well as of the delayed enhancement of frontal theta responses in children support the notion of the association between the theta response and frontal lobe processes. In this regard, since frontal lobe functioning has been assigned a major role for the occurrence and course of psychiatric disorders in children (Rothenberger, 1990), event-related theta activity may appear informative as a supplementary tool for such clinical studies (e. g., Rothenberger, 1995; Yordanova, Dumais-Huber, Rothenberger, & Woerner, 1997). It should also be noted that the developmental changes of single-sweep parameters, although occurring at different ages, were rather stepwise than gradual, which points to their possible relation with stages of cognitive development (Piaget, 1969) but the precise correlations of single theta response parameters with cognitive stage is still to be investigated.

Theoretical implications

The developmental time courses were different for theta response amplitude, phase-locking, and enhancement. These differential developmental courses might reflect sequential effects in the maturation of a common underlying mechanism. Alternatively, they may indicate that specific mechanisms might be involved in the maturation of the processes related to each of the three single-sweep parameters.

The strong phase-locking of theta responses in adults shows that repeatable and stable waveforms are produced after stimulation. In

the framework of the concept of the theta system in the brain (Başar, 1992), the strong phase-locking is likely to result from stable (facilitated or traced) connections between neuronal elements. Hence, it can be assumed that the theta networks involved in responding during the early stage (0–300 ms) of stimulus information processing are stabilized or traced with development in children so that repeatable patterns can be produced at the central but not at the frontal and parietal locations. The increase in repeatability of the early theta responses is accompanied by a decrease in magnitude, which might reflect a developmental specialization of the theta networks based on involving fewer but functionally defined elements (Courchesne, 1990). The large enhancement factors in adults suggest that the neuronal elements responding in the theta channel can be coactivated (synchronized) simultaneously by the external stimulus (Klimesch et al., 1994) but no developmental changes were observed for the enhancement of the theta responses. With regard to the three single-sweep parameters analyzed here, it might be assumed that the theta response system changes with development in a way that enables less but functionally specified elements to be coactivated simultaneously under defined conditions. Reduction of active elements, selection of networks, and capability of synchronizing them upon stimulation seem to follow differential time courses.

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