Chapter 11
The Maturing Brain

11.1 Introduction

Chapter 6 provided an analysis of the essentials of dynamics in the sensory and cognitive processes of the brain. This includes basic studies in the both the human and animal brain, demonstrating that oscillatory activities in the delta, theta, alpha, beta, and gamma bands govern control and communication processes in the brain. Accordingly, these oscillations constitute the "most general transfer functions" of brain function. The Preface proposed one of the guiding themes of the book, which is the introduction of a new Cartesian system with multiple causalities. To achieve this, it is necessary to understand the changes that occur during the maturation processes of the brain.

Chapter 10 on the evolution of the species added an important dimension for changes in brain dynamics by answering the following questions: What are essential features of the anatomy of invertebrate ganglia and electrical activity of the ganglia? What are essential features of electrical activity in the cat and human brain? Despite important anatomical changes and changes in the amplitude and degree of synchrony of oscillatory responses, an ensemble of common features provided a transfer of hereditary information from Aplysia to the human brain: There are common frequency codes (or quasi-invariants as denoted in Part VI, Chapter 22) that organize functions in diverse brains.

There are also important changes in the structure and electrical activity in the human brain from the fetus to the brain of elder subjects. How do these changes affect the transfer functions, i.e., communication processes in the maturing brain? A 2-year-old child does not have a full command of his or her native language and cannot solve mathematical problems. Also, a 2-year-old child does not show alpha activity. Furthermore, the frontal lobes are not completely developed; synaptic organization is in the process of steady development. This chapter includes measurements of three groups; 3-year-old children, adults, and middle-age people. To provide the basis of the ontogenesis of the maturing brain, the next section gives an anatomical description.

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11.2 Changes in Structure and Synaptic Organization of the Human Brain

In ontogeny, similar to the evolution of the species (Fig. 11.1), the neocortex develops much more in size and volume than any other neuronal structure of the brain. Also in the human, from embryo to adult, the relative growth of the white matter underlying the cortex with its connective structure by far surpasses that of white matter elsewhere in the central nervous system (CNS). Neuron generation seems to have been completed in the human neocortex by the end of the second trimester of gestation. Afterward, however, cortical neurons continue to grow in size even at the time

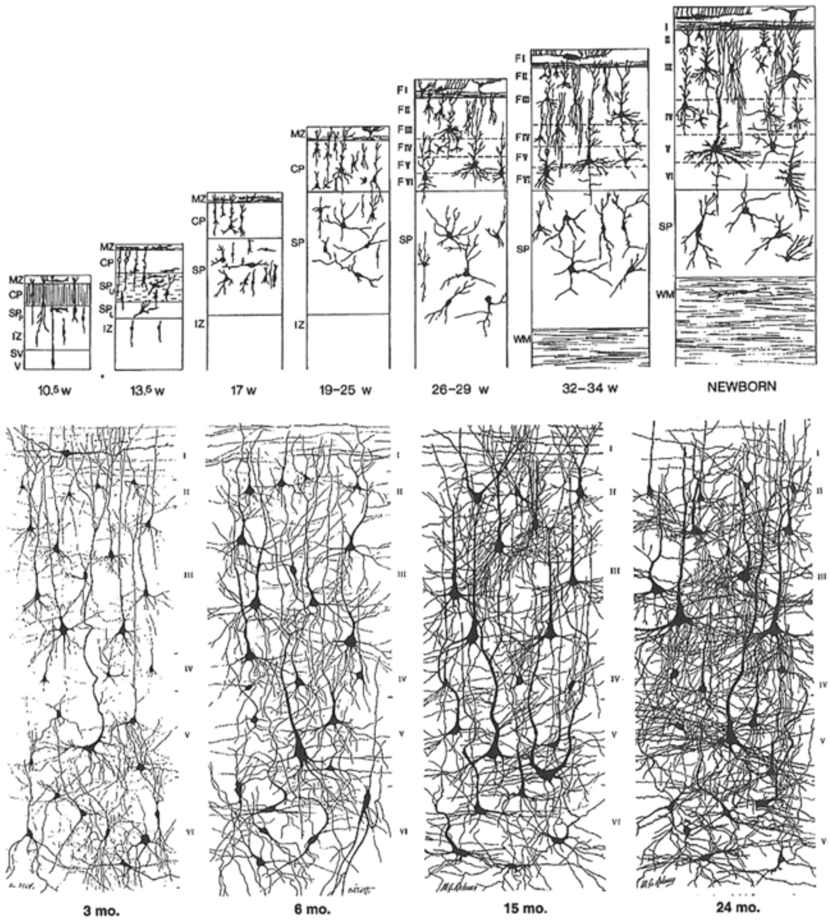

Fig. 11.1 Development of neurons in the human cortex. *Top:* Prenatal period from 10.5 weeks to birth. From Mrzljak et al. (1990). *Bottom:* Postnatal period at 3, 6, 15, and 24 months (modified from Conel 1963)

the infant is born; some neurons are still developing and migrating to their final location. Growing neurons develop their axons, which branch out to develop collaterals (see Fig. 11.1). Synaptogenesis begins in the third trimester of the pregnancy and continues until the age of 2 years. According to Changeux (2004), the main lines of the cellular architecture of the cerebral cortex are established before birth. This architecture is largely determined by the developmental genes and those responsible for the formation of nerve connections and the propagation of signals. According to Changeux (2004), about half of all adult humans synapses are formed after birth, and their number continues to change, rising and then falling until death. In humans the postnatal development of the brain lasts considerably longer than in other mammals. Cranial capacity increases 4.3 times after birth in humans. Moreover, cranial capacity reaches 70% of the adult human volume 3 years after birth. It is important to note that alpha activity in the child starts 3 years after birth, almost parallel with the development of speech. In human beings the rapid phase of synaptic growth is shorter in a sensory area such as the visual cortex, where it continues to grow until 2 or 3 years after birth, then in association areas such as the prefrontal cortex, where it grows up to 10 years after birth. Changeux (2004) further states that this observation has great importance from a functional point of view. The prefrontal cortex, which is very rich in neurons in layers two and three, plays a central role in cognitive functions.

In their book, *The Brain and the Inner World*, Solms and Turnbull (2002) indicate that the frontal cortex is crucial for the retrieval of memory. In this context, it is notable that the frontal cortex, no less than the hippocampus, is poorly developed in the first 2 years of life. There is a substantial growth spurt in the frontal cortex at around 2 years of age, and then a second spurt at about 5 years. Further, the frontal cortical volume continues to expand throughout adolescence. In the first few years the level of the organization of the frontal system may be considered so poor that the organized retrieval process is not available to the young child. The growth of volume and synaptic organization is seemingly accompanied with important changes of alpha activity in primary visual areas and crucial changes in frontal areas (association).

These relevant findings on anatomical organization of the neocortex are revisited later in this chapter.

11.2.1 The Aim of This Chapter

The age of the human subject is one of the most important factors influencing the amplitude and frequency of the electroencephalogram (EEG) (Dustman et al. 1993; Katada et al. 1981; Niedermeyer 1993; Obrist 1976). Within the brain response susceptibility concept, the evoked oscillations also can be expected to undergo important changes with increasing age in children and adults. To demonstrate these changes, a comparative analysis is made for oscillatory evoked potentials (EPs) of 3-year-old children who do not have developed occipital 10 Hz rhythm, adult subjects with expressed alpha (18–32 years old), and elder subjects with reduced occipital alpha (55 years old). The major results provide a model to show that the spontaneous and evoked alpha is interrelated.

The concept of *brain response susceptibility* is effectively supported by the evaluation of the comparative data (for the hypothesis the reader is referred to Chaps. 7, 8, 23, and 24).

11.2.2 Spontaneous and Evoked Alpha Activity at Occipital Sites in Three Age Groups

Figure 11.2a illustrates the instantaneous power spectra at occipital recordings of three subjects from each of the three age groups: 3-year-old child, young adult, and middle-aged adult. As known from earlier studies (Eeg-Olofsson 1971; Niedermeyer 1993; Petersén and Eeg-Olofsson 1971), the EEG in 3-year-old children does not have spontaneous activity in the 10 Hz frequency range. In fact, no 10 Hz activity was recorded in the EEG of a 3-year-old child (Fig. 11.2a). In contrast to the results from children, young adults had distinct and ample 10–12 Hz activity in the occipital recording (Fig. 11.2a, middle panel).

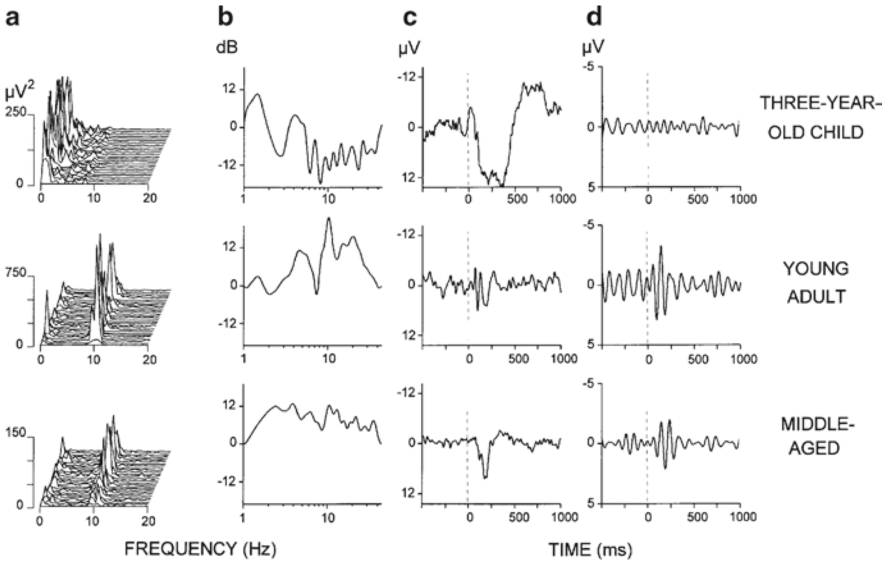

Fig. 11.2 Averaged VEPs of three representative subjects: 3-year-old child, young adult, and middle-aged adult. (**a**) Instantaneous power spectra of consecutive 2 s long EEG epochs, (**b**) amplitude-frequency characteristics of visual evoked potentials, (**c**) averaged VEPs, (**d**) filtered in the range of 8–15 Hz. All recordings are from the left occipital site O1. Stimulus onset occurs at 0 ms (from Başar et al. 1997c)

Results from experiments on middle-aged subjects showed a reduction in 10 Hz activity in the occipital areas. Figure 11.2a (bottom) illustrates the power spectra of a 55-year-old subject. The 10 Hz activity of this subject is apparent in comparison with the 3-year-old child, but drastically reduced in comparison with the young adult. Figure 11.2b shows the amplitude-frequency characteristics (AFCs), and Fig. 11.2c displays the averaged EPs on visual stimulation for the three subjects. Figure 11.2d illustrates the filtered average visual EP responses with band limits of 8–15 Hz. No alpha responses (defined as the oscillatory brain activity in the 8–15 Hz frequency range within approximately 200–300 ms following external stimulation) are recorded in the visual EPs of children. In young adults, the group mean amplitude of the peak-to-peak alpha responses in the averaged visual EPs was 4.5 μV. In the visual EPs of middle-aged adults, the peak-to-peak alpha response was 3.1 μV.

11.2.3 A Comparative Analysis of Frontal Vs. Occipital 10 Hz Activity in Young and Middle-Aged Adults

Figure 11.3a presents stack plots of power spectra of the spontaneous EEG of young and middle-aged adults to enable comparison between their frontal and occipital alpha activity. Although young adults had low 10 Hz activity at the frontal site (or sometimes no activity) as a rule, their posterior alpha had relatively high amplitude. (In this example the young adult manifests alpha power at approximately 100 μV^2 for the frontal, and more than three times higher for the occipital recording.) In the middle-aged adult, a most important phenomenon was observed; in the occipital recording (O1), alpha power was maximally 20 μV^2, whereas at the frontal (F3) recording site alpha power was approximately 80 μV^2.

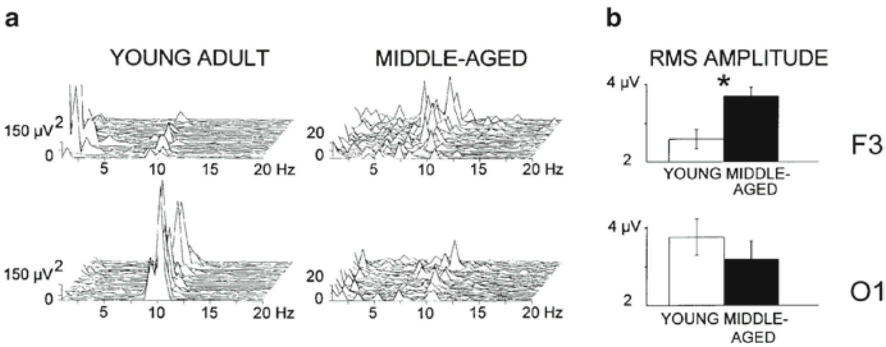

Fig. 11.3 (**a**) Instantaneous power spectra of EEG epochs in one representative young and one representative middle-aged adult recorded from the left frontal (F3) and left occipital (O1) electrode locations. (**b**) Group mean values ±1 standard error of the rms amplitudes measured in the pre-stimulus epoch from the same electrode locations. The significance of difference is $^{*}p \leq 0.05$ (from Başar et al. 1997c)

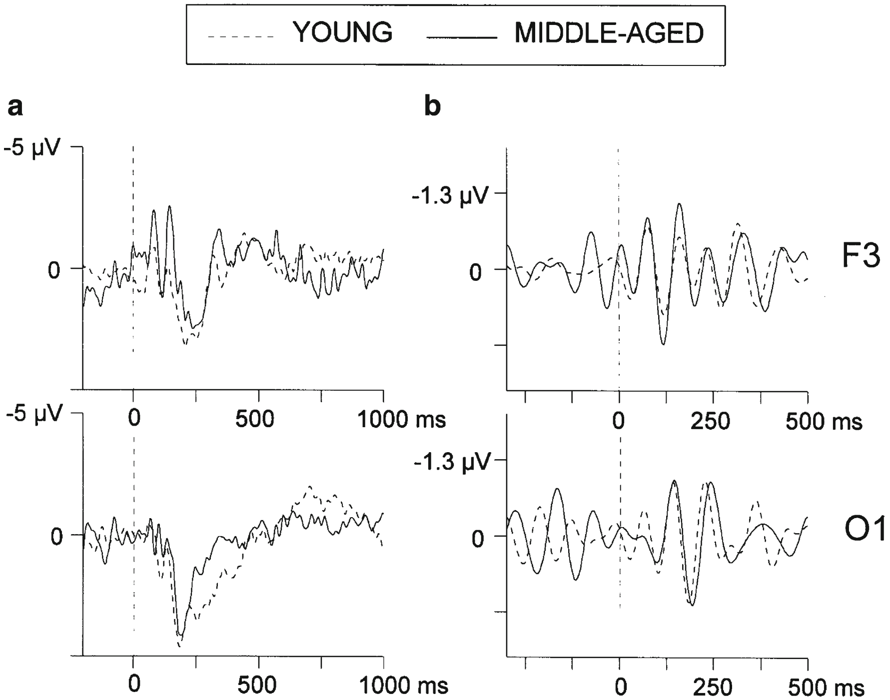

Fig. 11.4 Grand average VEPs in young and middle-aged adults from left frontal (F3) and left occipital (O1) locations. (**a**) Unfiltered, and (**b**) filtered in the range of 8–15 Hz. Stimulus onset occurs at 0 ms (from Başar et al. 1997c)

A significant increase of frontal alpha amplitude was obtained for middle-aged subjects as also revealed from the mean group rms values in Fig. 11.3b. In contrast, lower rms values were produced by the older subject for the occipital recordings.

Figure 11.4a illustrates unfiltered grand averaged visual EPs in young and middle-aged subjects. An increase in 10 Hz activity at the frontal (F3) site is observable already in the unfiltered curves. Figure 11.4b presents the grand average visual EPs digitally filtered in the alpha (8–15 Hz) range. It is clearly seen that the frontal alpha responses are larger in middle-aged than in young adults (in averaged visual EPs, 4.63 vs. 3.4 µV). The most important result illustrated in Fig. 11.4b is the frontal increase of about 40% in the alpha responses of middle-aged adults. This effect is visible even in the unfiltered visual EPs.

11.2.4 Single-Sweep Analysis of Visual EPs in Young and Middle-Aged Adults

In Fig. 11.5 single visual EPs recorded at the frontal F3 position and filtered in the 8–15 Hz range in two young and middle-aged subjects are shown. This figure serves to demonstrate the meaning of the parameters used and shows the following features:

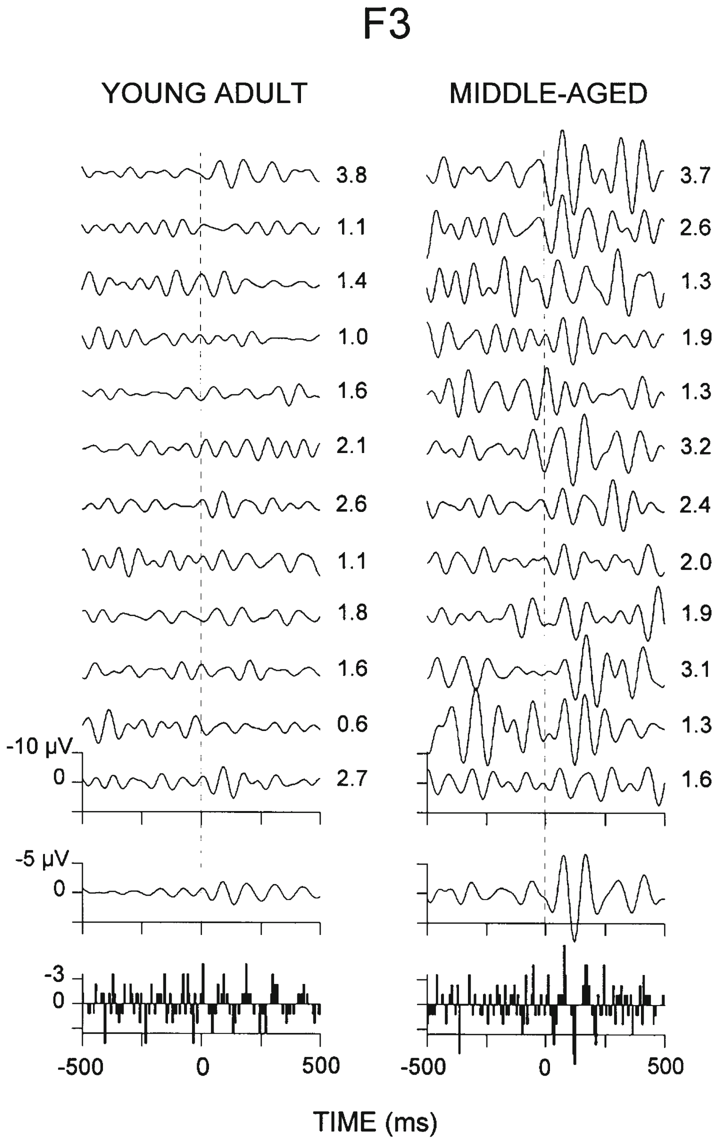

Fig. 11.5 Single sweeps from left frontal lead (F3) in one representative young and one middle-aged adult, filtered in the 8–15 Hz frequency range. The numbers on the right side of each single sweep are the corresponding enhancement factors (from Başar et al. 1997)

- Maximal alpha amplitudes within 0–300 ms are higher in the middle-aged than in young adult person.
- Consecutive alpha responses of the elder adult are better synchronized or much more congruent than those of the young adult.
- Although the pre-stimulus alpha activity is higher in the elder subject, the relative amplitude enhancement of the response is still somewhat higher than in the

young adult. The relative amplitude changes of alpha activity were estimated by computing the enhancement factors that, as examples, are presented in the figure for each single alpha sweep shown.

11.3 Brain Response Susceptibility

11.3.1 Excitability of the Brain: Spontaneous Electroencephalogram Rhythms and Evoked Responses

The expression *excitable physiological system* was introduced by Sato and his co-workers (Sato 1963; Sato et al. 1971, 1977). These authors studied the relation of visual EPs to EEG by comparing the power spectra of the spontaneous activity with the driven rhythmic activity of the brain. They found that the occipital recording of a relaxed human subject displays a rhythmic spontaneous activity before photic flicker stimulation. However, the shape and frequency positions of the maxima in the power spectrum of this activity are similar to the frequency characteristics obtained by the application of visual stimuli, thus indicating the system's selective excitability. Accordingly, the excitability of a physiological system may be considered one of the most important basic transfer functions of the system.

Başar (1980) extended and generalized this idea by analyzing (1) data for all EEG frequencies and (2) diverse brain structures in addition to the occipital cortex. The frequency domain description of EPs in the cortex, thalamus, reticular formation, hippocampus, and cerebellum shows an overall frequency content for each structure similar to that of ongoing EEG activity. In addition, a resonating universal mechanism is indicated because the sensory stimulus brings the brain into a "coherent" state. In response to the stimulus, the frequency bands of the activity in various brain structures becomes much sharper and narrower, and also coherent in phase and frequency. The magnitude of the response in a given frequency range is enhanced against the magnitude of the ongoing activity. These results enabled us to develop extensions of Sato et al.'s (1971) concept of excitability:

> If a brain structure has spontaneous rhythmic activity in a given frequency channel, then this structure is tuned to the same frequency, and is producing "internal evoked potentials" to internal afferent impulses originating in the CNS, or respond in the form of evoked potentials to external sensory stimuli with patterns similar to those of internal evoked potentials. Thus, knowledge of the spontaneous or ongoing activity preceding stimulation must be considered as an important prerequisite for evaluation of evoked potentials (Başar 1980).

The response susceptibility of a brain structure depends mostly on its own intrinsic rhythmic activity (Başar 1980, 1983a, b, 1992; Narici et al. 1990). A brain system could react to external or internal stimuli producing those rhythms or frequency components that are already present in its intrinsic (natural) or spontaneous activity, i.e., if the spontaneous brain rhythms are missing in a given frequency range, they will be absent in the evoked rhythms and vice versa.

11.3.2 Electroencephalogram in Children Might Provide a Useful Natural Model for Testing the Hypothesis of Brain Response Susceptibility

The intrinsic (spontaneous) oscillatory brain activity depends on several factors:

1. Age
2. Topology
3. Vigilance and/or cognitive states
4. Pathology

The effects of some of these factors are used in the following to demonstrate brain response susceptibility.

By measuring EPs in 3-year-old children, the developing brain was used as a "natural model" to investigate the following question: How do brain systems respond to external stimulation if their intrinsic (spontaneous) rhythms are different (or not yet developed) in comparison with EEG rhythms in adults? Spontaneous EEG activity in children and adults was hypothesized to represent different types of intrinsic background rhythmic activity with respect to both alpha and slow frequency ranges (Fig. 11.6). According to the concept of brain systems response susceptibility, it was expected that:

1. Upon sensory stimulation, the evoked rhythms (post-stimulus enhancement, time, and frequency-locking during the post-stimulus period) as well as the corresponding evoked frequency EP components, will differ between children and adults if their spontaneous EEG rhythms are different; ***and
2. The evoked rhythms in children and adults should reflect their spontaneous EEG frequency patterns, respectively.

11.3.3 Aging and Topology-Related Changes in Alpha Activity and Brain Response Susceptibility

Young adults manifested somewhat higher alpha amplitudes during ongoing EEG over occipital brain areas. Accordingly, only at occipital locations were they able to produce larger and better synchronized alpha responses than middle-aged adults. In contrast, over the frontal brain regions, middle-aged adults had significantly higher and much more strongly phase-locked alpha responses than young adults, which were accompanied by higher pre-stimulus alpha power in the group of elder subjects.

Several reports indicate that a shift occurs in the alpha activity toward the more anterior sites of the brain with increasing age in adults (Fisch 1991). The results from analysis of spontaneous and pre-stimulus alpha activity in young and middle-aged adults are in line with these previous reports. The most important step in this

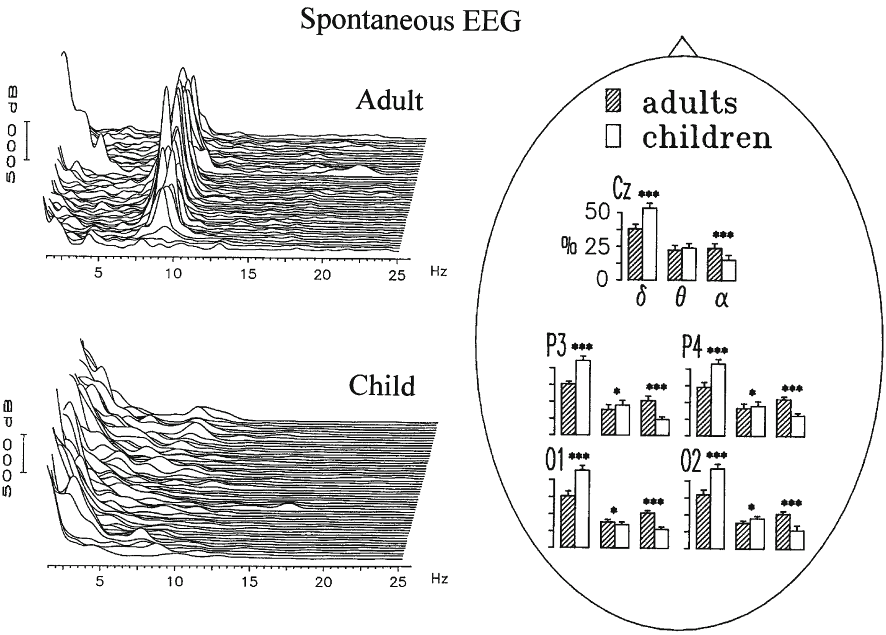

Fig. 11.6 Spontaneous EEG in 3-year-old children and adults. (*Left panel*) Instantaneous power spectra of EEG epochs recorded in one representative adult and one representative 3-year-old child (left occipital lead O1). Calculations are performed according to the method of compressed spectral arrays. Each curve presents a record of 1 s duration. Note the differences in the spectral characteristics in adults and children, as well as the different dynamics during the recording. (*Right panel*) Mean group values (+1 SE) of the root mean square amplitudes in the spontaneous EEG for delta (0.5–3.5 Hz), theta (4–7 Hz), and alpha (8–15 Hz) ranges, measured in percent from the sum of the amplitudes in all frequency ranges. The significance of difference is designated as: $^{*}p < 0.05$, $^{**}p < 0.01$, and $^{***}p < 0.001$ (with modifications from Başar-Eroğlu et al. 1994)

analysis is the finding that the age-related changes in the ongoing EEG are parallel with corresponding alterations in the visual and auditory evoked alpha responses. These results, as well as the results from children (Başar-Eroğlu et al. 1994; Kolev et al. 1994; Yordanova and Kolev 1996), show that EPs are controlled by spontaneous 10 Hz activity.

11.4 Conclusion: Importance of Maturation in Brain-Mind

This chapter gives a global description of the ontogenesis and synaptic organization of the human cortex as well as oscillatory spontaneous activity and responses in three important age groups. The results and interpretation of results have two important consequences.

1. It was stated at the beginning of the chapter that one of the major aims of this book is the development of a new Cartesian system to approach brain-body-mind integration. To do this, several chapters describe various properties of the brain related to brain-mind integration.

Does a child have a different type of mind than an adult? Does an elder subject have a different type of experience and “different type of mind” than a young adult? The findings emphasize the need for a “hyperspace” and presentations at different levels for the comparison of cognitive processes in babies, young adults, and elder subjects. Further, it can be seen that pathologies considerably change anatomical, biochemical, and electrical brain properties (see Chap. 13). This has the following implication: To be able to perform a real comparison of cognitive processes in children, adults, and older subjects, it is necessary to take various standardizations into account. This is discussed in Chaps. 14–16 as well.

2. It is also intriguing to observe that alpha activity grows in amplitude during the evolution of the species and maturation of the brain (Fig.17.2). Further, as humans age, the high amplitude alpha activity moves from the posterior to the frontal brain. Section 11.2 shows that synaptic organization of frontal areas does occur later in the maturating process. In comparison with the brains of animals, Bullock et al. (1995b) has shown that coherence is higher in the human cortex in comparison with lower animals. Because alpha activity is not found in the frontal areas in the brain of a young child, it is not possible to find high coherence. Altogether it seems that existence of mature alpha activity is of a major importance for the development of associative behavior of brain structures. Therefore, Chap. 10 and the present chapter introduce relevant thoughts on the connectivity and differentiation of mind in the brain.

11.4.1 Important Comment to the Parallelism of Alpha Activity During Maturation of the Human Brain and the Evolution of the Species

At this point it is suggested that the reader take into consideration an important parallel between the maturing of the brain (microevolution) with the increase of alpha activity during evolution of species (macroevolution). An increase in alpha activity is observed during the transition of the child brain to the adult brain. Moreover, alpha activity shifts from posterior areas to the frontal cortex in the brains of elder subjects. Also, the largest alpha activity is observed in the frontal areas in these subjects. In terms of evolution theory, this can be tentatively considered a *mutation* of alpha activity in the human brain. Frontal alpha activity becomes richer with the development of cognitive processes and the semantic experience of the maturing brain. The same situation is observed during the evolution of the species: 10 Hz oscillations in invertebrates have small amplitudes, and no coherent activity in the isolated ganglia is observed. In the human brain alpha activity shows high amplitudes and regular shapes. Are there parallels in the evolution of the species and the maturing brain? This is a very important question related to a type of maturation of alpha activity during evolution of the species. Is the increase of alpha activity a sign of augmentation of cognitive processes? Chap. 17 returns to this very important question.