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International Journal of Psychophysiology 39 (2001) 91–127

INTERNATIONAL
JOURNAL OF
PSYCHOPHYSIOLOGY

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Event-related oscillations are 'real brain responses' — wavelet analysis and new strategies

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Abstract

The EEG consists of the activity of an ensemble of generators producing rhythmic activity in several frequency ranges. These oscillators are active usually in a random way. However, by application of sensory stimulation these generators are coupled and act together in a coherent way. This synchronization and enhancement of EEG activity gives rise to 'evoked' or 'event-related oscillations'. The *compound evoked potential* manifests as superimposition of evoked rhythms in the EEG frequencies ranging from delta to gamma ('natural frequencies of the brain'). The superimposition principle is described with efficient strategies and by utilization of an efficient algorithm. The wavelet analysis confirms the results of the combined analysis procedure obtained by using the amplitude frequency characteristics (AFCs) and digital filtering. The AFC and adapted digital filtering methods are based on the first approach to analyze average evoked potentials. In contrast, the wavelet analysis is based on *signal retrieval* and *selection* among a large number of sweeps recorded in a given physiological or psychological experiment. By combining all these results and concepts, it can be stated that the wavelet analysis underlines and extends the expression that alpha-, theta-, delta-, and gamma-responses described in this report are the most important brain responses related to psychophysiological functions. The wavelet analysis confirms once more the expression 'real signals' which we attribute to EEG frequency responses of the brain. It will be demonstrated that the delta, theta, and alpha responses (i.e. the rhythms 'predicted' by digital filtering) are real brain oscillations. The frequency components of the event-related potential vary independently of each other with respect to: (a) their relation to the event; (b) their topographic distribution; and (c) with the mode of the physiological measurements. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Event-related oscillations (delta, theta, alpha, gamma); Cross-modality measurements; Hippocampus; Multiple sclerosis

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PII: S0167-8760(00)00135-5

1. New strategies in ERP research

The conventional averaged EP is widely used, but in the light of new ongoing studies it is considered to be only a rough estimate of the brain's EEG response: the averaged EP does not take into account dynamical changes in the brain's intrinsic activity. Although the concept of induced and evoked rhythms was introduced early on by Lord Adrian, only recently has it found great interest among physiologists and psychologists. A new working hypothesis considers *single-trial EPs* and *induced EEG rhythms* as follows.

1.1. Evoked potentials — ensembles of brain event-related oscillations in the alpha, theta, delta and gamma ranges

The conventional averaged EP is widely used, but in the light of new ongoing studies it is considered to be only a rough estimate of the brain's EEG response: the averaged EP does not take into account dynamical changes in the brain's intrinsic activity. Another way to verify the presence of time-locked theta responses after stimulation is to compute the amplitude frequency characteristics (AFC) of the averaged ERPs (Başar, 1976, 1980; Röschke et al., 1995). The AFC describes the brain system's transfer properties, e.g. excitability and susceptibility, by revealing resonant as well as salient frequencies. It therefore does not simply represent the spectral power density characterizing the transient signal in the frequency domain but the predicted behavior of the system (brain) if sinusoidally modulated input signals of defined frequencies were applied as stimulation. As reflecting the amplification in a given frequency channel, the AFC is expressed in relative units. Hence, the presence of a peak in the AFC reveals the resonant frequencies interpreted as the most preferred oscillations of the system during responding to stimulus. To calculate the AFCs, auditory ERPs were first averaged (Fig. 1a) and then transformed to the frequency domain by means of one-sided Fourier Transform (Laplace transform; for details see Appendix A and Solodovnikov, 1960; Başar, 1980).

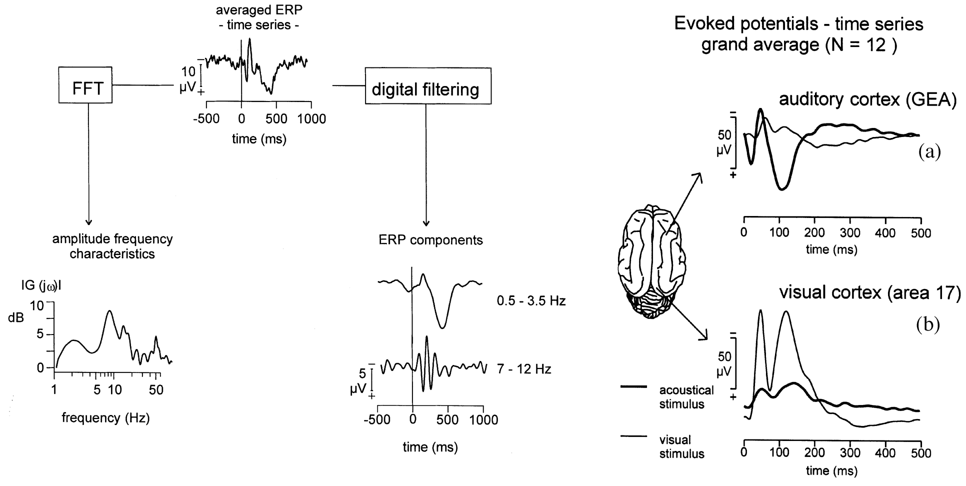

Fig. 1. (a) Principles of ERP frequency analysis. The averaged ERP is used to compute amplitude frequency characteristics (AFC, by means of Fast Fourier transform) and ERP frequency components (by means of digital filtering. For the AFC, the relative amplitude (in dB) is shown as a function of frequency (in Hz, logarithmic scale). AFC are normalized in such a way that the amplitude at 1 Hz equals 0 dB. (b) Averaged evoked potentials recorded from auditory and visual cortex of the cat brain. (A) Auditory cortex, (B) visual cortex. Solid curves: auditory stimulation; dashed curves: visual stimulation. Averages of $N = 12$ experimental sessions from four cats. GEA, gyrus ectosylvianus anterior (modified from Schürmann, M. Başar-Eroğlu, C., Başar, E., 1996. In: Başar, E., Hari, R., Lopes da Silva, F.H., Schürmann, M. (Eds), Brain Alpha Activity — New Aspects and Functional Correlates. Int. J. Psychophysiol., Special Issue 26: 149–170).

In the last decade a new technique called the wavelet analysis has been used increasingly by engineers, physicists and mathematicians who are interested in performing signal analysis in the frequency domain.

The wavelet analysis confirms the results of the combined analysis procedure obtained by using the amplitude frequency characteristics and digital filtering. The AFC and adapted digital filtering methods are based on the first approach to analyze average evoked potentials. In contrast, the wavelet analysis is based on *signal retrieval* and *selection* among a large number of sweeps recorded in a given physiological or psychological experiment. By combining all these results and concepts it can be stated that the wavelet analysis underlines and extends the expression that alpha-, theta-, delta-, and gamma-responses described in this report are the most important brain responses related to psychophysiological functions.

In summary, the wavelet analysis confirms once more the expression 'real signals' which we attribute to EEG frequency responses of the brain.

The EEG consists of the activity of an ensemble of generators producing rhythmic activity in several frequency ranges. These oscillators are active usually in a random way. However, by application of sensory stimulation these generators are coupled and act together in a coherent way. This synchronization and enhancement of EEG activity gives rise to 'evoked' or 'induced rhythms'.

Evoked potentials representing ensembles of neural population responses were considered as a result of transition from a *disordered* to an *ordered state* as illustrated in chapter 11 in Başar (1998).

The *compound evoked potential* manifests as a superimposition of evoked rhythms in the EEG frequencies ranging from delta to gamma ('natural frequencies of the brain'). In chapter 15 in Başar (1998) the superimposition principle is described with efficient strategies and by utilization of an efficient algorithm.

A number of investigators are working in the streamline of this concept following a synopsis given by Yordanova and Kolev (1998). Frequency domain analysis has demonstrated that the evoked oscillatory electroencephalographic (EEG) responses in different frequency bands also vary with sensory and cognitive processes (e.g. Başar and Bullock, 1992; Pantev et al., 1994). The stimulus-related EEG oscillations are defined as the EEG frequency responses or the frequency ERP components and can be extracted from the ERP by appropriate filtering procedures (Başar, 1980; Cook III and Miller, 1992; Farwell et al., 1993; Pantev, 1995). It has been assumed that the EEG frequency responses originating from a stimulus-induced reorganization (e.g. frequency stabilization, frequency selective enhancement or damping, and phase-reordering) of the spontaneous (ongoing) EEG (Sayers et al., 1974a,b; Başar, 1980; Parvin et al., 1980) give rise to the time-domain ERP components (Başar, 1992). In this framework, analysis of both the time and frequency components of the ERP may contribute to a better neurophysiological understanding of stimulus-related brain functioning.

The time domain analysis of ERPs has demonstrated that specific brain mechanisms are activated during the processing of infrequently occurring target stimulus events. Such events produce the parietal endogenous P300 (P3) ERP component, with larger P300 amplitudes obtained under task relevant compared to passive processing conditions (Pritchard, 1981; Johnson, 1986; Johnson Jr., 1988; Picton, 1992; Polich, 1993), and higher brain processes of attention allocation and memory updating thought to underlie P300 generation (Donchin and Coles, 1988; Polich and Kok, 1995).

In the frequency domain, higher cognitive and associative brain processes have been most consistently correlated with the EEG theta (4–7 Hz) activity (Mizuki et al., 1980, 1983; Lang et al., 1989; Inouye et al., 1994). Also, it is noteworthy that the EEG theta response has been found to manifest sensitivity to those task variables that are major determinants of the P300 component (Başar-Eroglu et al., 1992; Klimesch et al., 1994; Klimesch, 1995). For example, attended and highly relevant stimuli in both the auditory and visual modality have produced significantly higher theta response amplitudes than task-irrelevant stimuli in passive conditions in the first 250 ms after stimulation (Demiralp and Başar, 1992). Furthermore, oddball ERPs have manifested larger theta and delta EEG frequency components compared to passive ERPs (Stampfer and Başar, 1985). Enhanced theta responses with a prolongation up to 500 ms have also been observed for oddball target stimuli but not for passive stimuli (Başar-Eroglu et al., 1992), with a similar prolongation of theta oscillations up to 800 ms found when auditory perceptual difficulty was manipulated (Kolev and Schürmann, 1992). Visual stimuli inducing episodic memory processes have produced event-related theta synchronization that suggests a strong connection between theta activity and memory operations (Klimesch et al., 1994, 1996). Taken together, these findings imply firstly that the EEG theta responses in early and late post-stimulus epochs are functionally related to the cognitive processing in task conditions, and secondly, a relationship may exist between the EEG theta response and P300 ERP component. The aim of the present study was therefore to examine the effect of the 'oddball' task processing on the early and late theta ERP components and their association with the P300 typically elicited in this condition (Johnson, 1986).

Despite the overall consistency of the findings from averaged task-related ERPs, however, both single EEG response amplitudes and phase-locking have modified the averaged brain potential amplitude (Woody, 1967; Jervis et al., 1983; McGillem and Aunon, 1987; Ruchkin, 1988; Brandt et al., 1991). This is an important point to note with regard to functional significance, because single-sweep activity has been shown to reflect specific aspects of stimulus information processing that can be obscured by the averaging procedure (Ford et al., 1994; Unsal and Segalowitz, 1995; Yordanova et al., 1996).

Although the concept of induced and evoked rhythms was introduced early on by Lord Adrian, only recently has it found great interest among physiologists and psychologists. However, there are some questions to be dealt with that often arise from several investigators assuming that the interpretation of EPs as a superimposition of evoked rhythmicities of various frequencies might be a hypothetical one. The present report will deal with these questions.

Question 1: are the delta, theta, alpha and gamma responses distinct entities, or merely results of digital filtering. In particular, the gamma response might be a harmonic of the alpha response?

Reply: it will be demonstrated that the delta, theta, and alpha responses (i.e. the rhythms 'predicted' by digital filtering) are real brain oscillations. The frequency components of the event-related potential vary independently of each other with respect to (a) their relation to the event; (b) their topographic distribution; and (c) with the mode of the physiological measurements. Furthermore, pharmacological agents differentially modulate the frequency components.

Question 2: oscillatory responses recorded simultaneously in several positions might not be signs of distributed processing, but results of volume conduction.

Reply: hippocampal recordings will be presented to demonstrate that volume conduction is of minor importance. These results are demonstrated in detail by Başar-Eroglu et al. (1991a,b), see also Başar-Eroglu et al. (this volume).

Question 3: many technical artifacts arise from the specific method of band-pass filtering?

Reply: to exclude this possibility, results of band-pass filtering will be compared with results of wavelet analysis in one of the following sections and a biophysical approach is proposed (see also chapter 5).

Furthermore, the results have to be interpreted globally. Minor changes of filtered responses or minor peakings in the amplitude frequency characteristics should not be taken into account strongly. Only major and dominant changes in the filtered evoked potentials and in the amplitude frequency characteristics can be used to analyze psychophysiological correlates of the evoked potentials (see below in this section).

1.2. Biophysical strategies for justification of the functional component analysis of evoked potentials by means of Fourier techniques and digital filtering

As several reports of this special issue show, we can describe in terms of frequency components of 10 Hz, 2 Hz, 5 Hz, 20 Hz or 40 Hz. Critics might mention that Fourier analysis can dissect the transient response into several components, which are subharmonics of the first component. Our aim is to justify our method of analysis with the following argument:

1. For digital filtering, the filter limits are not chosen arbitrarily but according to the measured or evaluated band limits of the amplitude frequency characteristics. This precaution is very important.
2. If we perform a Fourier analysis of the impulse response, we can vary the Fourier spectrum by increasing the magnitude of the stimulating impulse. If in this given impulse response the first or the main component is increased, the first harmonic does usually increase proportionally to the change in impulse amplitude. This means that the subcomponents or subharmonics are not independent from each other. Our physiological aim was to show that this is not the case for the frequency components of evoked potentials. In other words: we assume that the 'theta response', 'alpha response' or '40 Hz response' in the evoked potential are not mathematical artifacts, but physiologically distinct components with different relations to sensory stimulation or cognitive events. Therefore it was clearly shown that frequency components are in most cases *not dependent* on each other but dependent on function, topology and intensity of the stimulation.

1.2.1. Real oscillatory responses are manifested only in major and dominant changes in the oscillatory responses

In an analogy with quantum mechanics in Heisenberg's sense, where the position, exact location or exact energy of a given elementary particle can only be described with the probability wave, the concept of wave packets in modern physics has been used in the analysis of ERPs in order to give a '*global description*' and not a very exact description of the observed oscillations. Accordingly, the analysis of brain compound potentials aims at obtaining 'cloudy information' about the frequency components: The results have to be interpreted globally. Minor changes of filtered responses or minor peakings in the amplitude frequency characteristics should not strongly be taken into account. Only major and dominant changes in the filtered evoked potentials and in the amplitude frequency characteristics can be used to analyze psychophysiological correlates of the evoked potentials (see Başar, 1998).

In particular, when we describe an increase in the '*alpha*', '*theta*' or '*delta*' responses, the significant changes must be at least in the range of 30% or more. Only such examples are given in this chapter and in the companion volume:

1. *Delta response increase* in visual odd ball experiments against simple sensory EPs are in the range of 200% (see chapter 15 in Başar, 1998).
2. Auditory odd-ball experiments evoke a *delta response increase* of 600% and a *theta response increase* of approximately 200% (see Başar, 1999).
3. In cross-modality experiments the *alpha response* is almost abolished in comparison to sensory evoked potentials obtained with adequate stimulation (see following sections of this chapter and companion volume).
4. Upon application of pharmacological agents the entire time course of the oscillatory response can be altered as in the case of hippocampal EP following application of ceruletide (see below in this section and companion volume).
5. EPs recorded in 3-year-old children do not contain phase-locked alpha responses whereas adults' EPs do (see Başar 1998), i.e. not every EP contains an alpha response as a real response.

These major changes were usually dependent: (a) on anatomical differences of the structures studied, resulting in *topographic differences*; or (b) on the type of experiments performed, resulting in *stimulus- or task-dependent differences*. Pathological changes also caused major changes of frequency components. Our examples serve to demonstrate that our analysis of frequency components is not arbitrary. The dissection of the evoked potential into frequency components can give us a very good idea as to the *real psychophysiological contents* of the potential, when the concept is carefully applied.

1.2.2. EP recordings in children

The previous sections showed that the frequency components of evoked potentials are distinct from each other. Taking into account the working hypothesis on a relationship between EEG and evoked potentials, the specific frequency contents of evoked potentials in children fits well with the other data given in this chapter. Alpha responses cannot be recorded in children who do not show spontaneous alpha rhythm in the EEG (for details see chapter 13). Nevertheless, oscillatory responses in other frequency ranges than alpha are recorded in children. This further supports the view that EP components in different frequency ranges are functionally distinct from each other.

1.3. Further biophysical justification: wavelet analysis

The recently introduced method of wavelet analysis confirms all results obtained by application of the Transient Response Frequency Characteristics (TRFC) analysis and adaptive digital filtering method (see the good congruence between adaptive digital filtering and wavelet analysis, Appendix and chapter 5 in Başar, 1998).

1.3.1. Ten-hertz frequency range

The alpha response in the cat brain — obtained in cross-modality experiments as described by Schürmann and Başar (1994) — was also demonstrated by means of wavelet analysis (see companion volume). Furthermore, analysis of the alpha response in the human brain with wavelet analysis confirms results of single sweep techniques by digital filtering. There is a large 10-Hz alpha response to visual stimulation in the occipital cortex, whereas an auditory stimulation does not create 10-Hz responses. The advantage of the wavelet analysis is the fact that the computer searches the phase locked signals in the 10-Hz frequency range. This is a method of single trial analysis enabling the automatic selection of some defined signals (see also Başar et al., in press).

1.3.2. Delta frequency range — P300

By the use of wavelet analysis the computer selects only responses to target stimuli. In case target and non-target stimuli are accumulated in the same file a certain program is in the position to select delta responses and differentiate target and non-target signals. With regard to the theta frequency range the wavelet analysis selects after target stimuli theta responses with a time delay of approximately 300 ms. These results are again in accordance with the analysis of TRFC and the adaptive digital filtering method (for details, see Schürmann et al., 1995).

The wavelet analysis confirms the results of the combined analysis procedure obtained by using the amplitude frequency characteristics and digital filtering. The TRFC (see Appendix A and Başar, 1980) and adaptive digital filtering methods are based on a first approach to analyze

Table 1
Amplitudes of the delta, theta, alpha, beta and gamma response components measured in GEA, HI, and OC electrodes of the cats during both AEP and VEP by using the band-pass filtering and wavelet decomposition methods[a]

Frequency band	Band-pass filtering	Wavelet decomposition
Delta	47.47 ± 55.20	45.01 ± 45.44
Theta	28.18 ± 19.20	35.14 ± 30.48
Alpha	46.42 ± 50.04	51.72 ± 55.18
Beta	28.90 ± 27.05	29.12 ± 27.11
Gamma	12.91 ± 9.64	15.75 ± 14.56

[a] Modified from Başar, E., Demiralp T., Schürmann, M., Başar-Eroğlu, C., Ademoglu, A., 1999. Brain Lang. 143–183.

average evoked potentials. In contrast, the wavelet analysis is based on *signal retrieval* and *selection* among a large number of sweeps recorded in a given physiological or psychological experiment. By combining all these results and concepts it can be stated that the wavelet analysis underlines and extends the assertion that alpha-, theta-, delta-, and gamma-responses described in this book are the most important brain responses related to psychophysiological functions.

In summary the wavelet analysis confirms once more the expression 'real signals' which we attribute to EEG frequency responses of the brain. The fact that the wavelet analysis is in good accordance with the procedure combining the TRFC method and digital filter analysis is demonstrated by the comparative presentation of amplitude measurements in Table 1. These results will be extensively explained in the companion volume.

1.4. Justification by means of physiological experiments

1.4.1. The alpha response in cross-modality measurements: intracranial EEG–EP measurements in cats (auditory and visual cortex)

As auditory and visual stimuli were used, the conditions were either 'adequate stimulation' (auditory cortex recording of auditory EP; visual cortex recording of visual EP) or 'inadequate stimulation' (visual cortex recording of auditory EP and vice versa). Such experiments are referred to as 'cross-modality' measurements (see Hartline, 1987; Başar, 1998, 1999; Başar and Schürmann, 1996).

One of the series of cross-modality experiments (Başar et al., 1991) was performed in cats with chronically implanted electrodes located in the auditory cortex (gyrus ectosylvianus anterior, GEA) and in the visual cortex (area 17). For further electrode sites, stereotactic coordinates and details on electrode implantation see Başar-Eroglu et al. (1991a,b). Two types of stimuli were used in different recording sessions:

1. Auditory EPs were recorded with sound stimuli of 80 dB sound pressure level, 2000 Hz frequency and 1000 ms duration.
2. Visual stimuli were delivered via a fluorescent bulb with 1000 ms duration.

Fig. 1b shows grand average EPs for $N = 12$ measurements in cats with auditory and visual stimulation. Two types of responses to adequate stimuli are shown: (1) auditory cortex recordings with auditory stimulation show high amplitude responses; (2) such high amplitude responses are also observed for the other condition of adequate stimulation, i.e. visual cortex with visual stimulation. With respect to inadequate stimulation, both the response to visual stimulation from the auditory cortex and the response to auditory stimulation from the visual cortex are of low amplitude. In both cases, however, there is a type of residual response.

As outlined in chapter 4 in Başar (1998) time domain averages shown in Fig. 1b were used to compute amplitude frequency characteristics and digitally filtered curves. Fig. 2 shows the amplitude frequency characteristics computed from the averaged EP shown in Fig. 1b (auditory cortex recordings). Comparing acoustical (adequate) vs.

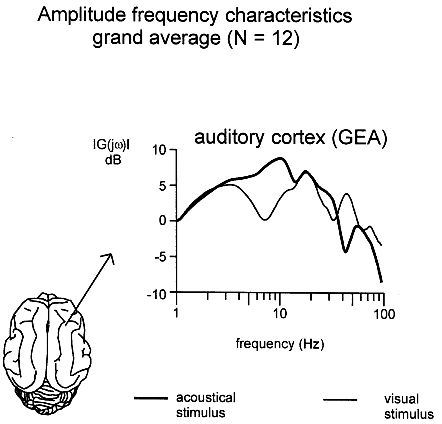

Fig. 2. Amplitude frequency characteristics computed from the cat evoked potentials shown in Fig. 18. *Abscissa:* frequency in Hz, logarithmic scale; *ordinate:* amplitude in relative units (decibels, dB). The curves are normalized in such a way that the amplitude at 1 Hz is equal to 0 dB. Recordings from the auditory cortex (Modified from Schürmann, M. Başar-Eroğlu, C., Başar, E., 1996. In: Başar, E., Hari, R., Lopes da Silva, F.H., Schürmann, M. (Eds), Brain Alpha Activity — New Aspects and Functional Correlates. Int. J. Psychophysiol., Special Issue 26: 149–170).

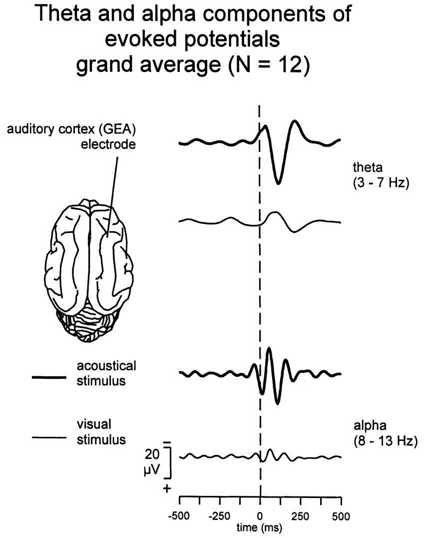

Fig. 3. Filtered components of averaged EPs computed from the curves shown in Fig. 18. Filter limits are chosen adequately according to the amplitude frequency characteristics shown in Fig. 18 (modified from Schürmann, M. Başar-Eroğlu, C., Başar, E., 1996. In: Başar, E., Hari, R., Lopes da Silva, F.H., Schürmann, M. (Eds), Brain Alpha Activity — New Aspects and Functional Correlates. Int. J. Psychophysiol., Special Issue 26: 149–170).

visual (inadequate) stimulation, the amplitude frequency characteristics had similar amplitudes in the delta–theta range, but considerable differences in the alpha range. The amplitude frequency characteristics being most markedly different in the alpha range, the frequency response in the alpha range appears to be correlated with the processing of adequate stimulation.

Fig. 3 shows filtered auditory cortex recordings. The upper panel shows theta responses whereas the lower panel shows alpha responses. A clear alpha response is seen with auditory — adequate — stimulation, whereas the alpha response to inadequate stimuli is minute. The amplitude ratio is approximately 1:6. Note that the adequate vs. inadequate difference is considerably smaller for theta responses, as shown in the upper panel. The amplitude ratio is approximately 1:3.

Panel A in Fig. 4 shows single-trial EPs filtered in the 8–15-Hz range. The left column refers to auditory stimulation with visual cortex recordings; the right column to visual stimulation with visual cortex recordings; i.e. inadequate vs. adequate stimulation. Responses to visual — adequate — stimulation show amplitude increase and time- and phase-locking. A distinct response is also seen in the filtered averaged EP in panel B. The unfiltered averaged EP also shows an alpha-like waveform. In contrast, responses to auditory stimulation — inadequate — show neither amplitude increase or phase locking, nor can we see an alpha response in the filtered average. There is a type of response in the unfiltered EP in panel C, but this is not an alpha response.

Fig. 5 gives another example of time-locking and amplitude increase in single trial responses to adequate stimulation: Single sweeps, filtered in the 8–15-Hz range — visual stimuli, visual cortex recordings — are superimposed. These superimposed single sweeps filtered in the 8–15-Hz range

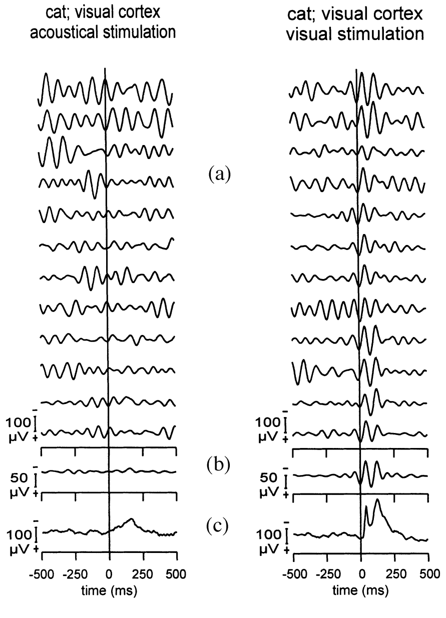

Fig. 4. EPs recorded from the cat brain by using intracranial electrodes. (a) single EEG-EP trials, filtered 8–15 Hz; (b) averaged EP, filtered 8–15 Hz; (c), averaged EP, wide-band filtered. *Left column,* inadequate stimulation (visual cortex recording with auditory stimulation). *Right column,* adequate stimulation (visual cortex recording with visual stimulation) (modified from Schürmann, M. Başar-Eroğlu, C., Başar, E., 1996. In: Başar, E., Hari, R., Lopes da Silva, F.H., Schürmann, M. (Eds), Brain Alpha Activity — New Aspects and Functional Correlates. Int. J. Psychophysiol., Special Issue 26: 149–170).

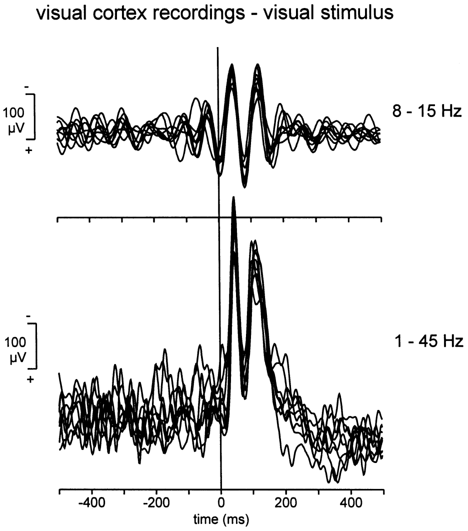

Fig. 5. Superimposed single trial EEG–EP epochs recorded from the cat brain with adequate stimulation (visual cortex recordings with visual stimulus). *Upper panel,* filter 8–15 Hz. *Lower panel,* wide-band filter (1–45 Hz) (modified from Schürmann, M. Başar-Eroğlu, C., Başar, E., 1996. In: Başar, E., Hari, R., Lopes da Silva, F.H., Schürmann, M. (Eds), Brain Alpha Activity — New Aspects and Functional Correlates. Int. J. Psychophysiol., Special Issue 26: 149–170).

(upper curves) are very similar in waveform to the wide-band filtered curves (lower curves). It is thus not only by filtering that the alpha response can be illustrated in these sweeps. Alpha responses are even visible in the broad-band filtered sweeps which are alpha-type responses. By contrast, Fig. 6 refers to a circumstance under which alpha responses *cannot be recorded,* i.e. to a measurement with inadequate stimulation. Note the lack of time-locking and the lack of amplitude increase.

As an interim summary it may be pointed out that alpha responses were recorded with adequate stimuli in primary sensory areas. Adequate vs. inadequate differences were larger for alpha responses than for theta responses, demonstrating the functional relevance of frequency components. As an aside, in ‘cross-modality’ recordings from the auditory cortex (gyrus ectosylvianus anterior) of the cat brain we observed a complementary effect: large alpha enhancements were present in auditory EP recordings. In visual EP recordings from the auditory cortex such alpha enhancements were not observed.

Critics might argue that the filtering procedure gives rise to this type of enhancements. However, even the averaged visual EP *without filtering* (Fig. 4, panel C and Fig. 5) shows a 10-Hz oscillatory waveform. Furthermore, the left column of Fig. 4, shows single sweeps of auditory EPs filtered in the same frequency range between 8 and 14 Hz, also recorded in the visual cortex.

We learned from these experiments that such damped alpha activity is not present in all parts of the brain or elicited by all types of stimuli: it is only by the combination of EP frequency analysis, of adequate stimuli and of appropriate electrode positions that such activities can be recorded. The results underline the following properties of the neural tissues under study. In the 10-Hz frequency range (filter limits: 8–14 Hz) we recorded large enhancements of single visual EPs in the visual cortex (also reflected in the amplitude fre-

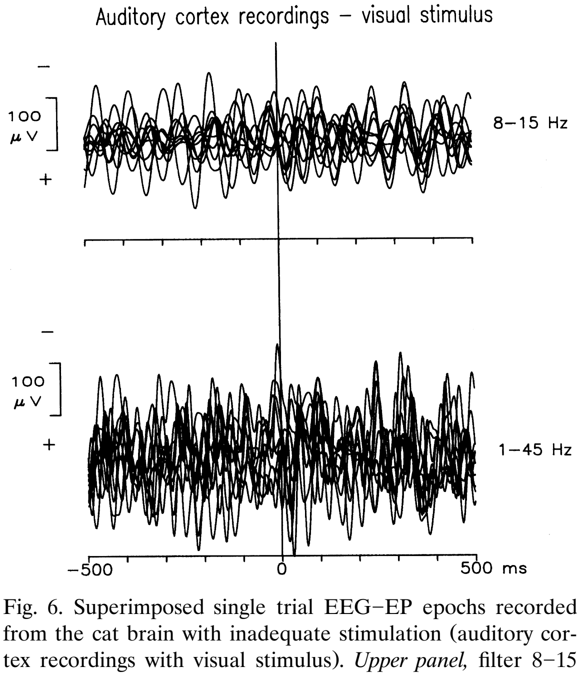

Fig. 6. Superimposed single trial EEG–EP epochs recorded from the cat brain with inadequate stimulation (auditory cortex recordings with visual stimulus). *Upper panel,* filter 8–15 Hz. *Lower panel,* wide-band filter (1–45 Hz) (modified from Schürmann, M. Başar-Eroğlu, C., Başar, E., 1996. In: Başar, E., Hari, R., Lopes da Silva, F.H., Schürmann, M. (Eds), Brain Alpha Activity — New Aspects and Functional Correlates. Int. J. Psychophysiol., Special Issue 26: 149–170).

quency characteristics in the shape of a dominant 12-Hz peak). In the language of systems theory significant (sharp) peaks in the amplitude characteristics of the transfer function characterize the resonant behavior of the studied system (see chapter 7 in Başar, 1998). One may also express this behavior as tuning of the 'device', or one might express the resonant frequency channels as the 'natural frequencies' of the system. In our case we may say that neural tissues in the occipital cortex are tuned to respond with 12 Hz and 1–5 Hz to adequate (visual) stimuli and with 1–5 Hz to inadequate (auditory) stimuli. The response magnitudes to both visual and auditory stimulation are similar in the low 1–5-Hz frequency range. It is important to note that the 10–12-Hz response peak has almost disappeared in the case of inadequate (auditory) stimuli, which, in turn, did not evoke alpha enhancements in single EEG–EP epochs of Fig. 4, panel A. This phenomenon is more marked in experiments with a single cat in comparison to mean value curves of Fig. 1b, panel B.

1.4.2. Hippocampal alpha responses as real brain oscillatory responses

Başar (1999) has shown that the hippocampus of the cat brain is able to generate alpha responses upon sensory stimuli and that the 10-Hz response oscillations are more stable than cortical and thalamic 10-Hz responses. In the following the hippocampal 10-Hz responses serve as examples of single EP-trials behaving like a short damped 10-Hz oscillation (visible without filtering; see also Başar, 1999).

The amplitude frequency characteristics recorded from hippocampal EPs have several maxima, in this example the most dominant response is in the 10-Hz frequency range (Fig. 7, bottom). The filtered response has also very high response amplitude (Fig. 7, top). The single trials shown were selected according to their enhancement factors (Başar, 1980) as applied previously for delta response in single P300 trials (Schürmann et al., 1995): Single sweeps with high enhancement factors for 10-Hz frequency range and low enhancements for the theta frequency range were selected. In Fig. 8 such wideband filtered single trials with the pattern of an almost pure 10-Hz response together with the average signals are shown. This is again a very convincing example showing (a) that the evoked potential is a manifestation of a superimposition of several frequency responses; and (b) that in ensembles of

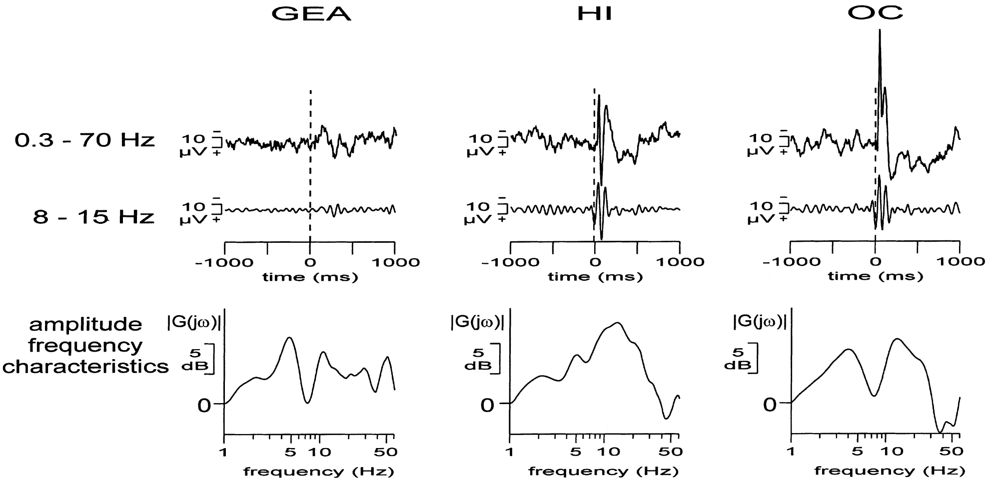

Fig. 7. Alpha responses in the cat brain, recorded from GEA (auditory cortex, gyrus ectosylvianus anterior), HI (hippocampus), and OC (visual cortex, occipital area 17). Wide-band filtered curves and the respective amplitude frequency characteristics are also shown.

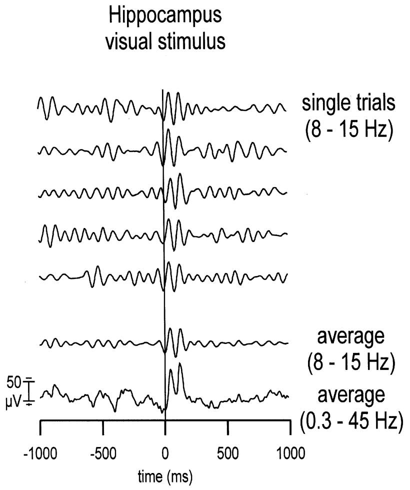

Fig. 8. Alpha responses in the cat brain, hippocampal recordings. Single trials (filtered 8–15 Hz) are shown as well as the filtered average (8–15 Hz) and the wide-band filtered average.

single evoked potentials — it is possible to record pure 10-Hz responses. The reader should compare the results concerning the superimposition principle in chapter 15 in Başar (1998).

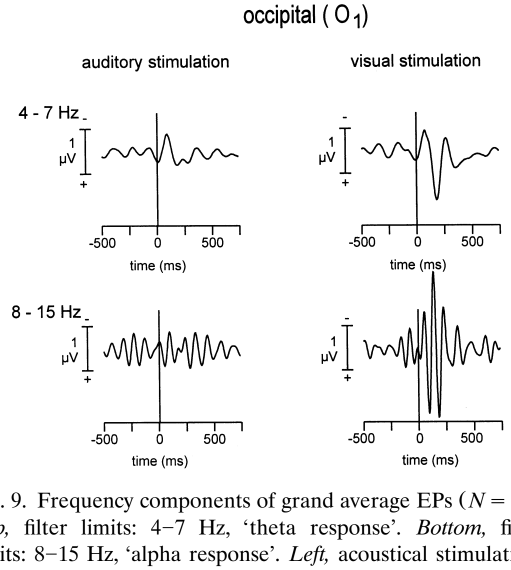

Fig. 9. Frequency components of grand average EPs ($N = 11$). *Top,* filter limits: 4–7 Hz, 'theta response'. *Bottom,* filter limits: 8–15 Hz, 'alpha response'. *Left,* acoustical stimulation. *Right,* visual stimulation (modified from Schürmann, M. Başar-Eroğlu, C., Başar, E., 1996. In: Başar, E., Hari, R., Lopes da Silva, F.H., Schürmann, M. (Eds), Brain Alpha Activity — New Aspects and Functional Correlates. Int. J. Psychophysiol., Special Issue 26: 149–170).

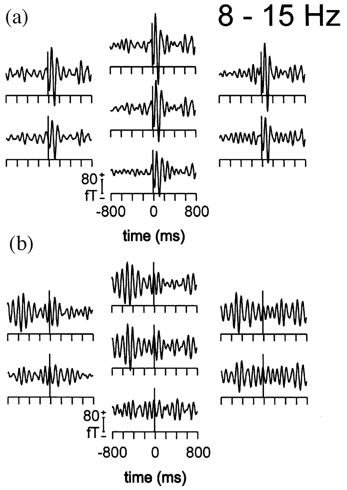

Fig. 10. Human MEG responses to auditory stimulation: averaged evoked fields recorded in a typical subject (filter limits: 8–15 Hz). (a) Seven channels with 'pure temporal' location. (b) Seven channels with 'pure occipital' location (modified from Schürmann, M. Başar-Eroğlu, C., Başar, E., 1996. In: Başar, E., Hari, R., Lopes da Silva, F.H., Schürmann, M. (Eds), Brain Alpha Activity — New Aspects and Functional Correlates. Int. J. Psychophysiol., Special Issue 26: 149–170).

1.4.3. Alpha responses in human EEG and MEG in cross-modality experiments

It is useful to compare the cat data to EEG and MEG recordings in humans. EEG measurements were performed in 11 subjects (Başar and Schürmann, 1994). Fig. 9 shows filtered curves computed from grand averages of occipital recordings (O1). The upper half of the figure shows theta responses whereas the lower half shows alpha responses. The alpha response to auditory stimulation (inadequate for the visual cortex, occipitally located) is on the left, where the response is of low amplitude. The response to visual stimulation, however, is on the right, with a distinct alpha response. Note that the adequate–inadequate difference is less for the theta response. The hypothesis as given previously is thus supported: As observed in cats it is mainly the alpha response which is dependent on whether or not a stimulus is adequate. A correlation between the alpha response and primary sensory processing is thus plausible both for human and for cat EEG–EP data.

MEG measurements were performed both with a BTI 7 channel MEG system (Saermark et al., 1992) and with a PHILIPS 19-channel MEG system (Başar et al., 1992; Schürmann et al., 1992a,b). The methods used were similar to those used for EEG recordings where possible. We used auditory stimuli (2000 Hz; 80 dB sound pressure level) and selected sensor positions close to the auditory cortex and close to the visual cortex.

The data shown in Fig. 10 were obtained with the 7-channel system where the different positions required two experimental sessions. Panel A shows temporal recordings, Panel B occipital recordings, in both cases with auditory stimuli. The underlying cortical areas being the primary auditory cortex and the primary visual cortex, auditory stimuli are regarded as adequate in the first case (Fig. 10, panel A) and as inadequate in

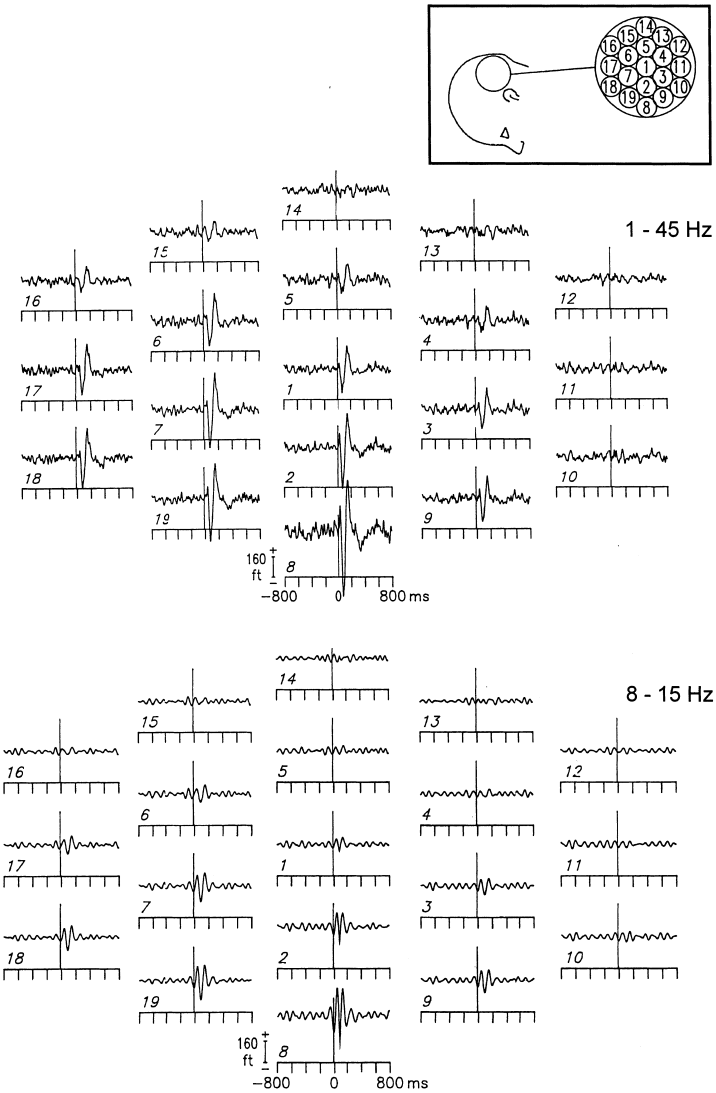

Fig. 11. Human MEG responses to auditory stimulation in a typical subject. *Upper panel:* Wide-band filter (1–45 Hz). *Lower panel:* filter 8–15 Hz. *Inset:* Localization of 19-channel PHILIPS SQUID sensor array and position of single SQUIDS within the array (modified from Schürmann, M. Başar-Eroğlu, C., Başar, E., 1996. In: Başar, E., Hari, R., Lopes da Silva, F.H., Schürmann, M. (Eds), Brain Alpha Activity — New Aspects and Functional Correlates. Int. J. Psychophysiol., Special Issue 26: 149–170).

the second case (Fig. 9, panel B). High amplitude alpha responses are visible in panel A with adequate stimulation. In contrast, panel B with inadequate stimulation does not show such alpha responses.

Fig. 11 shows recordings obtained with the 19-channel system. As visible in the sketch of the measurement position (see inset), the sensor array covers both temporal and occipital areas of the skull. The upper panel shows wide-band filtered curves whereas the lower panel shows alpha-filtered curves (8–15 Hz). With auditory stimuli, clear alpha responses can be observed 'close to the auditory cortex' (sensor above temporal area, e.g. channel 8), whereas no such responses are present 'close to the visual cortex' (sensors above occipital area, e.g. channels 12–14). The wide-band filtered curves are in agreement with the 8–15-Hz filtered curves; in some cases the degree of similarity is very high. Note that the wide-band filtered curves show some kind of response close to the visual cortex with inadequate stimulation. These responses, however, do not correspond to alpha responses. Another example of single MEG epochs with auditory stimulation is given in Fig. 12. The single trials are filtered in the 8–15-Hz range. Both time- and phase-locking can be observed. The filtered averaged MEG response closely resembles the unfiltered averaged MEG response. Fig. 13 is a close-up of the data shown in Fig. 11; the congruence between the filtered MEG response (lower panel) and the unfiltered MEG response (upper panel) is easily visible.

1.4.4. Summary: oscillatory responses in cross-modality experiments

As outlined above, we observed marked differences — in intracranial recordings in cats and in human occipital EPs — between responses to adequate and inadequate stimuli. In the context of the present chapter, it is important to note that these 'adequate/inadequate' differences were marked for alpha responses and less marked for theta responses, thus hinting at a functional significance of the frequency components.

With respect to responses to 'inadequate' stimuli it is remarkable that 'in cats approximately one-third of the neurons in area 17 (striate cortex), 18, and 19 are reported to be responsive to sound as well as to visual input' (Hartline, 1987). Furthermore, 'a large number of neurophysiological studies showed that primary sensory stimuli elicit impulses or volleys converging over thalamic centers to primary sensory areas. On the other hand, the 'sensory stimulation of second order' usually reaches the cortex over association areas (see for example Shepherd, 1988). Due to this consideration it is conceivable that the responses in the lower frequency ranges (theta, delta) might reflect the responsiveness of various brain areas in cases of association processes involved in global associative cognitive performance' (Başar et al., 1991).

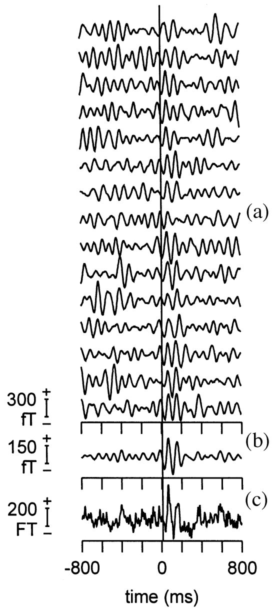

Fig. 12. MEG responses to auditory stimulation. (a) Single trials, filtered 8–15 Hz; (b) averaged response filtered 8–15 Hz; (c) wide-band filtered averaged response (modified from Schürmann, M. Başar-Eroğlu, C., Başar, E., 1996. In: Başar, E., Hari, R., Lopes da Silva, F.H., Schürmann, M. (Eds), Brain Alpha Activity — New Aspects and Functional Correlates. Int. J. Psychophysiol., Special Issue 26: 149–170).

Note that the human occipital EP contains a 'residual response' to auditory stimulation which, however, does not contain any significant 10-Hz component. The response is dominated by a theta response component (which is visible even with-

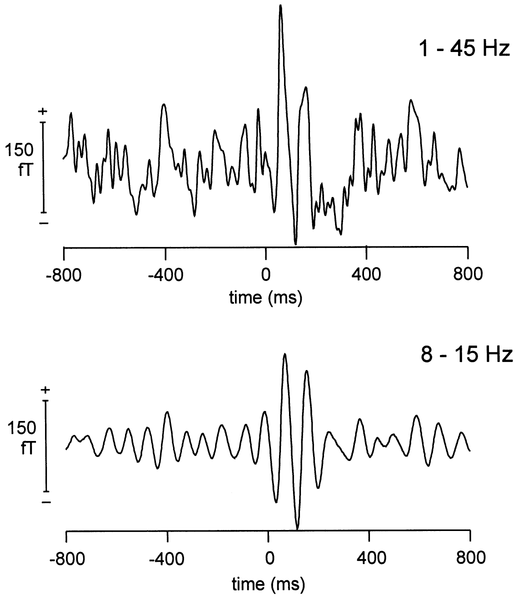

Fig. 13. Averaged MEG responses shown in Fig. 11. *Upper panel:* wide-band filter (1–45 Hz). *Lower panel:* filter 8–15 Hz (modified from Schürmann, M. Başar-Eroğlu, C., Başar, E., 1996. In: Başar, E., Hari, R., Lopes da Silva, F.H., Schürmann, M. (Eds), Brain Alpha Activity — New Aspects and Functional Correlates. Int. J. Psychophysiol., Special Issue 26: 149–170).

out Fourier analysis). On the basis of cognitive ERP measurements, Başar-Eroglu et al. (1992) assumed that the brain's delta and theta responsiveness is functionally related to cognitive processes such as selective attention, learning, and decision making. The cross-modality responses of this study support this hypothesis: we assume that the occipital response to auditory stimuli is a cross-modality response which is probably not elicited directly by visual stimulation. Instead it may be evoked or induced through cognitive mechanisms acting mostly in association areas of the brain including the forebrain, parietal areas, and the limbic system. This last aspect provides further justification of regarding the theta response as a predominantly cognitive component.

This interpretation is also supported by results obtained with a different paradigm: it is mainly slow frequencies that contribute to differences between EPs obtained in an omitted stimulus paradigm and EPs recorded in a session without cognitive load: In a time prediction task, selective averaging of responses to the last stimulus before omission showed increased delta–theta amplitudes (Demiralp and Başar, 1992).

To differentiate the responses of different neural populations in the hippocampus, two gross electrodes were chronically implanted in the hippocampus (with a tip diameter of approx. 100 μm). One was very close to the pyramidal cells, the other was in a rather distant position (Fig. 14). The electrode positions were verified histologically after the experiments; only those six cats with appropriate positions were included in the analysis. The EPs recorded from both electrodes (pyramidal and distant) revealed the component at approximately 40 Hz.

Fig. 15 shows mean value curves of the amplitude frequency characteristics obtained from measurements of six cats, both for the pyramidal and distant electrodes. In the amplitude characteristics obtained from the pyramidal electrode, the 40-Hz selectivity was the dominant selectivity, whereas in the characteristic of the distant electrode, the 40-Hz selectivity was less prominent. The pyramidal electrode detected marked 4 Hz (theta) selectivity whereas the 4 Hz selectivity of

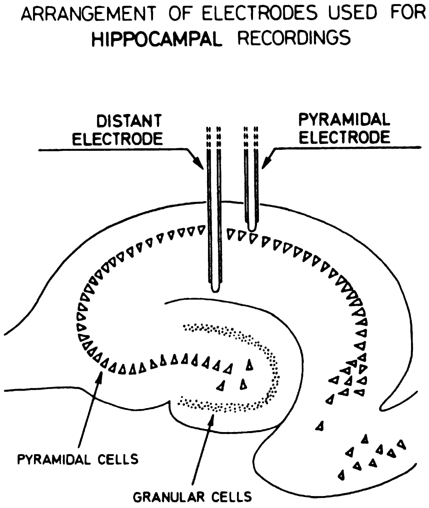

Fig. 14. A schematical cross-section of the dorsal hippocampus and the arrangement of electrodes used (modified from Başar, E., 1980. EEG Brain Dynamics. Elsevier, Amsterdam).

the distant electrode was mostly attenuated. In other words, the amplitude characteristics revealed important differences in the response activity recorded from both electrodes (i.e. both neural areas). This difference can be shown in a more marked manner by comparing the absolute magnitude of 4 Hz and 40 Hz components in the time domain.

Fig. 16 shows two selectively averaged EPs obtained from both hippocampal electrodes. The same figure illustrates further, the pass-band filtered components of 4 Hz and 40 Hz (for the filtering procedure see chapter 4). The components detected from the pyramidal electrode are approximately five times larger than the same components detected from the distant electrode. This experiment added the following information to the justification with physiological measures. In the companion volume it will be shown that the hippocampus of the cat brain is able to generate alpha responses upon sensory stimuli and that the 10-Hz response oscillations are more stable than cortical and thalamic 10-Hz responses. In the following the hippocampal 10-Hz responses serve as examples of single EP-trials behaving like a short damped 10-Hz oscillation (visible without filtering).

The amplitude frequency characteristics recorded from hippocampal EPs have several maxima, in this example the most dominant response is in the 10-Hz frequency range. The filtered response has also a very high response amplitude.

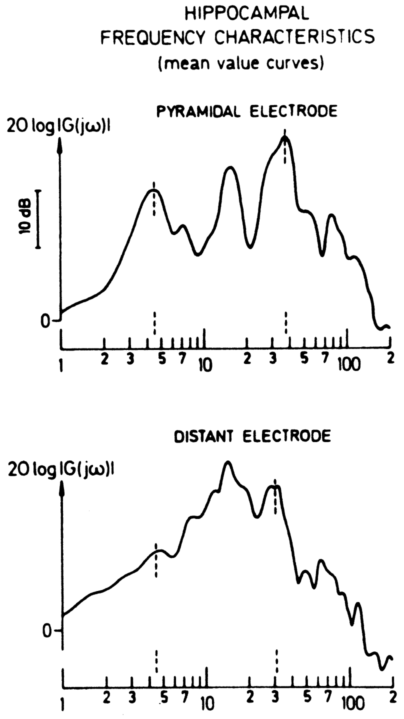

Fig. 15. Mean value amplitude characteristics which are computed from the hippocampal responses recorded by using the electrode locations specified in Fig. 14. Each curve is obtained from experiments on six cats (modified from Başar, E., 1980. EEG Brain Dynamics. Elsevier, Amsterdam).

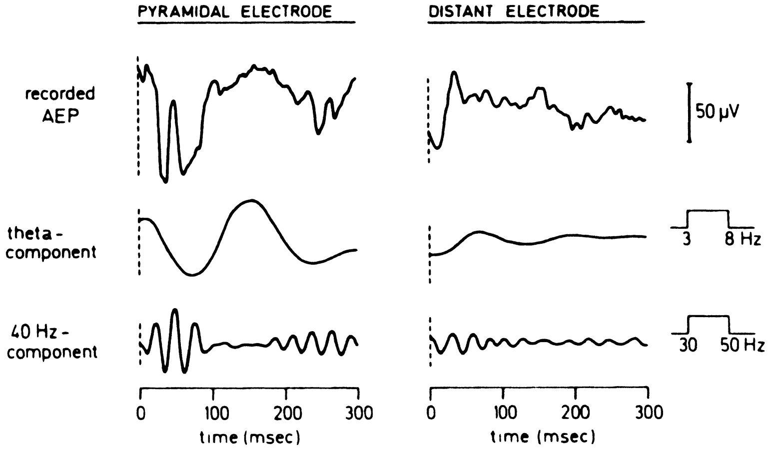

Fig. 16. Selectively averaged EPs (upper curves) which are recorded from the same cat by using the electrode locations specified in Fig. 14. The lower curves for each electrode location are the theta and 40-Hz components of the respective averaged EPs (modified from Başar, E., 1980. EEG Brain Dynamics. Elsevier, Amsterdam).

The single trials shown were selected according to their enhancement factors (Başar, 1980) as applied previously for delta response in single P300 trials (Schürmann et al., 1995): Single sweeps with high enhancement factors for the 10-Hz frequency range and low enhancements for the theta frequency range were selected. In Figs. 18 and 13 in Başar (1998) such wideband filtered single trials having the pattern of almost pure 10-Hz responses together with the average signals are shown. This is again a very convincing example showing (a) that the evoked potential is a manifestation of a superimposition of several frequency responses; and (b) that — in ensembles of single evoked potentials — it is possible to record pure 10-Hz responses. The reader should compare the superimposition results concerning the superimposition principle in chapter 15 in Başar (1998).

1.4.4.1. Summary concerning hippocampal EPs. With the help of gross electrodes, it is possible to detect response activity which can be measured with the unit recording techniques. The gross electrode picks up with different weights all the response activities existing in the neural populations in the vicinity. (Hippocampal electrodes picked up 4-, 10- and 40-Hz response activities which were also recorded with microelectrode techniques.)

By adequate choice of location of the gross electrodes and by considering the experiments with single recording techniques, one has the possibility to evaluate the responses of defined neural populations.

The implications of the hippocampal measurements for the question of volume conduction will be relevant for the comparison of amplitude frequency characteristics recorded simultaneously from various structures of the brain (see companion volume). These frequency characteristics often revealed common response components (mostly in alpha and beta frequency ranges). The fact that the electrodes with the distance of several hundred micrometers record the source activity in a highly attenuated degree indicates that the common responses of various distant nuclei cannot be the result of volume conduction.

1.5. Justification in terms of a pathological condition: break of the alpha response in multiple sclerosis

Further results supporting the hypothesis of a special role of the alpha response in primary sensory processing have been obtained in a study in multiple sclerosis (MS) patients (see Başar-Eroglu et al., 1993; Schürmann et al., 1993). In these patients, it was assumed that primary sensory input to the visual cortex is frequently impaired due to optic neuritis. According to the above-mentioned hypothesis, it was assumed that the alpha response might be reduced in subjects with MS. The alpha response in the occipital location is related to sensory perception induced with light if the sensory nerve (in this case the optic nerve) is injured. Accordingly, in these patients the alpha response should not be registered upon visual stimulation.

In fact, the attenuation or absence of alpha responses in the occipital cortex of MS patients clearly supports the above-mentioned considerations about the functional relevance of alpha responses (Başar-Eroglu et al., 1993; Schürmann et al., 1993). Here we have again an important explanation to correlate the frequency components with function and pathological influence on change of the function. When the patient is blindfolded, no 10-Hz response is observed in the evoked potentials elicited with light signals.

A single sweep analysis presented in Fig. 17 clearly demonstrates that single EEG–EP epochs contain no alpha responses upon light stimulation. A filtering artifact phenomenon or a Fourier artifact would still produce 10-Hz enhancements. Alpha response is a physiological real response abolished in injury of the optic nerve.

1.6. Psychophysiological justification

1.6.1. 'Pure' theta responses

Demiralp and Başar (1992) have measured significant theta responses following expected visual and auditory targets. These experiments are very pertinent to the understanding of the function of the diffusely distributed theta system of the brain. EPs as well as ERPs were recorded from 10 healthy subjects in auditory and visual modalities

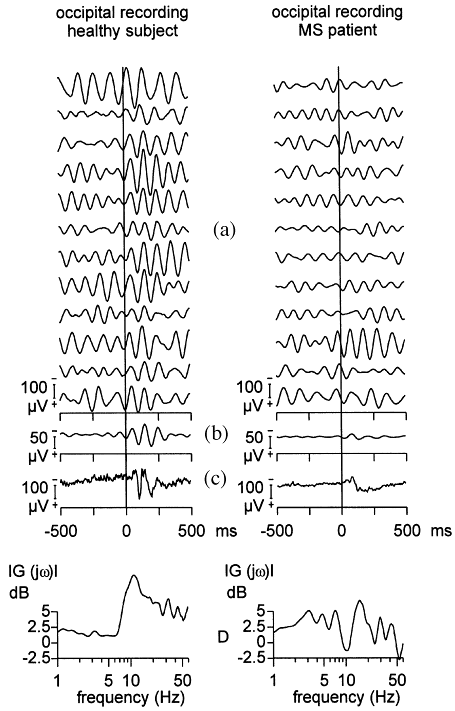

Fig. 17. (a) single EEG-sweep, filtered 7–12 Hz; (b) filtered averaged EP (7–12 Hz); (c) unfiltered averaged EP; (d) amplitude frequency characteristics computed from averaged EP. Left column: one subject of the control group. Right column: one subject of the MS group (modified from Başar-Eroğlu, C. Warecka, K., Schürmann, M. Başar, E., 1993. Int. J. Neurosci. 73: 235–258).

(only visual EPs will be shown in this report). For ERP recordings 'the omitted stimulus paradigm' was employed, in which the subjects were expected to mark mentally the onset time (time prediction task) of the omitted stimulus (target).

The light stimulator was a 20-W fluorescent bulb which was electrically triggered with steps of 800-ms duration. A regular recording session in three parts, with short resting periods in between, was carried out on the same day. In standard EP recordings, the interstimulus interval varied randomly between 2.5 and 4 s with a mean value of 3 s whereas in omitted stimulus paradigm, the stimuli were delivered with 3-s regular intervals. In the omitted stimulus paradigm, every 4th stimulus was omitted and the subject's task was to predict and to mark mentally the time of occurrence of omitted signals. Subjects had not been informed of the task beforehand to avoid their unwanted cooperative efforts during the preceding (EEG, EP) of the experiments (for details see Demiralp and Başar, 1992; Başar-Eroglu and Demiralp, this volume).

Although no strategy for fulfilling the time prediction task was imposed, at the end of the experiments all subjects reported that their '*expectancy*' was maximal at the time of the third stimulus (the predecessor of the omitted stimulus) in the omitted stimulus paradigm. They said that they could attain the rhythm of the stimulations just after the second stimulus by comparing the onset times of the first and second stimulus, and that they attended to the third stimulus to test their feeling for the rhythm. The first stimulus after the omission served also as a control of their performance in the prediction of the virtual onset of the omitted stimulus. Considering the subjects' reports we focused our attention on the comparison of the responses to third attended stimuli with the standard EPs. For limitation of space only data obtained from F3, P3 and O1 are shown.

The bottom row of Fig. 18 shows the unfiltered averaged responses, superimposed, of 10 subjects recorded from F3, P3 and O1 leads upon application of the standard visual EP paradigm (VEP). The upper row of Fig. 18 illustrates the responses of the same subjects to the third attended visual stimuli (3.ATT) in the visual omitted stimulus paradigm. In this paradigm, theta responses are visible even without filtering. Especially the frontal EP response looks like an 'almost pure theta oscillation' visible without filtering.

The averaged responses were filtered in various frequency bands by means of digital filters with zero phase-shift (band limits selected according to maxima in amplitude frequency characteristics). Fig. 19 shows the visual EPs (VEP, bottom) and the responses to the third attended light stimuli (3.ATT, top) in the omitted stimulus paradigm (superimposed) and the grand averages obtained in both conditions filtered in the theta frequency band (3–6 Hz). Note that the similarity between wide-band filtered curves (Fig. 18) and theta-filtered curves (Fig. 19) is highest for frontal recordings ('pure theta' responses). Further de-

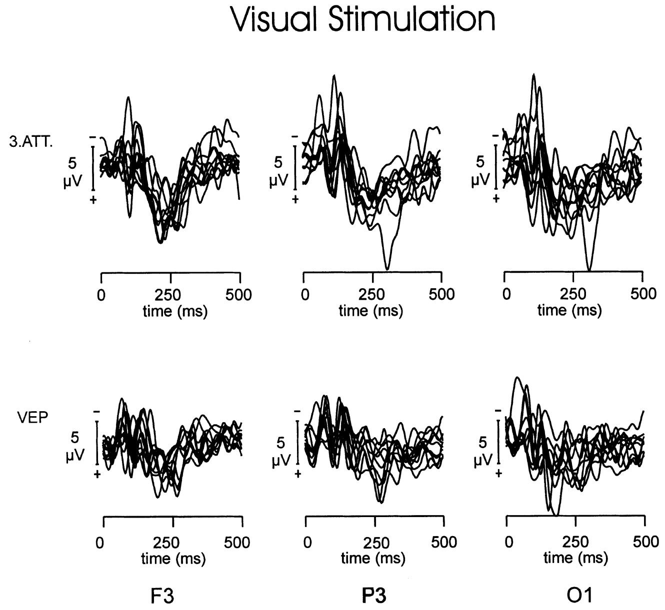

Fig. 18. Superimposed standard visual EPs (VEP) and responses to 3rd attended light stimuli in the visual omitted stimulus paradigm (3.ATT) of 10 subjects obtained from frontal (F3), parietal (P3) and occipital (O1) regions. Wide-band filtered recordings (modified from Demiralp, T., Başar, E., 1992. Int. J. Psychophysiol. 13: 147–160).

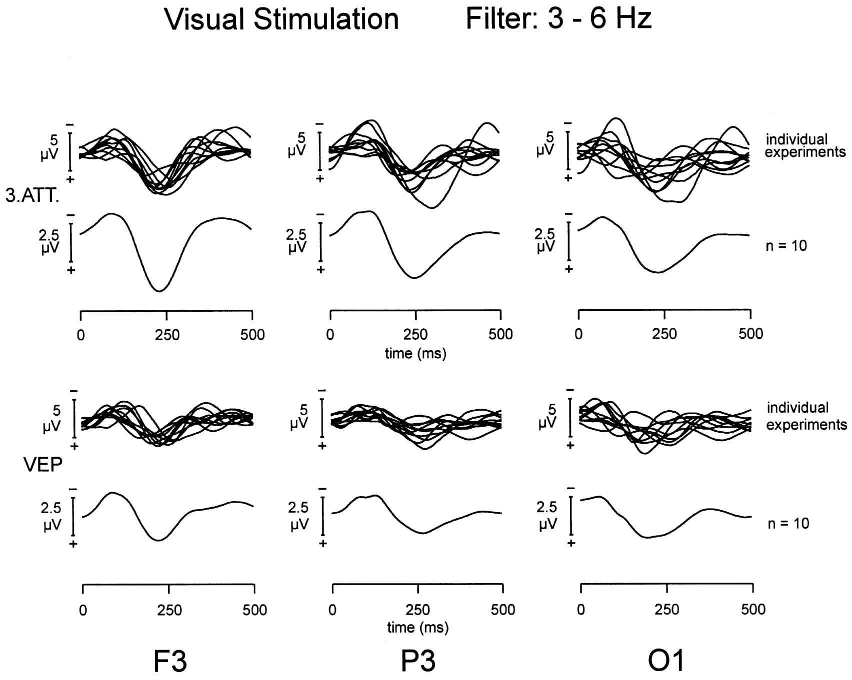

Fig. 19. Superimposed standard visual EPs (VEP) and responses to 3rd attended light stimuli in the visual omitted stimulus paradigm (3.ATT) of 10 subjects and their grand averages filtered in theta frequency band (3–6 Hz) (modified from Demiralp, T., Başar, E., 1992. Int. J. Psychophysiol. 13: 147–160).

tails of the results will be presented in the companion volume.

The highest, statistically significant, theta increases during cognitive performance were obtained in frontal and parietal recording sites. In the visual modality the theta response increase in the frontal recording site was slightly higher than that in the parietal recording site (48% vs. 45%). Since the cognitive task in this study was also mainly based on anticipation of an expected stimulus, it is not surprising that the greatest changes are in frontal regions.

1.6.2. *'Pure delta' response — examples from experiments with 'cognitive' paradigms*

The P300 human response to a special type of auditory stimuli shows that delta responses can be considered as 'real brain responses' with precise functional correlates. This was demonstrated in a study using an auditory oddball paradigm (Başar-Eroglu et al., 1992). Standard auditory EPs (delta response amplitude set to 100%) were compared with responses to oddball stimuli where the normalized delta amplitude was approximately 600% (see Başar-Eroglu et al., this volume). This remarkable increase is an example of a major change in the frequency contents of an EP as mentioned in the beginning of this chapter. Taking into account the psychophysiological foundation of the P300 paradigm, this hints at cognitive processing as a functional correlate of the delta response. The same conclusion was drawn from a study employing a visual oddball paradigm with standard vs. target checkerboard stimuli (Schürmann et al., 1995, this volume).

A different approach for the investigation of delta responses was chosen by Parnefjord and Başar (1995) and Parnefjord (1996): auditory EPs were recorded in several sessions with decreasing stimulus intensities. While responses to 80-dB stimuli contained marked alpha and theta components, stimuli close to the subjective auditory threshold elicited nearly 'pure' delta responses. These delta responses were interpreted as correlates of decision making ('tone heard' or 'tone not heard'; see also Başar, 1999).

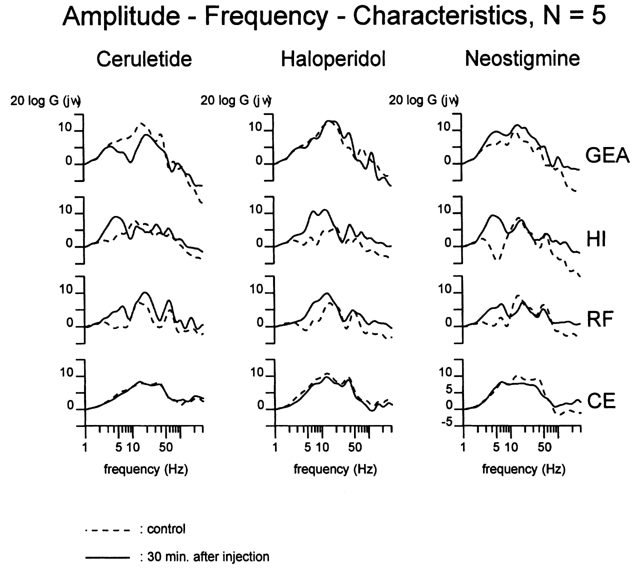

Fig. 20. Amplitude frequency characteristics computed from averaged auditory EPs recorded from auditory cortex (GEA), reticular formation (RF), hippocampus (HI) and cerebellum (CE) of five cats. Interrupted lines refer to averaged control auditory EPs, solid lines to auditory EPs after applications of either ceruletide (left column), or haloperidol (middle column) and neostigmine (right column).

1.7. Application of pharmacological agents

Application of pharmacological agents induces important changes in evoked potentials. This was demonstrated in several studies, some of them performed in cats with chronically implanted electrodes (Başar-Eroglu et al., 1996).

Ceruletide is chemically related to the C-terminal octapeptide of cholecystokinin (CCK-8), which is supposed to be a modulator rather than a transmitter of neuronal activity (review: Zetler, 1985). In addition to ceruletide, the following reference drugs were used: a neuroleptic (haloperidol) and an indirect cholinergic (neostigmine). The experiments were performed on nine freely moving female cats with electrodes in the auditory cortex (gyrus ectosylvianus anterior; GEA), dorsal hippocampus (HI), mesencephalic reticular formation (RF), and cerebellum (acoustical vermis: CE). Ceruletide induces an important change in the amplitude frequency characteristics, especially in the hippocampus of the cat, and in the slow frequency range of approximately 4 Hz (Fig. 20). The entire evoked potential recorded in the hippocampus turns out to be a 'theta oscillation' also visible without application of filters.

By application of acetylcholin the hippocampal EPs show major increases again in the theta frequency range, whereas other frequency components were not influenced so relevantly (see wide-band filtered curves in Fig. 21 and amplitude frequency characteristics in Fig. 21).

1.8. Defined brain states show oscillatory behavior without filtering

A general statement must be emphasized here: in some particular states of the brain the evoked potentials turn out to be oscillatory responses with a homogenous frequency. Also, in experiments described in chapter 15 in Başar (1998), we have used a strategy in which two groups of auditory evoked potentials are recorded during the same experimental session. A large amount of examples stating single evoked potentials with almost homogeneous theta oscillations or almost homogeneous alpha response oscillations can be found. If we use these groups or subsets also as a single EP as average evoked potentials without filtering we can register oscillatory response waves with a unique frequency. In other words, although the filtered potentials give a global idea of the frequency contents of the response, they are re-

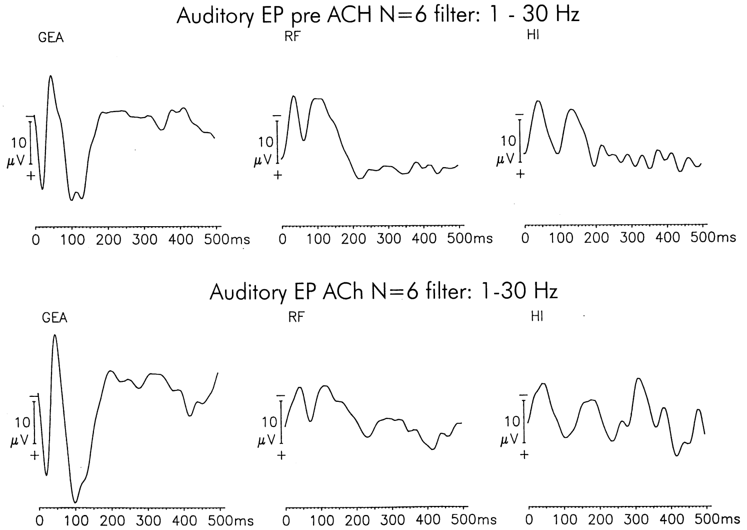

Fig. 21. Grand mean averaged auditory EPs recorded from auditory cortex (GEA), reticular formation (RF), and hippocampus (HI) of six cats, pre- and post-acetylcholine (ACh). Stimulus onset at 0 ms.

flected here as a real process because of the fact that the compound potentials contain superimposed activities originating from several neural populations. Consequently, we can only be sure about the function correlates if changes in the frequency components are huge.

The examples stated in this report do not cover all the findings presented in this special issue or in experiments described by other authors or in Başar (1998, 1999). It is impossible to encounter here all types of experiments and all results supporting the idea that the frequency components are real ones, correlated with diverse types of brain function and/or sensory modalities. These examples are stated here in order to respond to a frequent question: 'Are theta or alpha components or 40-Hz components somewhat not harmonics of a large response?' For example, if an impulse response is analyzed with Fourier techniques, then we would find several components due to the nature of the applied mathematical methodology. Results shown in this book reject the possibility of encountering such harmonic components, if we take into account the precautions stated above. Minor peakings in response can certainly be due to harmonic components, but an increase in the range of 200% or 600% (see Başar-Eroglu et al., this volume) in the delta frequency range without any change in the alpha range, as observed in an oddball paradigm, can never be explained with such harmonic changes (see Başar, 1999).

Changes in the harmonic components do occur in a parallel manner if the largest component increases or disappears then the harmonics increase or disappear in a parallel manner. We insist, however, that changes in the frequency response amplitudes must be relevant components and major peakings and not presented with small deviations. Every research scientist has to find strategies in order to correlate the frequency components with psychophysiological correlates. This is not just the application of a mathematical method, but an ensemble of strategies with biological knowledge, behavior knowledge, and computer application. The EEG-Integrative Neurophysiology searches global sensory and cognitive components, accordingly we have to use the expression 'cloudy information'.

Appendix A: Methods

A.1. Method of transient response analysis

The method of transient response analysis is a common method from the *general systems theory*. This method studies the system's response in the time domain by application of either step or impulse functions at the input of the system. The method of transient responses has the advantage that the observer immediately obtains the responses of the system under study when sudden changes (jumps or steps) in the input function occur.

A practical method of obtaining the evoked potential (*brain system transient response*) is averaging, where the mean value being a function of time is taken from EEG records that follow a number of identical stimulus presentations. In such processing, the averaged values of time-unlocked activities and noise (brain response unrelated activities) tend toward zero, whereas the average of the evoked potential (e.g. the event-locked and repeatable signal) tends to remain constant. This approach has been most commonly used and has led to accumulation of enormous amount of results (for mathematical description and extended survey see, e.g. Başar, 1980; Regan, 1989).

The greatest disadvantage of the method stems from the fact that the information about the distinct components of the system is obscure in the transient response. When two, three or more components exist in the system response, the observer cannot distinguish these different components without further mathematical analysis. Usually, physiologists prefer the method of transient response analysis, but peak identification of distinct components (subsystems) in the time domain is often erroneous. Simple-looking system transient responses sometimes have a large number of components and vice versa, a large number of peaks in the transient response do not necessarily reveal the existence of a large number of system components. For verification of these remarks the reader should refer to the examples presented in Başar (1998, 1999).

Another important disadvantage is that by applying averaging, certain information about the dynamic properties of the brain is lost. The methods that follow in our brain dynamics research program (BDRP) are introduced in an attempt to overcome these shortcomings.

A.2. Frequency characteristics and TRFC-method

Before describing the method used we would like to explain the theoretical basis of the analyses. When the transfer properties of a system are studied, the investigator is often confronted with the resonance phenomenon. Resonance is the response that may be expected of underdamped systems when a periodic signal of a characteristic frequency is applied to the system. The response is characterized by a 'surprisingly' large output amplitude for relatively small input amplitudes, i.e. the gain is large.

Resonance phenomena or forced oscillations can be analyzed in the direct empirical way as follows: a sinusoidal signal of a frequency f is applied to the system. After a certain period sufficient for the damping of the transient, only forced oscillations will remain, having the frequency of the input signal. Then the amplitude of the applied signal (input), the amplitude of the forced oscillations (output) and the phase difference between input and output will be measured. By gradually increasing the frequency from $f = 0$ to $f = f_0$, the output amplitude relative to the input amplitude and the phase differences will be measured as a function of frequency called amplitude and phase characteristics, respectively.

Although this approach reveals the natural frequencies of the system, only a small number of scientists have investigated the EEG response using sinusoidally modulated light or sound signals (for details on pioneering experiments with sinusoidally modulated light, see Van der Tweel, 1961). Difficulties result from the requirement to record evoked responses to sinusoidal signals of over at least three decades of stimulation frequencies, with the evoked responses in each stimulation frequency being averaged for at least 100 single stimulus applications. Another difficulty comes from the frequent changes in brain activity stages: they may change within a few minutes and have a limited duration, which is not sufficient for the application of many sinusoidal stimuli of different frequencies.

There is, however, another way of obtaining the frequency characteristics of a system. This is the transient response frequency characteristics (TRFC) method: according to general systems theory, all information concerning the frequency characteristics of a linear system is contained in the transient response of the system and vice versa. In other words, knowledge of the transient response of the system allows us to predict how this system would react to different stimulation frequencies, if the stimulating (input) signal was sinusoidally modulated. If the step response $c(t)$ of the system — in our case the sensory evoked potential — is known, the frequency characteristics, $G(j\omega)$, of this system can be obtained with a Laplace transform (or one-sided Fourier transform) of the following form:

$$G(j\omega) = \int_0^\infty \frac{\mathrm{d}\{c(t)\}}{\mathrm{d}t} \exp(-j\omega t)\mathrm{d}t$$

or,

$$G(j\omega) = \int_0^\infty \exp(-j\omega t)\mathrm{d}\{c(t)\}$$

$$G(j\omega) = \int_0^\infty \exp(-j\omega t)\lambda(t)\mathrm{d}t$$

where $G(j\omega)$ represents the frequency characteristics of the system; $c(t) =$ step response of the system; $\lambda(t) =$ impulse response; $\omega = 2\pi f$, the angular frequency, and f is the frequency of the input signal.

The frequency characteristic $G(j\omega)$ — including the information of amplitude changes of forced oscillations and the phase angle between output and input — is also called the *frequency* *response function*. It is a special case of the transfer function and is, in practice, identical with the transfer function (Bendat and Piersol, 1968).

For numerical evaluation a Fast Fourier transform (FFT) is used as follows: Let X_n be a discrete time series $(X_n = X(n\Delta t),\ T = ((N-1)\Delta t)$. Then the Fourier transform Y_k of X_n is:

$$Y_k = Y(\omega_k) = \sum_{n-0}^{N-1} X_n \exp(-i2\pi N^{-1}nk);$$
$$\omega_k = 2\pi k T^{-1}$$

where $Y_k = a_k + ib_k$ are the complex Fourier coefficients the geometric mean of which is the amplitude spectrum.

Although this transform is valid only for linear systems, it can be applied to non-linear systems as a first approach because the errors due to system non-linearities are smaller than errors resulting from the length of measurements in sinusoidal stimulation experiments given the rapid transitions of the brain's activity from one stage to another (Başar, 1980).

In the mathematical literature, the TRFC-method is simply called one-sided Fourier transform or the Laplace transform. We use the expression TRFC-method in order to indicate that this method gives all characteristics in the time and frequency domains. In particular, the physiologist is used to observing the experimental parameters in the time domain by obtaining the transient responses of the studied system (see above in this chapter). Using this method, the most frequently used physiological transient responses are obtained. Moreover, it is possible to analyze the frequency content or the components in the frequency domain by computing the amplitude–frequency characteristics from the same transient response. Therefore, we find it more useful and descriptive to call this method the TRFC-method.

The determination of the abstract frequency characteristics or the transfer function of the biological system under study usually causes experimental and sometimes also conceptual difficulties. Knowledge of the abstract frequency characteristics is only a useful tool for the mathematical representations of the biological system. The mathematical representation alone (transfer function or the law of the system) does not tell much about the biological, physical or chemical properties of the system. It merely helps to identify the frequency positions of all the components without determining the exact nature (biological, physical or chemical nature) of these components. Using the measured frequency characteristics (i.e. having knowledge of different system components), the investigator should search for other parameters or methods in order to have a clearer idea of the inside of the black box or gray box (studied system). In other words, he also has to try to elucidate the black box or enlighten the gray box. As stated in the BDRP, the TRFC method should also deal with some supplementary experimental methods and 'methods of thought'.

Finally, a limitation of this approach has to be mentioned: by application of sensory stimuli, the brain is not directly excited with the proper input signal — there are physiological transducers (cochlea, retina, skin, etc.) between the input signal and the measured electrical output. Therefore, a direct comparison of the input and output signal is impossible; instead, the relative output amplitudes — or the magnitude of the maxima in the amplitude characteristics — are to be compared.

In view of practical application, the methodology to evaluate EPs, AFCs and digitally filtered data have been previously described (e.g. Başar, 1980). The essential steps are as follows:

1. *Recording of EEG–EP epochs:* With every stimulus presented a segment of EEG activity preceding and following stimulus application are digitized and recorded. This operation is repeated for each trial.
2. *Selective averaging of EPs*: The stored raw single EEG–EP or EEG–ERP epochs are selected with specified criteria after the recording session: EEG segments showing movement artifacts, sleep spindles or slow waves were eliminated.
3. *Amplitude–frequency characteristics (AFC)* are

computed according to the formula given above.

4. *Adaptive digital filtering* is performed, as will be described in the next section.

A.3. Response adaptive filtering

Response adaptive filtering is the ideal theoretical filtering of the transient response of a system in such a way that a selective blocking of one or more components (or subsystems) is obtained. Ideal filters are defined as transmission elements which, within a given frequency range, transfer the input signal without any change in amplitude and with a fixed (independent of frequency) time shift. Outside this frequency range they have zero transmission (or vice versa, depending on whether the filter has a band-pass or a band-stop characteristic). They are not physically realizable, but they should be considered as useful analytical tools when the contribution made to a signal by a frequency band is to be deduced without any distortion.

Let us assume a system, $G(j\omega)$, which should result from the interconnections of the subsystems,

$$G_1(j\omega),\ G_2(j\omega),\ G_3(j\omega),\ldots,G_K(j\omega),\ldots G_N(j\omega),$$

in such a way that

$$G(j\omega) = G_1G_2G_3\ldots G_K\ldots G_N$$

If we already know the amplitude frequency characteristics of the system $G(j\omega)$ under study, and we further want to know how the transient system response would be affected if one or more of the components of the system were missing, we first of all determine the frequency band limits of the component to be eliminated (or the component which should be removed from the system). The procedure consists of the following steps:

(1) The amplitude characteristics $|G(j\omega)|$, of the system under study are obtained by means of Laplace transform (or one-sided Fourier transform) using the transient evoked response, $c(t)$:

$$|G(j\omega)| = |L(d\{c(t)\}/\mathrm{d}t) = \left|\int_0^{\infty} \exp(-j\omega t)\mathrm{d}\{c(t)\}\right|$$

(2) Frequency band limits of theoretical filters are determined according to the frequency and band-width of amplitude maxima in the amplitude–frequency characteristics, $|G(j\omega)|$.

(3) After determination of the ideal filter characteristics in the frequency domain, $G_{KF}(j\omega)$, the weighting function, $g_{KF}(t)$, of the filter is computed by means of the inverse Fourier transform:

$$g_{FK}(t) = F^{-1}\{G_{KF}(j\omega)\} = \frac{1}{2\pi}\int_{-\infty}^{+\infty}(|G_{KF}(j\omega)|\exp(-j\omega\tau))\exp \times (j\omega t)\mathrm{d}\omega$$

By taking t to be equal to zero, any fixed or frequency-dependent time shift (which would have been inevitable in the case of a real electrical filter) can easily be avoided.

(4) The experimentally obtained transient evoked response, $c(t)$, is theoretically filtered by means of the convolution integral using the weighting function, $g_{KF}(t)$, of an adequately determined ideal filter:

$$c_F(t) = g_{KF}(t) * c(t) = \int g_{KF}(\tau)c(t-\tau)\mathrm{d}\tau$$

where, $c_F(t)$ is the filtered evoked response. Since the time response is available in the form of discrete data with sampling interval of Dt, the integrals in the above equations can be replaced with iterative summation. Evaluation of these integrals is achieved by using the fast Fourier Transform algorithm (FFT).

The method of response adaptive digital filtering has a very important advantage in the study of biological systems: Usually it is very difficult to remove or attenuate subsystems from the biological system under investigation. But, if the frequency characteristics of the system are known, we can do it theoretically by using the theoretical isolation method. This is the theoretical version of the method of selective blocking by application of pharmacological agents or by surgical ablation techniques.

Although some electronic filtering methods have already been used in the study of brain waves and evoked potentials, the theoretical isolation method presented here gives us the possibility to choose amplitude and phase frequency characteristics of the filters separately. Therefore, the investigator can apply ideal filters without phase shift. It is also possible to use filters with exact characteristics and change them adequately according to the amplitude characteristic of the system under study. Therefore, the use of theoretical filters is much simpler and more flexible than the use of electronic filters. Theoretical filters are designed as digital filters. They can be applied because they introduce no phase shift in the signal (Başar and Ungan, 1973; Başar, 1980; Cook III and Miller, 1992; Farwell et al., 1993). However, filter characteristics, especially for narrow filter pass-bands as well as for abrupt amplitude changes typical for averaged EPs, should be chosen such as to avoid the production of filter-related oscillations (Wastell, 1979; De Weerd, 1981; Farwell et al., 1993).

We should mention here that the choice of filters used can be made independently of any frequency characteristics. This choice, however, would be arbitrary. Adaptive filtering, however, aims at a component analysis in the study of a given brain response. Important examples of how powerful this method can be are given in Başar (1998, 1999).

A.3.1. Combined analysis procedure: EEG and EP comparison

The theoretical background for developing the combined analysis procedure is the concept of the EEG as an active signal in the brain: The spontaneous EEG is regarded as a signal that determines or governs the responses of the brain. Within this framework, we need a technique providing for analysis of both the spontaneous (ongoing) and evoked EEG activity. The methodology for comparing the brain's spontaneous activity and EPs can be briefly described as follows:

1. A sample of the spontaneous activity of the studied brain structure just prior to stimulus is recorded.
2. A stimulation signal is applied to the experimental subject (animal or human). Visual, acoustical, somato-sensory, etc., inputs may serve as stimulation, for example, an auditory step function in the form of a tone burst with frequency of 2000 Hz and intensity of 80 dB SPL.
3. Single-sweep evoked response following the stimulation is recorded. As a result, the EEG activity prior and following stimulation are stored together as a combined record.
4. The operations explained in the three steps above are repeated approximately 100 times (the number of trials depends on the nature of the experiment and the behavior of the experimental subject).
5. The stored single-sweeps are averaged using a selective averaging method (Başar, 1980).
6. The selectively averaged EP is transformed to the frequency domain with the Fourier transform in order to obtain the amplitude–frequency characteristics, $|G(j\omega)|$, of the studied brain structure.
7. The frequency band limits of the amplitude maxima in the amplitude–frequency characteristics, $|G(j\omega)|$, are determined, according to which the cut-off frequencies of the digital pass-band filters are justified.
8. The stored EEG-EPogram's are filtered within the properly chosen pass bands, as described in step 7.
9. The maximal amplitudes of the filtered EPs, and the so-called enhancement factor for each EEG-EPogram, are evaluated.

A.3.1.1. Definition of the enhancement factor EHF. In a given experimental record of EEG-EPogram, the enhancement factor EHF is the ratio of the maximal time-locked response amplitude (max) to the rms value of the spontaneous activity just prior to the stimulus, with both signals (spontaneous and evoked activities) being filtered within the same frequency pass bands:

$$\mathrm{EHF} = \frac{\max}{2\sqrt{2}\,\mathrm{rms}}$$

A.3.2. New methods for studying oscillatory brain potentials

As explained above, the transient response of a system can be fully described in either the frequency or the time domain. The frequency domain presentation, however, looses the information about the time characteristics (timing) of the signal and vise versa. Thus, it is of great importance to introduce methods that can achieve a reliable resolution in both domains such as to extract essential information about the dynamics over time of the frequency EEG components. What is also crucial is to go deeper into oscillatory behavior by describing single sweep dynamics. The new methods proposed relate directly to these issues.

A.4. The wavelet analysis

Recently, a new technique called wavelet analysis has been used frequently by engineers, physicist and mathematicians who are interested to perform signal analysis in both time and frequency domain (Grossman and Morlet, 1984; Mallat, 1989; Daubechies, 1990). The wavelet transform is based on multiresolution decomposition of the signal and allows us to investigate oscillations in different frequency bands forming the electrical brain activity.

1. The wavelet transform is free of limitations for the signal analyzed such as stationarity, normal distribution, etc.
2. The wavelet transform allows for the optimal adjustment of the time and frequency resolution simultaneously.
3. By using wavelet coefficients, it is possible to characterize the frequency components of the evoked potentials in single EEG responses. Thus, dynamic changes in single sweeps can be precisely evaluated. Furthermore, the wavelet coefficients can be used to select homogenous groups of single sweeps from a set of recorded responses, and to further form averaged wave forms, each reflecting a different synchronization property functionally related to the brain system. An example is described for the P300 component by Demiralp et al. (in press).
4. The wavelet analysis provides us with the unique possibility to search for internal evoked potentials hidden in the 'spontaneous' EEG.

In this article, we mainly describe the methods and results of Fourier Transform for the analysis of evoked potentials. This theory treats constant and discrete time cases, and in particular, it is interesting for the analysis of non-stationary signals (which is the main rationale for applying this technique to event-related potentials; see also Heinrich et al., 1991; Bartnik et al., 1992; Ademoglu, 1995). In contrast to the Fourier Transform analysis, which uses a 'single' window, the wavelet techniques use short windows at high frequencies and long windows at low ones. The aim of this signal analysis extracts relevant information from a signal by transforming it. Such methods make a priori assumptions on the signal to be analyzed. They may yield sharp results if these assumptions are valid.

Further advantages of the wavelet analysis are the following: the computer is able to search and find repeatable and phase locked signals in *a given frequency window*. Therefore, the investigator has to define a frequency window for the discovery of the activity in this range. In order to get knowledge about the center frequencies of these signals, it is useful to apply firstly the Fourier transform or phase spectra analysis to the EEG or EPs during a given series of experiments. As an example, we mention the analysis of P300 experiments indicating a dominant delta response in subjects following target signals. If we did not have the information related to frequency characteristics we could not apply wavelet analysis in the delta frequency range. Another example is the analysis of the alpha response. By means of the Fourier Transform we have been able to show that the brain response contains large 10-Hz responses to sensory adequate stimuli. Furthermore, wavelet analysis was applied to check the occurrence of responses in the gamma frequency range. Investigating the gamma band response is an important application of wavelet analysis. According to these facts it can be stated that the TRFC method and wavelet analysis are complementary methods to investigate brain oscillatory wave forms. Although the description of the application of these analyses is restricted to a few examples in the present volume and in the companion volume, the concept of this signal analysis enriches the brain dynamics analysis described step-by-step in Başar (1998).

The application of conventional frequency domain analysis techniques to transient signals contains a major drawback: a signal in time-domain has a perfect resolution in time domain without any frequency information and vice versa. When dealing with transient signals such as ERPs, where the spectral properties of the signal might be time-varying, it is necessary to avoid such extremities and try to find a representation in between. One approach is the short-time Fourier transform which divides the time domain into uniformly spaced epochs and applies Fourier transform to these intervals. Its major drawback is the limitation of time-frequency localization coming from Heisenberg's uncertainty principle which succinctly states that $\Delta f\,\Delta t = 1/4\pi$ where Δf is the frequency resolution and Δt is the time resolution. The Wavelet transform may be a better alternative for its choice of logarithmically ordered frequency bands which requires shorter time intervals for higher frequencies and longer time intervals for lower frequencies. It also permits us to decompose the signal onto a space with basis functions which can be chosen as orthogonal and having compact support (well-localized in time). In short, the Wavelet transform with its better time–frequency localization allows for the non-stationary nature of the transient ERPs.

A.4.1. Description of the method

A.4.1.1. Spline basis functions. The recent growth in studies of time-frequency or multiresolution decompositions that perform a signal analysis in both time and frequency (Grossman and Morlet, 1984; Mallat, 1989; Daubechies, 1990) allows us to investigate the time occurrence of different components of VEPs by their characterizations in different frequency bands. The spline wavelets which are semi-orthogonal and have a compact support are used for their near optimal time–frequency localizations (Unser et al., 1992).

The B-Splines of order n are a basis of the subspace of all continuous piecewise polynomial functions of degree n with derivatives up to $n-1$ that are continuous everywhere on the real line (Schumaker, 1981). For equally spaced integral knot points, any function $\phi^n(x)$ of this space can be expressed as (Prenter, 1975)

$$\phi^n(x) = \sum_{i=-\infty}^{\infty} c(i)\beta^n(x-i) \tag{1}$$

where $\beta^n(x)$ denotes the normalized B-Spline function of order n with $n+2$ equally spaced knots. The definition for the $\beta^n(x)$ is

$$\begin{aligned}\beta^n(x) &= \beta^{(n-1)}(x) * \beta^0(x)\\ &= \beta^0(x) * \beta^0(x) * \ldots * \beta^0(x)\\ &\quad n+1 \text{ times}\end{aligned} \tag{2}$$

where '*' is the convolution operation and $b^0(x)$ is the indicator function in the interval [0,1) defined as

$$b^0(x) = \begin{Bmatrix} 1 & \text{for } 0 \le x < 1 \\ 0 & \text{otherwise} \end{Bmatrix} \tag{3}$$

The function $\phi^n(x)$ in Eq. (1) can be uniquely determined by its B-Spline coefficients $\{c(i)\}$. For the B-Spline interpolation, the essential point is to determine the coefficients of this expansion such that $\phi^n(x)$ matches the values of some discrete sequence $\{f(k)\}$ at the knot points: $\phi^n(x) = f(k)$ for $\{k = -\infty \ldots + \infty\}$. This problem is termed Cardinal Spline Interpolation whose fundamental theoretical results have been treated in Schoenberg (1969).

A.4.1.2. Discrete B-Splines. The discrete B-Splines are obtained by sampling the corresponding continuous functions $b^n(k) = \beta^n(k)$ with the following starting conditions:

$$b^0(k) = \begin{Bmatrix} 1 & \text{for } 0 \leq k < 1 \\ 0 & \text{otherwise} \end{Bmatrix} \tag{4}$$

A similar convolution relation as for the continuous case is

$$b(k) = b^0(k) * b^0(k) * \ldots * b^0(k) * b^n(k)$$
$$n+1 \text{ times} \tag{5}$$

The additional convolution in Eq. (7) by $\{b^n(k)\}$ is required to guarantee that discrete B-Spline provides the same values as the continuous basis functions at the node points $\{k = -\infty \ldots + \infty\}$. The interpolating function $\phi^n(x)$ of the form

$$f(k) = \phi^n(k) = \sum_{i=-\infty}^{\infty} c(i) b^n(k-i) \tag{6}$$

which can also be described by a convolution

$$f(k) = b^n(k) * c(k) \tag{7}$$

The B-Spline filter coefficients $\{c(k)\}$ in Eq. (7) can be efficiently computed for the quadratic case (where $n = 2$) by using

$$c^+(k) = f(k) + b_1 c^+(k-1) \qquad (k = 2,\ldots,K) \tag{8a}$$

$$c^-(k) = f(k) + b_1 c^-(k+1) \qquad (k = K-1,\ldots,1) \tag{8b}$$

$$c(k) = b_0(c^+(k) + c^-(k) - f(k)) \tag{8c}$$

where $b_0 = -8\alpha/(1-\alpha^2)$, $b_1 = \alpha = \sqrt{8} - 3$ (Unser et al., 1992).

A.4.2. Spline wavelet transform

The attractiveness of the Gabor representation of a signal comes from its optimal time–frequency localization (Gabor, 1946). However, the use of fixed window size, redundancy and non-orthogonality are the major limitations of the Gabor analysis. The use of B-Spline wavelets were shown to have near optimal time-frequency localization by Unser et al. (1992). Although they are not orthogonal as the Battle/Lemarie polynomial spline wavelets used by Mallat (1989) which are exponentially decaying, they are semi-orthogonal and have a compact support. The quadratic B-Spline function and its associated wavelet are shown in Figs. 22 and 23, respectively. The B-Spline function, in some sense, acts as a low-pass filter and the B-Spline wavelet acts as a band-pass

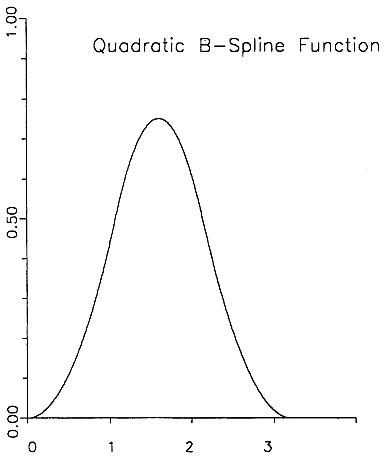

Fig. 22. β^2 (x) the quadratic spline function (modified from Demiralp, T., Ademoglu, A., Schürmann, M., Başar-Eroğlu, C., Başar, E., 1999. Brain Lang. 66: 108–128).

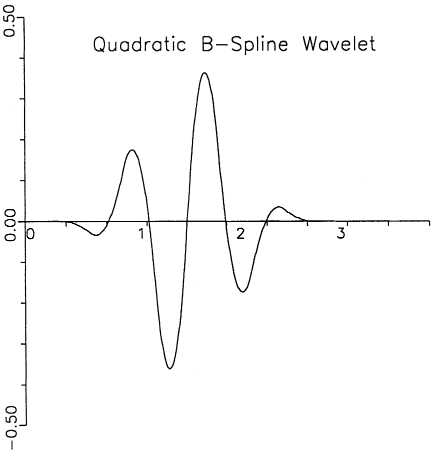

Fig. 23. β_2^2 (x) the quadratic spline wavelet (modified from Demiralp, T., Ademoglu, A., Schürmann, M., Başar-Eroğlu, C., Başar, E., 1999. Brain Lang. 66: 108–128).

Table 2
Coefficients of the truncated decomposition filters h, g (IIR) and reconstruction filters p^2, q^2 (FIR) for quadratic spline filters[a]

k	$h(k)$	$g(k)$	$p^2(k)$	$q^2(k)$
−10	+0.00157	−0.00388		
−9	+0.01909	−0.03416		
−8	−0.00503	+0.00901		
−7	−0.04440	+0.07933		
−6	+0.01165	−0.02096		
−5	+0.10328	−0.18408		
−4	−0.02593	+0.04977		+1/480
−3	−0.24373	+0.42390		−29/480
−2	+0.03398	−0.14034	+1/4	+147/480
−1	+0.65523	−0.90044	+3/4	+303/480
0	+0.65523	+0.90044	+3/4	−303/480
1	+0.03398	+0.14034	+1/4	−147/480
2	−0.24373	−0.42390		+29/480
3	−0.02593	−0.04977		−1/480
4	+0.10328	+0.18408		
5	+0.01165	+0.02096		
6	−0.04440	−0.07933		
7	−0.00503	−0.00901		
8	+0.01909	+0.03416		
9	+0.00157	+0.00388		

[a] Modified from Başar, E., Demiralp T., Schürmann, M., Başar-Eroğlu, C., Ademoglu, A., 1999. Brain Lang. 108–128.

filter. The wavelet basis functions are formed by logarithmically scaled and linearly shifted versions of these functions. The logarithmic scaling yields the logarithmically ordered band-pass filters falling into different octaves. The linear shifting of the wavelet basis functions allows for the time localization of the several frequency components observed in the band-pass filters.

A.4.2.1. Fast algorithm. The initial step for the wavelet decomposition up to a level I is to find the B-Spline coefficients $\{c(k)\}$ at the resolution level 0 [Eqs. (8a), (8b) and (8c)]. The wavelet coefficients $\{d_i(k)\}$ are then computed iteratively for $i = 0$ to $i = I - 1$ by filtering and decimating by a factor of 2

$$c_{(i+1)}(k) = [h * c_{(i)}] \downarrow_2(k) \qquad (9a)$$

$$d_{(i+1)}(k) = [g * c_{(i)}] \downarrow_2(k) \qquad (9b)$$

where $i = 0, 1, 2......, I - 1$, $\downarrow_2$ indicates downsampling by 2 and where h and g are the low-pass and the high-pass filters for decomposition, respectively. The coefficient values for these filters are given in Table 1 for the quadratic spline wavelets. The reconstruction filters $p^2(k)$ and $q^2(k)$ given in Table 2 may be used to interpolate the wavelet coefficients into continuous waveforms by using the Interpolatory Graphics Algo-

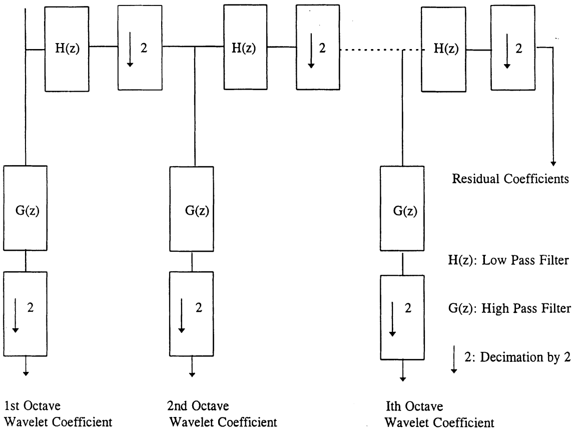

Fig. 24. The basic computational block diagram of I octave wavelet decomposition algorithm (modified from Demiralp, T., Ademoglu, A., Schürmann, M., Başar-Eroğlu, C., Başar, E., 1999. Brain Lang. 108–128).

rithm proposed by Chui (1992). The basic computational block diagram for the one octave wavelet decomposition is given in Fig. 24.

A.5. Results of wavelet analysis of EPs

A.5.1. Typical animal

The analysis of auditory and visual EPs in all three structures (GEA, HI, OC) by means of the wavelet method shows distinct response components in delta, theta, alpha, beta and gamma frequency ranges, which are differently weighted according to the investigated brain structure and the stimulus modality.

Fig. 25 shows auditory and visual evoked potentials for a typical cat. Fig. 26 shows the amplitude frequency characteristics (grand averages) computed from transient responses such as those shown in Fig. 25 [by means of the Fourier Transform (TRFC) method].

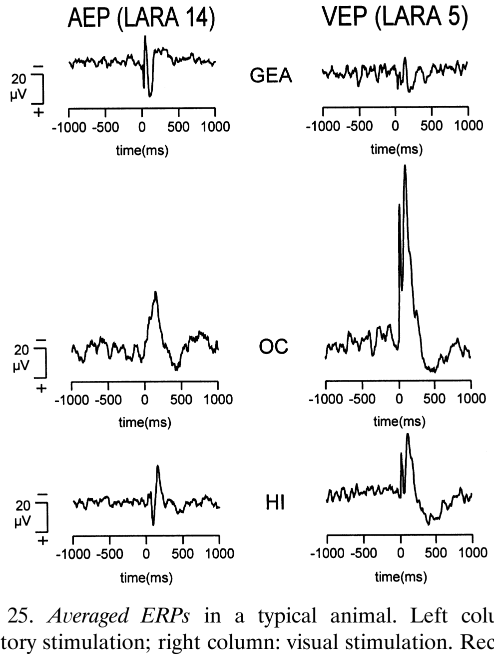

Fig. 25. *Averaged ERPs* in a typical animal. Left column, auditory stimulation; right column: visual stimulation. Recordings from auditory cortex (GEA), visual cortex (OC) and hippocampus (HI). Along the x-axis, time in ms; along the y-axis, amplitude in μV (negativity upwards) (modified from Başar, E., Demiralp T., Schürmann, M., Başar-Eroğlu, C., Ademoglu, A., 1999. Brain Lang. 146–183).

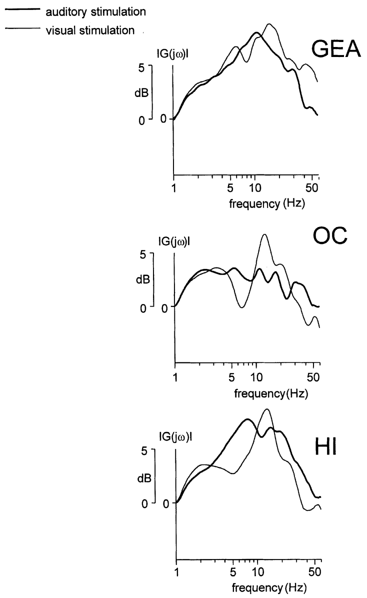

Fig. 26. *Amplitude frequency characteristics,* grand averages ($N = 6$). Solid lines, auditory stimulation; dashed lines, visual stimulation. Data from auditory cortex (GEA), visual cortex (OC) and hippocampus (HI). Along the x-axis, frequency in logarithmic scale. Along the y-axis, relative amplitude in decibels (dB). The amplitudes are normalized in such a way that the amplitude at 1 Hz is equal to 0 (frequency domain averages.) (modified from Başar, E., Demiralp T., Schürmann, M., Başar-Eroğlu, C., Ademoglu, A., 1999. Brain Lang. 146–183).

Fig. 27 shows the results of band-pass filtering of the auditory EP and visual EP recorded from the GEA, HI and OC leads of a representative cat (lara 14/5). In contrast, Fig. 28 shows the results of the five octave wavelet analysis applied to the respective EPs in the same cat (note that the uppermost rows in Figs. 27 and 28 are identical and show wide-band filtered EPs). The basic observations on the averaged EPs in Fig. 28 were in general in accordance with the results shown in Fig. 27 (obtained by using Fourier transform and adaptive digital band-pass filtering). However, especially in higher frequency bands the time-localization capability of the wavelet analysis was significantly better compared with the conventional band-pass filters. The ringing effects occurring by the conventional band-pass filtering techniques, which lead to oscillations before the stimulation time point, were absent or clearly smaller in alpha, beta and gamma frequency ranges. The results support our earlier studies (see chapters 2 and 10 in Başar, 1999). Here we mention only two remarkable items:

1. The dominant frequency components of the visual EPs recorded in the OC area were in delta and alpha ranges with comparable weights, whereas the auditory EPs (recorded in GEA) had a dominant component in the alpha range (Figs. 26 and 27).
2. Alpha response components were most pronounced in the responses of OC and GEA to adequate stimuli and in HI in visual modality, whereas their amplitudes decreased extremely in responses of both GEA and OC to inadequate stimuli.

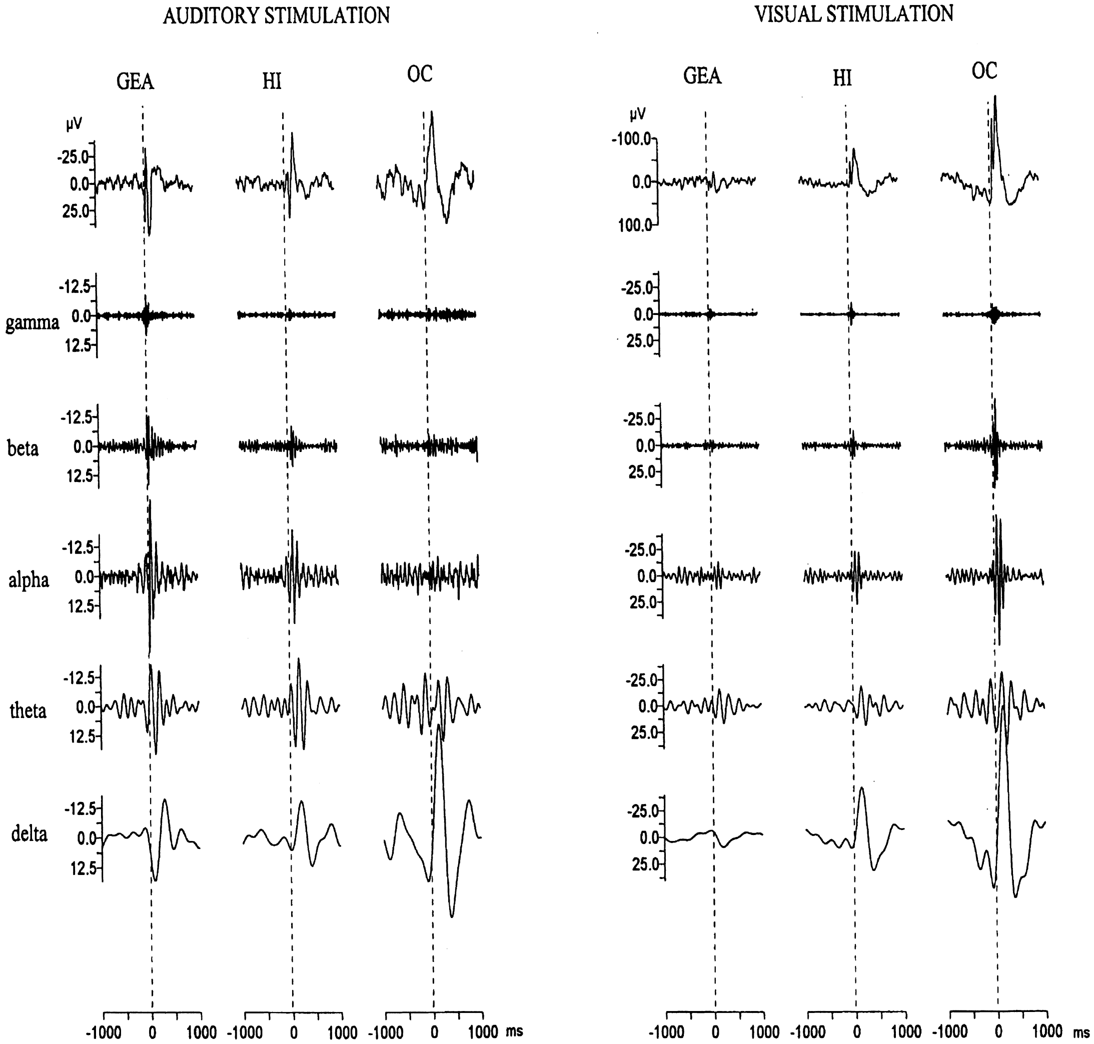

Fig. 27. Results of *band-pass filtering* in a typical animal (same as in Fig. 25). Left, auditory stimulation; right, visual stimulation. Each *column* refers to an electrode site (auditory cortex: GEA; visual cortex: OC; hippocampus: HI). The uppermost *row* shows the wide-band filtered curve. The further *rows* show the frequency components gamma (32–64 Hz), beta (16–32 Hz), alpha (8–16 Hz), theta (4–8 Hz), and delta (0.5–4 Hz) (Modified from Başar, E., Demiralp T., Schürmann, M., Başar-Eroğlu, C., Ademoglu, A., 1999. Brain Lang. 146–183).

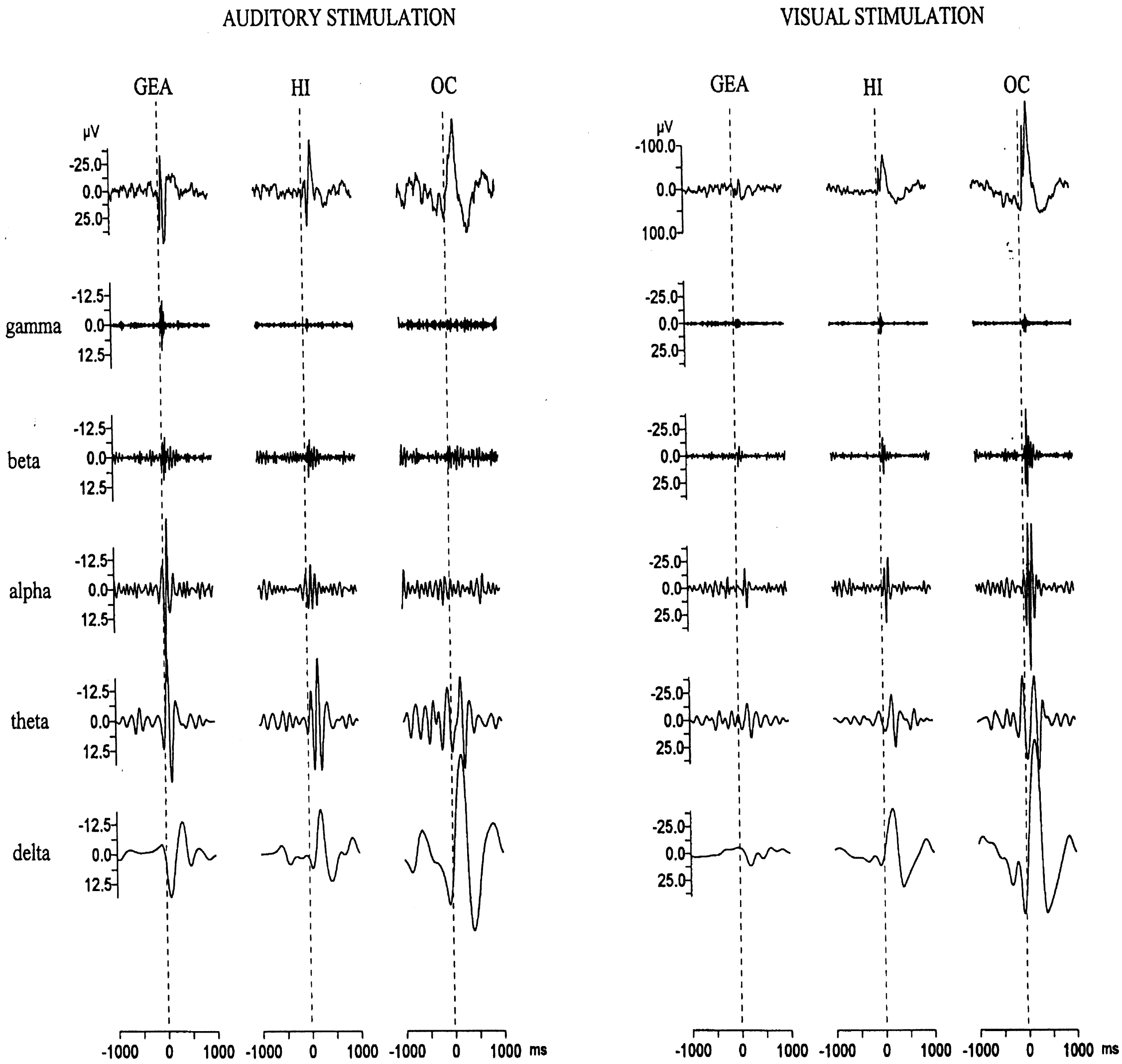

Fig. 28. Results of *wavelet decomposition* in a typical animal (same as in Fig. 25). Left, auditory stimulation; right, visual stimulation. Each *column* refers to an electrode site (auditory cortex: GEA; visual cortex: OC; hippocampus: HI). The uppermost *row* shows the wide-band filtered curve. The further *rows* show the frequency components gamma (32–64 Hz), beta (16–32 Hz), alpha (8–16 Hz), theta (4–8 Hz), and delta (0.5–4 Hz) (modified from Başar, E., Demiralp T., Schürmann, M., Başar-Eroğlu, C., Ademoglu, A., 1999. Brain Lang. 146–183).

A.5.2. Wavelet analysis of single trials

In Fig. 29, a further improvement in the analysis of EPs by using the wavelet transform is shown. In this example, the alpha component of the EP was used to classify different types of single sweeps. Because the wavelet transform represents the time course of different frequency components of the signal by distinct coefficients with a relevant time resolution for that frequency range, it yields a significant data reduction, which allows a simpler analysis of the frequency components of the response. In this example, we classified the sweeps, showing (i) early alpha enhancement; and (ii) prolonged or late alpha enhancement. The averages of these subgroups showed significantly different shapes. Additionally, even by superimposing the broad-band filtered single sweeps of each group, the early and late or 'prolonged alpha phase locking' can be clearly observed. In the early-alpha-response sweeps, a phase locking effect can only be obtained in the first cycle of the post-stimulus alpha activity whereas in the other subgroup phase locking is visible during two alpha cycles.

A.6. Interpretation of wavelet analysis

A further possibility to obtain such responses consists of selective averaging: when inspecting the set of single trials ERPs, examples with almost homogeneous theta oscillations or almost homogeneous alpha response oscillations can be found. If we group these examples into different subsets and compute averages for each of the subsets we obtain oscillatory response waves with a unique frequency (Başar, 1988). In other words, although the only goal of EP filtering is to give a *global idea* of the frequency contents of the response, the EP components obtained by digital filtering are related to *a real process:* this is because the compound potentials contain superimposed activities originating from several neural populations. Consequently, we can only be certain about the functional correlates *if changes in the EP frequency components are large.*

These examples are stated here in order to respond to answer a frequent question: 'are theta or alpha components or 40-Hz components somewhat not harmonic of a strong response?' For example, if an impulse function analyzed with Fourier techniques, i.e. if a filtered analysis was applied to an impulse function, then we would find several components on account of the nature of the applied mathematical methodology. Results shown here reject the possibility of encountering such harmonic components, if we take into account the results given above. Minor peakings in response can be certainly due to harmonic components, but an increase in the range of 600% in the delta frequency range without any change

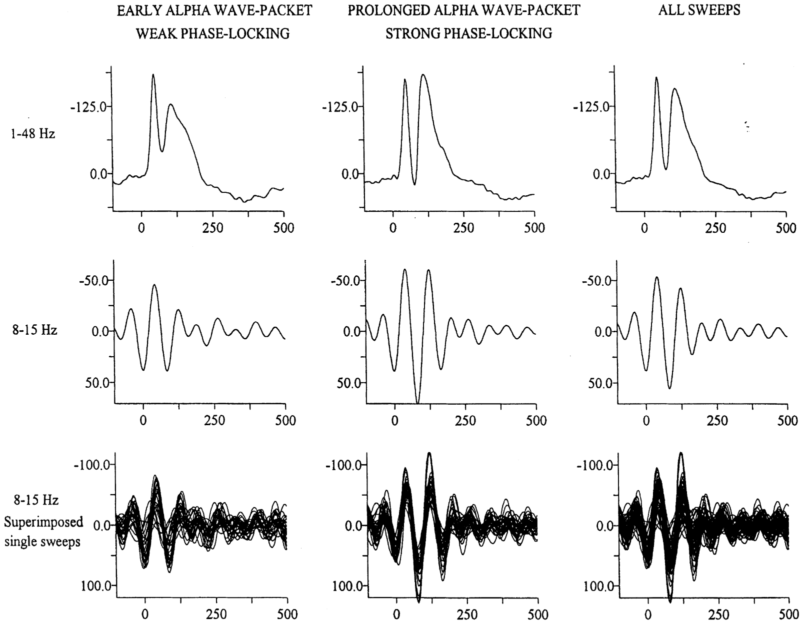

Fig. 29. *Selective averaging* according to results of wavelet decomposition (see text for details). The left *column* refers to single trials with early alpha (8–15 Hz) wave packet, the middle column to single trials with prolonged alpha wave packet, and the right column to all single trials. The *rows* show the wide-band filtered averaged ERP, the averaged ERP filtered in the alpha (8–15 Hz) range, and the single trials filtered in the alpha (8–15 Hz) range (modified from Başar, E., Demiralp T., Schürmann, M., Başar-Eroğlu, C., Ademoglu, A., 1999. Brain Lang. 146–183).

in the alpha frequency domain, as observed in a study of the P300 response (Başar-Eroglu et al., 1992; cf. Demiralp et al., companion report), can never be explained with such harmonic changes.

Changes in the harmonic components do occur in a parallel manner: if the largest component increases or disappears then the harmonics increase or disappear in a parallel manner. We emphasize, however, that changes in the frequency response amplitudes are not harmonic but *relevant components* as long as major peakings — and not small deviations — are evaluated. On the other hand, in our search for global sensory and cognitive components the expression ‘cloudy information’ is appropriate. Every scientist has to find strategies in order to correlate the frequency components with psychophysiological correlates. This is not just the application of a mathematical method, but an ensemble of strategies with biological knowledge, behavior knowledge, and computer application.

A.7. Role of wavelet transform methods in the analysis of functional ERP components

The TRFC method (together with digital filtering) and wavelet analysis are *complementary methods* to investigate brain oscillatory waveforms. The investigator has to define a frequency window for the discovery of the activity in this range. In order to get knowledge about the center frequencies of these signals, the investigator has to apply firstly the Fourier Transform or phase spectra analysis to the EEG or EPs during a given series of experiments:

1. As an example, we mention the analysis of P300 experiments indicating a dominant delta response of subjects following target signals. If we did not have the information related to frequency characteristics we could not apply wavelet analysis in the delta frequency range (see companion volume).
2. Another example is the analysis of the alpha response. By means of the Fourier Transform we have been able to show that the brain response contains large 10-Hz responses to sensory adequate stimuli. Then the wavelet analysis was applied to check the occurrence of 10-Hz responses.

The advantages of using the wavelet analysis in the decomposition of ERPs into frequency components are threefold:

1. Due to the possibility of using functions with compact support, the time-localization of the frequency components can be obtained with a higher precision.
2. As the wavelet analysis does not require the use of a fixed time window, it is especially advantageous when dealing with signals such as ERPs which contain wave packets that differ significantly in duration and frequency content.
3. By using time windows with relevant duration for each frequency range, the wavelet transform yields a significant data reduction or data compression. This feature is extremely helpful in identifying and isolating EP features in single EP sweeps, where the information content is significantly higher and more complex to analyze compared with the averaged response. As we have shown in the example, where we can identify the different response subgroups by using the wavelet coefficients in different frequency bands of the single responses, this property opens an important window to a finer analysis of ERPs and extends the conventional averaging technique in terms of obtaining more homogeneous sub-averages with significantly lower variance.

The results given above demonstrate that wavelet analysis confirms all results obtained by application of the TRFC analysis and adaptive digital filtering: The above-mentioned properties of the alpha response in the cat brain were demonstrated by wavelet analysis as well as by digital filtering.The alpha response in the human brain with wavelet analysis confirms results of single-trial ERP analysis by means of digital filtering. There is a large 10-Hz alpha response to visual stimulation in recording from a position close to the occipital cortex, where an auditory stimulation does not create 10-Hz responses.

A particular advantage of the wavelet analysis is in the field of single trial analysis: the improvement over digital filtering is that *phase locked signals* can be automatically searched for. This applies to both the 10 Hz frequency range (see above) and signals in the delta frequency range (Demiralp et al., in press). The results obtained so far by wavelet analysis underline and extend the view that alpha-, theta-, delta-, and gamma-responses are related to psychophysiological functions. The properties of the wavelet analysis imply that it may be used to evaluate experiments where physiological tasks will be altered without informing the subjects. In summary the wavelet analysis confirms once more the expression 'real signals' which we attribute to EEG frequency responses of the brain.

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