ELECTROENCEPHALOGRAPHY (EEG)

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Electroencephalography is a domain concerning recording and interpretation of the electroencephalogram. Electroencephalogram (EEG) is a record of the electric signal generated by the cooperative action of brain cells, or more precisely, the time course of extracellular field potentials generated by their synchronous action. Electroencephalogram derives from the Greek words enkephalo (brain) and graphein (to write). EEG can be measured by means of electrodes placed on the scalp or directly on the cortex. In the latter case, it is sometimes called electrocorticogram (ECoG). Electric fields measured intracortically were named Local Fields Potentials (LFP). EEG recorded in the absence of an external stimulus is called spontaneous EEG; EEG generated as a response to external or internal stimulus is called an event-related potential (ERP). The amplitude of EEG of a normal subject in the awake state recorded with the scalp electrodes is 10–100 μV. In case of epilepsy, the EEG amplitudes may increase by almost an order of magnitude. In the cortex, amplitudes are in the range 500–1500 μV.

1. EEG RHYTHMS

The following rhythms have been distinguished in EEG (Fig. 1): delta (0.5–4 Hz), theta (4–8 Hz), alpha (8–13 Hz), beta (13–30 Hz), and gamma (above 30 Hz). Gamma components are difficult to record by scalp electrodes and their frequency does not exceed 45 Hz; in ECoG components, up to 100 Hz, or even higher, may be registered. The contribution of different rhythms to the EEG depends on the age and behavioral state of the subject, mainly the level of alertness. Considerable intersubject differences in EEG characteristics also exist. EEG pattern is influenced by neuro-pathological conditions, metabolic disorders, and drug action (1).

- Delta rhythm is a predominant feature in EEGs recorded during deep sleep. In this stage, delta waves usually have large amplitudes (75–200 μV) and show strong coherence all over the scalp.
- Theta rhythms rarely occur in adult humans. However, they are predominant in rodents; in this case, the frequency range is broader (4–12 Hz) and waves have a high amplitude and characteristic sawtooth shape. It is hypothesized that theta rhythms in rodents serve as a gating mechanism in the information transfer between the brain structures (2). In humans, activity in the theta band may occur in emotional or some cognitive states; it can be also connected with the slowing of alpha rhythms caused by pathology.
- Alpha rhythms are predominant during wakefulness and are most pronounced in the posterior regions of the head. They are best observed when the eyes are closed and the subject is in a relaxed state. They are blocked or attenuated by attention (especially visual) and by mental effort. Mu rhythms have a frequency band similar to alpha, but their topography and physiological significance are different. They are related to the function of motor cortex and are prevalent in the central part of the head. Mu rhythms are blocked by motor functions.
- Beta activity is characteristic for the states of increased alertness and focused attention, as was shown in several animal and human studies.
- Gamma activity is connected with information processing (e.g., recognition of sensory stimuli) (3) and the onset of voluntary movements. In general, it can be summarized that the slowest cortical rhythms are related to an idle brain and the fastest to information processing.

The EEG is observed in all mammals, the characteristics of primate EEG being closest to the human. Cat, dog, and rodent EEGs also resemble human EEGs, but have different spectral content. In lower vertebrates, electric brain activity is also observed, but it lacks the rhythmical behavior found in higher vertebrate recordings.

2. SHORT HISTORY OF ELECTROENCEPHALOGRAPHY

Richard Caton (1842–1926) is regarded as the first scientist to investigate brain potentials. He worked on the exposed brains of cats and rabbits, measuring electric currents by means of a galvanometer, where a beam of light reflected from its mirror was projected onto a scale placed on a nearby wall. The results (presented in 1875) showed that "feeble currents of varying directions pass through the multiplier when the electrodes are placed at two points of the external surface, or one electrode on the gray matter and one on the surface of skull." This observation can be regarded as a discovery of electroencephalographic activity.

Adolf Beck (1863–1939) also investigated spontaneous activity of the brains of rabbits and dogs. He was the first to discover (in 1890) the rhythmical oscillations of brain electrical activity. He also observed the disappearance of these oscillations when the eyes were stimulated with light, which was the first discovery of so-called "alpha blocking." Later, his co-worker Napoleon Cybulski (1854–1919) presented the electroencephalogram in a graphical form by applying a galvanometer with a photographic attachment and was the first to observe epileptic EEG activity in a dog elicited by an electric stimulation (4). In 1929, the first electroencephalogram was recorded from the surface of the human scalp by Hans Berger (5).

1935 witnessed birth of the major fields of today's clinical electroencephalography. F. Gibbs and H. Davis showed association of 3/sec spike-wave complexes in EEG with epileptic absences and A. L. Loomis et al. studied human sleep patterns. Also in 1935, the first electroence-

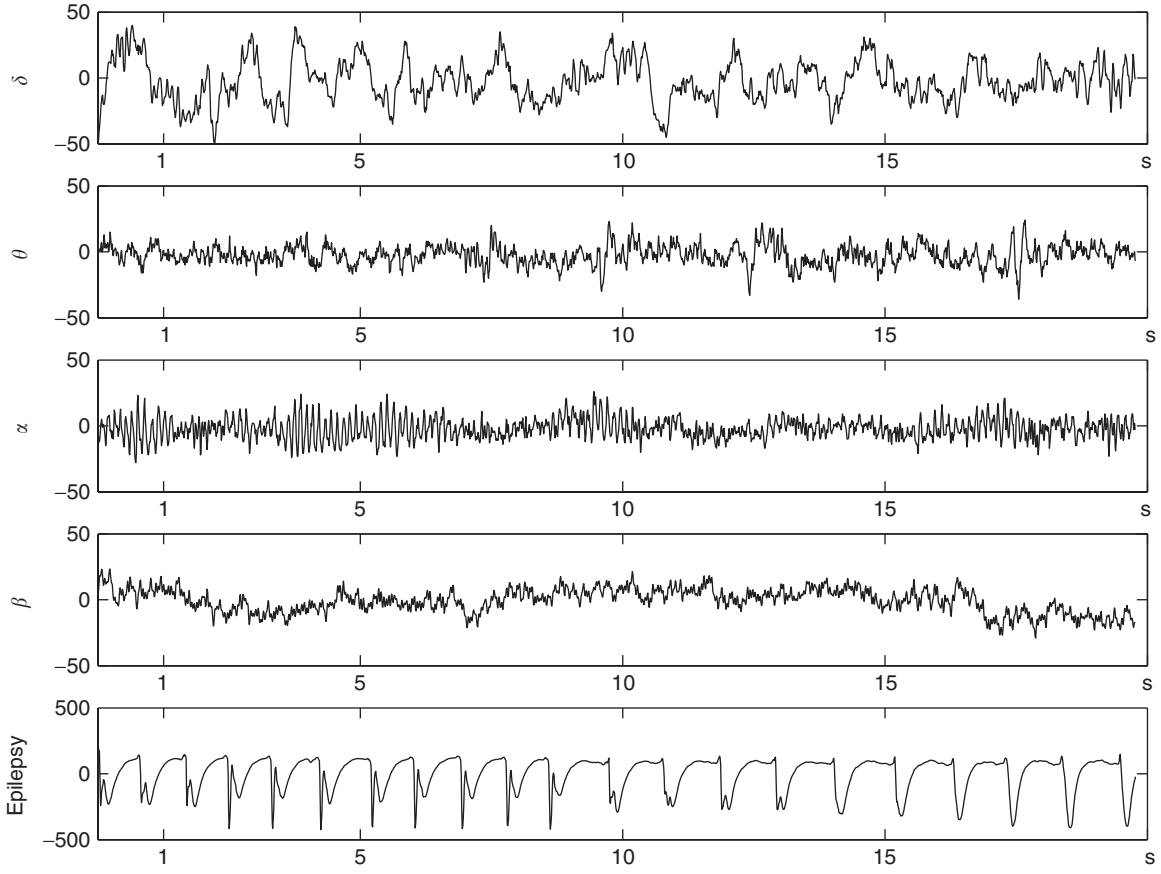

Figure 1. Characteristic EEG rhythms, from the top: δ (0.5–4 Hz), θ (4–8 Hz), α (8–13 Hz), β (13–30 Hz). The lowest trace–EEG during epileptic seizure, note that the amplitude scale is an order of magnitude bigger.

phalograph (Grass Model I) started the era of contemporary EEG recording. More information about the history of electroencephalography may be found in (1) and (4).

3. NEUROPHYSIOLOGICAL BASIS OF EEG

In the brain, two main classes of cells exist: nervous cells, called neurons (Fig. 2), and glial cells. In both, the resting potential is approximately -80 mV, with the inside of cells being negative. The difference of potentials across a cell membrane comes from the difference of concentration of cations: K^+, Na^+, anions Cl^-, and large organic anions. Ca^{++} ions are less abundant, but they have an important regulatory role. The potential difference is maintained by the active transport of cations K^+ to the inside of the cell and Na^+ to the outside, using the energy supplied through metabolic processes.

Electric activity of neurons is manifested by generation of action potentials and postsynaptic potentials (PSP). Action potentials occur when the electrical excitation of the membrane exceeds a threshold. Postsynaptic potentials are subthreshold phenomena. The generation of action potentials is connected with rapid increase of permeability for Na^+ ions. Their influx in the cell causes a rapid increase of the potential inside the cell and the change of polarity of the inside of the neuron from negative to positive (about $+30$ mV). A subsequent increase of membrane permeability to K^+ ions (leading to their outflow from the cell), and a decrease of permeability for Na^+ ions makes the inside of the cell negative again with respect to the surrounding medium. In this way, action potential of characteristic spike-like shape (duration about 1 ms) is created. It obeys the "all or nothing" rule: for supra-threshold stimuli, a pulse of a constant amplitude is generated; for subthreshold excitation, the neuron doesn't fire.

PSPs are connected with the phenomena occurring on the postsynaptic membrane. When action potential arrives at the synapse, it secretes a chemical substance, called mediator or transmitter, which causes a change in the permeability of the postsynaptic membrane of the next neuron. As a result, ions traverse the membrane and a difference in potentials across the membrane is created. When the negativity inside the neuron is decreased (e.g., by the influx of Na^+ ions), the possibility of firing is higher and an excitatory postsynaptic potential (EPSP) is generated. An inhibitory postsynaptic potential (IPSP) is created when the negativity inside the neuron is increased and the neuron becomes hyperpolarized. Unlike the action potential, the PSPs are graded potentials, their ampli-

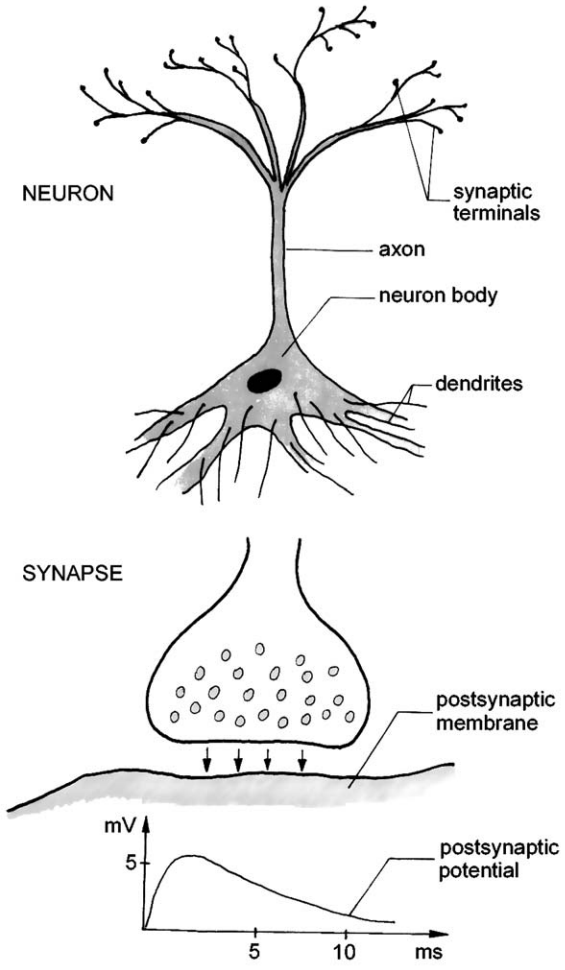

Figure 2. From the top: neuron, synapse, postsynaptic potential.

tudes are proportional to the amount of secreted mediator, which depends on the excitation of the input neuron. Postsynaptic potentials typically have amplitudes of 5–10 mV and a time span 10–50 msec. In order to obtain supra-threshold excitation, the amplitudes of many postsynaptic potentials have to be superimposed in the soma of a neuron. A neuron can have very abundant arborizations, making up to 10,000 synaptic junctions with other neurons (in the human brain, about 10^{11} neurons exist).

The electrical activity of neurons generates currents along the cell membrane in the intra- and extracellular spaces, producing an electric field conforming approximately to that of a dipole. Macroscopic observation of this electric field requires the synchronization of electrical activity of a large number of dipoles oriented in parallel (6). Indeed, pyramidal cells of the cortex are, to a large degree, parallel and, moreover, they are synchronized by virtue of common feeding by thalamocortical connections (2). The condition of synchrony is fulfilled by the PSPs, which are relatively long in duration. The contribution from action potentials to the electric field measured extracranially is negligible. EEG comes from the summation of synchronously generated postsynaptic potentials. The contribution to the electric field of neurons acting synchronously is approximately proportional to their number, and, for those firing nonsynchronously, as a square root of their number. For example, if the electrode records action of 10^8neurons (which is typical for scalp electrode) and 1% of them are acting synchronously, their contribution will be 100 times bigger than the contribution of neurons acting asynchronously, because $10^6/\mathrm{sqrt}(10^8) = 100$.

The problem of the origins of EEG rhythmical activity has been approached by electrophysiological studies on brain nerve cells and by the modeling of electrical activity of the neural populations (2,3). The question emerges whether the rhythms are caused by single cells with pacemaker properties or by the oscillating neural networks. It has been shown that some thalamic neurons display oscillatory behavior, even in the absence of synaptic input (7). Evidence exists that the intrinsic oscillatory properties of some neurons contribute to the shaping of the rhythmic behavior of networks to which they belong. However, these properties may not be sufficient to account for the network rhythmic behavior (2). It is generally accepted that cooperative properties of networks consisting of excitatory and inhibitory neurons connected by feedback loops play the crucial role in establishing EEG rhythms. The frequency of oscillation depends on the intrinsic membrane properties, on the membrane potential of the individual neurons, and on the strength of the synaptic interactions.

In the past, the role of EEG in information processing has not been fully recognized. However, strong evidence exists that coherent oscillations in the beta range in a population of neurons might be the basic mechanism in feature binding of the visual system (8). It seems that this observation is not limited to the visual system and that synchronized oscillatory activity provides an efficient way to switch the brain system between different behavioral states and to cause a qualitative transition between modes of information processing. In this way, neuronal groups with a similar dynamic functional state can be formed, subserving perceptual processes. It has also been postulated that the role of synchronized oscillatory EEG activity in the alpha and theta range is to serve as a gating mechanism to the flow of the information through the network. Bursts of oscillatory activity may constitute a mechanism by which the brain can regulate changes of state in selected neuronal networks and change the route of information (2).

4. RECORDING STANDARDS

EEG is usually registered by means of electrodes placed on the scalp. They can be secured by an adhesive (like collodion) or embedded in a special snug cap. The resistance of the connection should be less than 5 KOhms, so the recording site is first cleaned with diluted alcohol, and conductive electrode paste applied to the electrode cup.

Knowledge of exact positions of electrodes is very important for both interpretation of a single recording as well as comparison of results, hence the need for standardization. The traditional 10–20 electrode system (9) states

positions of 19 EEG electrodes (and two electrodes placed on earlobes A1/A2) related to specific anatomic landmarks, such that 10–20% of the distance between them is used as the electrode interval (Fig. 3). The first part of derivation's name indexes the array's row—from the front of head: Fp, F, C, P, and O. The second part is formed from numbers even on the left and odd on the right side, in the center "z" or "0". Progress in topographic representation of EEG recordings brought demand for a larger amount of derivations. Electrode sites halfway between those defined by the standard 10–20 system were introduced in the extended 10–20 system (10).

EEG is a measure of potential difference; in the referential (or unipolar) setup, it is measured relative to the same electrode for all derivations. This reference electrode is usually placed on the earlobe, nose, mastoid, chin, neck, or scalp center. No universal consent exists regarding the best position of the reference electrode, because currents coming from bioelectric activity of muscles, heart, or brain propagate all over the human body. In the bipolar setup (montage), each channel registers the potential difference between two particular scalp electrodes. Data recorded in a referential setup can be transformed into any bipolar montage, for the sake of display or further processing. The common "average reference" montage can be obtained by subtracting from each channel the average activity from all the remaining derivations. The Hjorth transform references each electrode to the four closest neighbors, which is an approximation of the Laplace transform (LT). LT is calculated as a second spatial derivative of a signal, offering information about vertical current density. For best performance, it needs an adequate spatial sampling-interelectrode distance around 20 mm (e.g., 128 electrodes on the scalp). The estimates obtained by means of LT for the electrodes lying at the scalp periphery are biased and have to be excluded.

Contrary to the open question of the reference, the necessity of artifact rejection is universally acknowledged. The main problem lies in the lack of a working definition for an EEG artifact—it can stem from muscle or heart activity (EMG, ECG), eye movement (EOG), external electromagnetic field, poor electrode contact, subject's movement, etc. Corresponding signals (EMG, EOG, ECG, and body movements) registered simultaneously with EEG are helpful in the visual rejection of artifact-contaminated epochs.

EEG is usually digitized by a 12-bit ADC (analog-digital conversion) with the sampling frequency ranging from 100 Hz for spontaneous EEG and several hundred Hz for ERP to several kHz for recording short latency far-field ERP. A black diagram of a recording setup is shown in Fig. 4. Prior to sampling, low-pass anti-aliasing filters are used; high-pass filters are applied in order to eliminate artifacts of lowest frequencies.

5. MATURATION OF EEG

EEG evolves with age and achieves its final character at 30 years, when it stabilizes and then starts to change again in the old age. The rate of change is correlated with mental health. EEG development in infancy and adolescence is characterized by a shift of the EEG rhythm toward higher frequencies. In newborns, slow delta rhythms predominate, then the basic frequency shifts toward theta at the age of 12 months. The posterior slow activity characteristic in young children constantly diminishes during adolescence. Alpha rhythm appears at the age of 10 years (1). In young adults (21–30 years), the EEG still shows mild signs of immaturity including contribution of 1.5–3 Hz and 4–7 Hz waves during awake state, normally not seen past the age of 30.

Physiologically, the maturation process is connected with the development of dendritic trees and myelination. Myelin layers produced by glial cells cover the axons of neurons and act as an insulator of electrically conductive cells. The propagation of electrical activity is faster and less energy-consuming in myelinated fibers.

6. SLEEP EEG

Sleep EEG reveals a characteristic alternating pattern. The classic description of sleep involves division into stages originally defined by Rechtschaffen and Kales

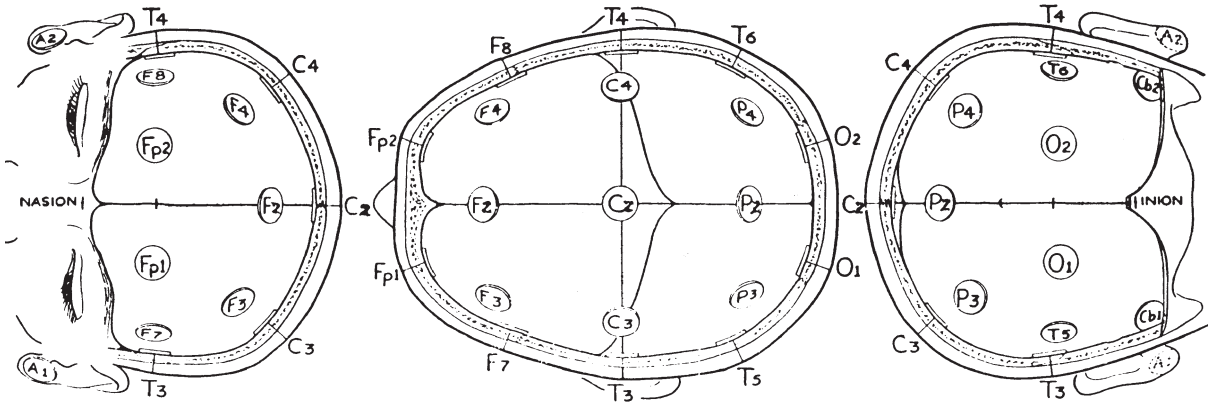

Figure 3. Electrodes placement in 10–20 system.

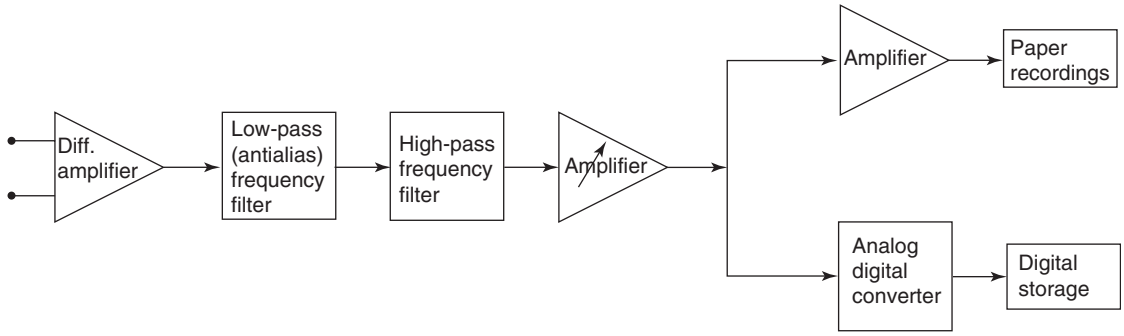

Figure 4. Block diagram of recording of a single EEG channel. Differential amplifier measures potential between two electrodes (one of them is treated as the reference). Analog filters and adjustable; amplifier prepares the signal for analog-digital conversion (ADC) and storage (lower path). Before the proliferation of digital media, EEG was stored on folded paper (upper path).

(R&K) (11): stage 1 (drowsiness), stage 2 (light sleep), stage 3 (deep sleep), stage 4 (very deep sleep), and REM (dreaming period accompanied by rapid eye movements). The differentiation of the sleep stages involves measurement of several signals. Their recording, called a polysomnogram, includes not only EEG, but also electrooculogram (EOG), electromyogram (muscular activity), and respiration. It may also include measurement of blood flow, electrocardiogram (ECG), and oxygen level in blood. EOG is recorded by means of the electrodes placed at the canthi of the eyes. As a result of the cornoretinal standing potential (the cornea is positive relative to the fundus), the eye movements produce changes in the potential between electrodes. The EOG and EMG help to distinguish REM state. The sequence of sleep stages is usually illustrated in the form of the hypnogram (Fig. 5). Recognition of stages is based on the contribution of the different rhythms and the occurrence of characteristic signal transients absent in wake EEG, namely sleep spindles, vertex waves, and K complexes. Sleep spindles are rhythmic waves of frequency 11–15 Hz and duration longer than 0.5s; characteristic increase and then gradual decrease of amplitude is not always observed. They are most prominent in the central derivations; low-frequency spindles (11–12.5 Hz) are more pronounced in the frontal and high-frequency spindles (12.5–15 Hz) in more posterior derivations (12). Vertex wave is a compound potential: a small spike discharge of positive polarity preceding a large spike and followed by a negative wave of latency around 100 ms and often another small positive spike. Vertex waves are a kind of auditory-evoked response (AER), as can be judged from their shape and place of occurrence. The K complex consists of an initial sharp component, followed by a slow component that fuses with a superimposed fast component. The sharp component may be biphasic or multiphasic. Sometimes the K complex is described only as having slow and fast components; the initiating sharp component is equated with a vertex wave (1).

Sleep stages may be briefly characterized as follows.

- Stage 1 (drowsiness) is associated with a decrease of alpha rhythm, rhythms in 2–7 Hz frequency band and low-amplitude rhythms of 15–25 Hz band. Deepening of drowsiness is connected with enhancement of slow activity and occurrence of vertex waves and slow rolling eye movements. According to R&K, the stage 1 is scored when less than 20% of the epoch contains any alpha activity and EEG consists of medium amplitude mixed frequency (mainly theta) activity, sometimes with vertex sharp waves.
- Stage 2 is characterized by appearance of sleep spindles, which are usually considered as a signal of sleep onset. Slow frequencies ranging from 0.75 Hz to 4 Hz are usually predominant in stage 2 of sleep; however, fast frequencies (15–30 Hz) may be present too. Summarizing, stage 2 is characterized by spindles and K complexes, less than 20% of the epoch may contain delta waves.
- Stage 3 is associated with preponderant slow rhythm in the delta frequency (0.75–3 Hz) range; activity of lower amplitude in 5–9 Hz range is also quite common. In a sizeable number of healthy subjects, alpha activity (7–11 Hz) may be intermingled with delta rhythm, and, in this alternating pattern, certain periodicities may occur. K complexes are still present in sleep stage 3; spindles are less abundant than in stage 2. Stage 3 is scored when 20–50% of the epoch contains delta waves of 0.5–2.5 Hz frequency and of 75 μV or greater peak-to-peak amplitude.
- Stage 4 is dominated by slow-wave activity of high amplitude; K complexes may appear. Stage 4 is scored when more than 50% of the epoch contains delta activity conforming to the criteria defined above.
- REM is characterized by a decrease of EEG amplitude, occurrence of faster rhythms, rapid eye movements, and loss of muscular activity. Spectral characteristics in REM is polyrhythmic and, on the basis of EEG only, it is difficult to distinguish REM from stage 1.

The evolution of slow-wave activity and spindles during overnight sleep is shown in Fig. 5.

Evidence exists that when the sleep becomes deeper, the sources that drive EEG activity move from the poster-

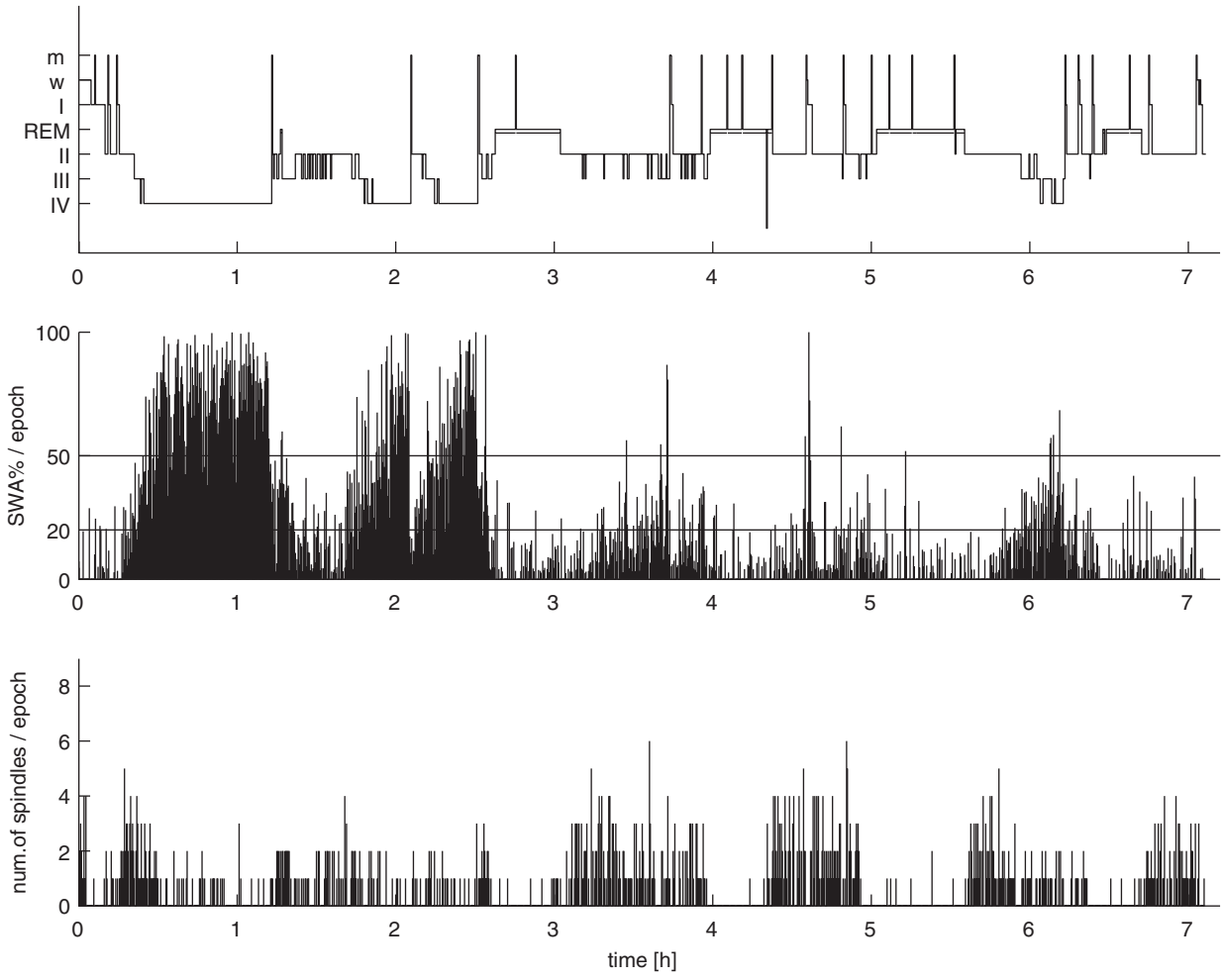

Figure 5. Time evolution of the overnight sleep (horizontal scale in hours). Top: – Hypnogram (by human expert; bottom: SWA and sleep spindles detected automatically from matching pursuit parameterization of the EEG signal: % SWA denotes the percentage of epoch occupied by waveforms classified as SWA. Continuous description of the slow-wave sleep is compatible with the III/IV stages delineation defined R&K (11), as indicated by the 20% an 50% lines. Artifacts not removed from analysis.

ior regions of the head (prevalent during awake state with eyes closed) to the centro-frontal regions (13).

During the night, nonREM (NREM) and REM periods occur in cycles. Slow-wave sleep is concentrated in the first one-third of the night and is predominant in childhood. The sleep pattern changes very much during childhood and adolescence. For newborn babies, REM takes most of the sleep time, and in young children, only REM and nonREM stages can be distinguished. Diminuition of deep slow-wave sleep and increase in wakefulness continues through entire life span after the age of 1 year. In old age, the contribution of stages 3 and 4 decreases markedly and the first REM stage appears later at night. The changes of the sleep pattern may be caused not only by a normal aging, but also by degenerative diseases. An atypical polysomnogram may be observed in a variety of situations (e.g., sleep deprivation, abnormal sleep habits, drug and drug withdrawal effects, sleep pathologies). Dissociated or otherwise atypical sleep patterns may be manifested by intrusion of the alpha rhythm on the slow waves in stages 3 and 4 or the appearance of sleep spindles in REM. Also, normal ultradian NREM/REM cyclicity may be altered or lost. The normal REM onset in adults appears after about one hour or later. Early (about 10 minutes) onset of REM sleep, called SOREM, may be an effect of previous REM deprivation, alcoholism, drug withdrawal, irregular sleep habits, severe depression, or narcolepxy-catalepsy. In the latest case, a poor REM cyclicity is observed.

From the clinical point of view, not only sleep macrostructure described by hypnogram, but also its microstructure, is important. Transient arousals associated with unstable sleep conditions are reflected in the EEG. A set of guidelines for arousal scoring has been proposed by the American Academy of Sleep Medicine (14). An EEG arousal is defined as an abrupt shift in EEG frequency, which may include theta, alpha, or frequencies greater than 16 Hz, but not spindles. A set of additional conditions is given in Guilleminault et al. (14). A certain number of

spontaneous arousals seems to be an intrinsic component of physiological sleep, but their frequent occurrence may be connected with respiratory sleep disorders, nocturnal myoclonus, and other clinical conditions.

7. PATHOLOGICAL CONDITIONS INFLUENCING EEG

EEG is affected by the CNS disorders (e.g., cerebral anoxia, cerebral inflammatory processes, cerebral palsy, Creutzfeld–Jacob disease, and metabolic and degenerative nervous system disorders such as senile and presenile dementias). It is influenced by brain tumors and craniocerebral traumas; in the second case, it can serve as a measure of patient recovery. EEG is also an important test in psychiatric diseases, sleep disorders, and developmental disorders. In particular, analysis of evoked potentials is very helpful in diagnosing dyslexia and differentiation between psychogenic and neurogenic disorders. The character of EEG changes dramatically in epileptic condition and its analysis is a basic tool in this case (1).

8. EPILEPTIC SEIZURE DISORDERS

An epileptic seizure is caused by the massive synchronization of neuronal electrical activity. During the seizure, groups of neurons discharge synchronously, creating a large amplitude signal and leading to uncontrollable oscillations. Tumors, infections, trauma, or metabolic and toxic disorders may be responsible for the synchronized discharges. Epilepsy is the second most common neurological disease (15). Its clinical symptoms may involve the loss of awareness, drop attacks, facial muscles and eye movements, aggressive outbursts, prolonged confusional states, and flexor spasms of a whole body.

Seizure types can be divided into three main categories (15):

1. Local—the synchronized electrical activity starts in a well localized part of the brain. The seizure, lasting a few seconds, is accompanied by jerking or spasms, as well as by a loss of consciousness.
2. Generalized—the EEG patterns are bilaterally symmetrical and roughly synchronous; the epileptic activity is spread over wide areas of both hemispheres simultaneously from the onset of attack.
3. Unclassifiable—different from those described in (1) and (2).

In epileptic discharges, the membrane potential of cortical and deeper located neurons changes in a dramatic way, which leads to massive bursts of action potentials and large fluctuations of intra- and extracellular fields. The seizure initiation is probably connected with the breakdown of the local inhibitory mechanisms. The crucial factor in generation of epileptic activity is the synchronization of neural pools. Mechanisms of this synchronization are probably connected with recurrent excitation operating through positive feedback loops.

An important diagnostic problem is localization of the epileptic focus, which, in severe cases, can be possibly removed by surgical intervention. Intracranial electrodes are usually placed in the suspected region, found from the scalp EEG, in order to better localize the focus. Tests involving measurement of ERP are performed in order to check if the removal of a given part of the brain will not impair some vital brain functions. The epileptic focus may not necessarily be detected by imaging techniques such as tomography, so the information contained in EEG is essential for localization of epileptic foci.

9. INFLUENCE OF DRUGS

EEG is very sensitive to the action of a wide range of pharmacological substances, especially psychotropic drugs, anaesthetics, and anticonvulsants. It is also affected by some drugs targeted to organs other than the central nervous system (CNS), such as antihistamines and antihypertensives. Influence of drugs on EEG primarily include changes in its spectral content and topographic characteristics. Effects of psychoactive drugs on EEG could be used to assess their action on the CNS. A particular effect of a drug on EEG may be used as an indication for its potential therapeutic efficiency.

10. EVENT-RELATED POTENTIALS

Event-related potentials (ERPs) are the changes of spontaneous EEG activity related to a specific event. ERPs triggered by particular stimuli, visual (VEP), auditory (AEP), or somatosensory (SEP), are called evoked potentials (EP). It is assumed that ERPs are generated by activation of specific neural populations, time-locked to the stimulus, or that they occur as the result of reorganization of ongoing EEG activity. The basic problem in analysis of ERPs is their detection within the larger EEG activity. ERP amplitudes are an order of magnitude smaller than that of the ongoing EEG. Averaging is a common technique in ERP analysis; it makes possible the reduction of background EEG noise. However, assumptions underlying the averaging procedure, namely (1) the background noise is a random process, (2) the ERP is deterministic and repeatable, and (3) EEG and ERP are independent, are not well justified.

The ERP pattern depends on the nature of the stimulation, placement of the recording electrode, and the actual state of the brain. ERPs are usually described in terms of the amplitudes and latencies of their characteristic waves (Fig. 6). The components occurring at different times are different in nature; they are named early and late ERP. The early ERPs of latency below 10–12 ms (called sometimes “far fields”) are connected with the response of the receptors and peripheral nervous system; late ERPs (“near-field” potentials) are generated in the brain. In late ERPs, exogenous components (primarily dependent on characteristics of the external stimulus) and endogenous components (which are dependent on internal cognitive processes) can be distinguished. Endogenous components of latencies above 100–200 ms are influenced

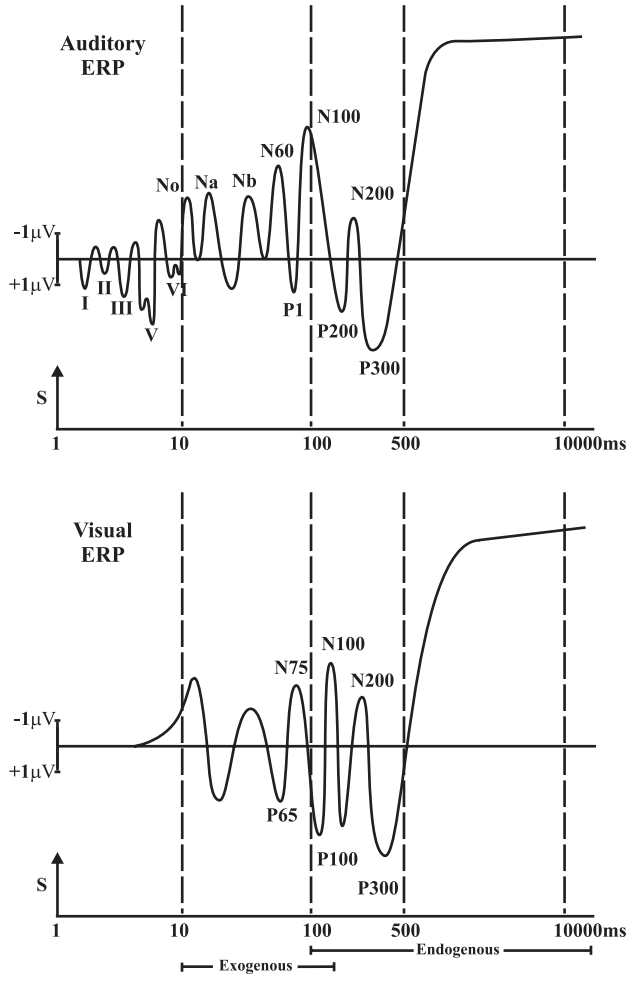

Figure 6. Schematic representations of average auditory ERP (upper picture) and visual ERP (lower picture) in logarithmic time scale, showing the commonly recognized components. Letter "N" denotes negative polarity, "P" positive polarity, usually followed by the number denoting latency in ms. The components of auditory potentials marked by roman numbers are the brain stem-evoked responses (BAEP). They are followed by mid-latency exogenous components (MAEP) in the frequency range 10–100 ms. The first peak in exogenous visual ERP comes from ERG (electroretinogram). Exogenous ERP exhibit modality–specific features; endogenous ERP are similar in both modalities.

by the attention to the stimulus. The later components around 300 ms (P300) reflect recognition and discrimination between stimuli. P300 amplitude is considered as a manifestation of CNS activation that reflects attention to incoming stimulus, when memory representations are updated. P300 latency is dependent on the stimulus classification speed (it is smaller for known stimuli) and the latency is connected with individual cognitive capability.

ERPs are widely used in clinical practice as tests of the integrity of the sensory pathways or their different dysfunctions. They are also helpful in the diagnosis of diffused brain diseases (e.g., multiple sclerosis or psychiatric disorders).

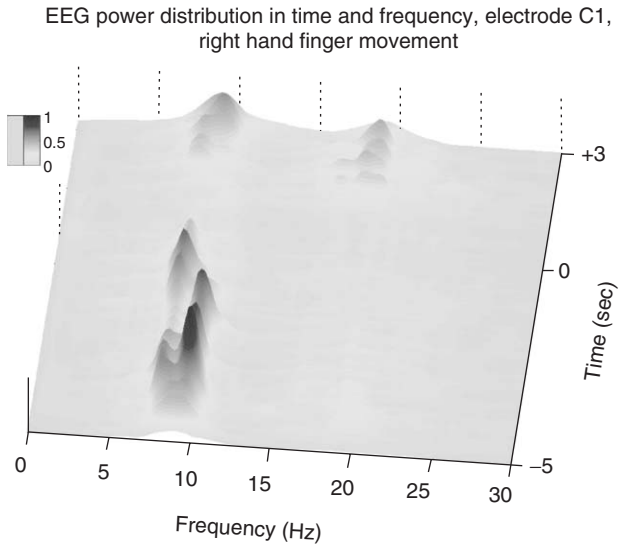

Figure 7. EEG power distribution in time and frequency during voluntary finger movement (movement onset at time 0) for electrode placed above sensorimotor cortex. The desynchronization (decrease of amplitude) is visible for alpha and beta band before the movement and their synchronization may be observed after the movement. (EEG filtered in 0.5–100 Hz frequency range. The power was divided by 1/f in order to suppress the frequency-dependent background.)

ERPs need not to be time-locked to the stimuli, they can occur without the fixed phase to the trigger. ERPs caused by continuous stimuli (e.g., wave-modulated light or amplitude-modulated tone) or those that are not time-locked to the stimulus are preferably analyzed in the frequency domain. As an example, ERPs can serve preceding voluntary actions such as speech or movements. They are usually accompanied by the change in the spectral content of the signals. Specifically, before the movement onset and during the movement, a decrease of activity occurs in the alpha and beta band in cortical regions connected with sensorimotor cortex (Fig. 7). This phenomenon is called event-related desynchronization (16). After the movement, an increased synchronization in both these bands occurs. During the action, an increase of activity in the high frequencies (gamma band) takes place. It is not always present in scalp recordings, but it is well visible in electrocorticogram.

11. EEG ANALYSIS

The traditional method of EEG analysis is visual inspection of the signals plotted on paper. Modern computer analysis can extend electroencephalographer's capabilities by supplying information not directly available from the raw data. However, visual analysis is still a widespread technique, especially for detection of transient features of signal. In most cases, the agreement of an automatic method with visual analysis is a basic criterion for its acceptance.

As a result of its complexity, the EEG time series can be treated as a realization of a stochastic process, and the statistical properties can be evaluated by typical methods based on the theory of stochastic signals. These methods include probability distributions and their moments (means, variances, higher-order moments), correlation functions, and spectra. Estimation of these observables is usually based on the assumption of stationarity, which means that the statistical properties of the signal do not change during the observation time. Although the EEG signals are ever changing, they can be subdivided into quasi-stationary epochs when recorded under constant behavioral conditions. On the basis of empirical observations and statistical analysis performed by several authors, quasi-stationarity can be assumed for EEG epochs of approximately 10 seconds in length, measured under constant behavioral conditions (1).

EEG signals can be analyzed in the time or frequency domain, and one or several channels can be analyzed at a time. The applied methods involve spectral analysis by Fourier Transform (FT), autoregressive (AR) or autoregressive-moving average (ARMA) parametric models, Kalman filters, and time-frequency and time-scale methods (Wigner distributions, wavelets, matching pursuit). The most common methods used for postprocessing include cluster analysis, discriminant analysis, or artificial neural networks (ANN).

Estimation of power spectra is one of the most frequently used methods of EEG analysis. It provides information about the basic rhythms present in the signal and can be easily and rapidly calculated by means of the Fast Fourier Transform (FFT). Maximum entropy power spectrum may be obtained by means of the autoregressive model, which can be recommended for the EEG analysis. The AR model represents a filter with a white noise at the input and the EEG series at the output; it is compatible with a physiological model of the alpha rhythm generation (17), but this link is neither specific nor essential. The AR model provides a parametric description of the signal and makes possible its segmentation into stationary epochs. It also offers the possibility of detecting nonstationarities by means of the inverse filtering (1).

Autoregressive or autoregressive-moving average models (ARMA), sometimes used for EEG analysis, belong to the class of linear models. Some authors use nonlinear methods for EEG analysis, based on estimators derived from chaos theory, such as attractor dimension or Lyapunov coefficients. However, these parameters have a very limited value for EEG, because this signal has a character of colored noise and reveals chaotic character only in some epochs of epileptic seizures, as was shown by surrogate data tests (18,19) and linear forecasting (20). Moreover, the above-mentioned chaotic estimators require long stationary data epochs, are subject to systematic errors, and are very sensitive to noise.

The representation of EEG activity for a complete ensemble of channels records from scalp electrodes is usually performed by mapping. The features of EEG can be extracted from multivariate statistics, so, in this respect, graphic representation in the form of maps is neither necessary nor sufficient. However, it is more effective for a human observer to look at a map than at a table of numbers. A map may help to make a direct comparison between the topographic distribution of EEG features and an anatomic image given, for example, by the tomographic brain scan. Three types of features are most commonly mapped for clinical applications (1) direct variable such as amplitude, (2) transformed variable such as total spectral power or relative spectral power in frequency band, and (3) the result of statistical test applied to given EEG feature.

The appearance of a map depends very much on the electrode reference system. The recommended representation involves surface Laplacians, because this approach approximates source current density and cancels a common component caused by volume conduction (6,21). However, a reliable computation of surface Laplacian requires at least 64 electrodes and adequate spatial sampling is obtained for 128 electrodes. Therefore, quite frequently an approximation of the Laplacian operator by Hjorth transform (22) is applied [e.g., it was used as a preprocessing method improving spatial resolution for estimation of synchronization and desynchronisation of EEG activity (16)]. Results obtained by application of Laplacian operator may be further ameliorated by deblurring; that is, using a mathematical model of volume conduction through the skull and scalp to downwardly project scalp-recorded potentials, which provides a computational estimate of the electrical potentials, that would be recorded near the superficial cortical surface (23).

Interdependence between two EEG signals can be found by a cross-correlation function or its analogue in the frequency domain—coherence. Cross-correlation can be used for comparison of EEGs from homologous derivations on the scalp. A certain degree of difference between these EEGs may be connected with functional differences between brain hemispheres, but a low value of cross-correlation may also indicate a pathology. The cross-covariance functions have been extensively used in the analysis of event-related potentials for the study of the electrophysiological correlates of cognitive functions (24). Inter-relationships between EEG time series recorded at different sites can also be quantified by information measures (25) and coherences (26). Usually, an ordinary coherence calculated pair-wise between two signals is used. However, for the ensemble of channels taken from different derivations, the relationship between two signals may come from the common driving from another site; therefore, partial and multiple coherences should be taken into account as well (27).

If the signals are modeled as a linear mixture of statistically independent "sources," their activities can be found by means of the Independent Component Analysis (ICA) (28). This class of algorithms, usually based on the neural networks scheme, is used in general for the "blind source separation" problems (BSS). ICA can be seen as an extension to the principal component analysis and factor analysis.

In order to find intrinsic relationships between signals from different locations, multivariate autoregressive model (MVAR) may be applied simultaneously to the whole set of EEG channels. From the MVAR coefficients,

partial, multiple, and ordinary (bivariate) coherences can be found as well as the transfer function of the system. Elements of the transfer matrix of the MVAR model have the meaning of Granger causality (19). It relies on prediction of the future of one channel from the past of the other channels, which allows for the determination of the activity propagation. Normalized Granger causality is equivalent to the directed transfer function (30), which was used, for example, for the determination of the direction of the propagation of EEG activity during overnight sleep (13), during epileptic seizure (31), and for the assessment of information flow between brain structures of behaving animals (32). For the set of mutually dependent signals, as is the case for most of the recorded EEG signals, all involved channels have to be processed simultaneously. Bivariate estimates of Granger causality or DTF can bring quite misleading results (33). Recently, short-time directed transfer function (Fig. 8) was introduced, which makes possible calculation of EEG flows not only as a function of frequency, but also of time when multiple repetitions of experiments are available (29,34,35).

The assessment of the time evolution of EEG and ERP is crucial for understanding the information processing by the brain. Detection of transient EEG features is important in diagnosis as well; therefore, time-frequency methods operating in a short time scale are needed. The first method aiming at dynamic analysis is the windowed Fourier transform with a sliding window. Substantial progress was also achieved by introduction of wavelet analysis.

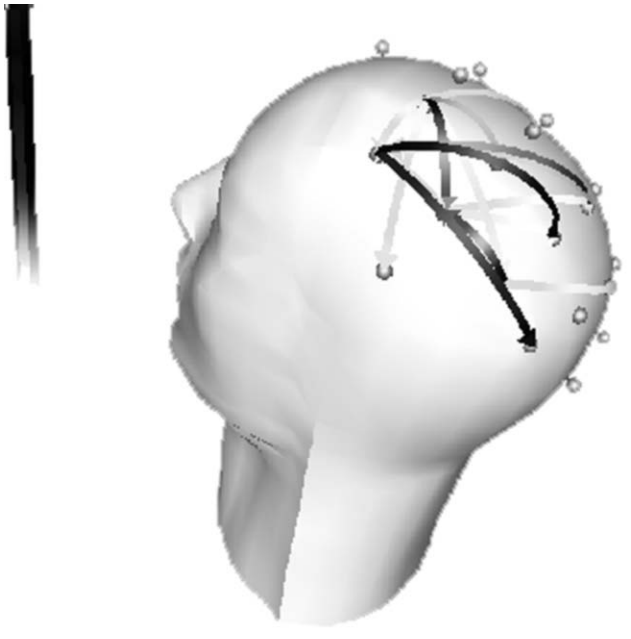

Figure 8. Determination of the EEG propagation by means of the SDTF. The arrows represent increase of EEG activity flows in the beta band in the 1–2 seconds after voluntary movement of the right index finger. (Flows calculated as: SDTF functions integrated in the beta band and time 1–2 s after movement in respect to SDTF in beta band in reference period before movement.) Based on the results described in (33). Dynamic propagation of EEG activity in time in the form of movie is available from Internet at http://eeg.pl.

Wavelet transform (WT) describes signals in terms of coefficients representing their energy content in specified time-frequency region. This representation is constructed by means of decomposition of the signal over a set of functions generated by translating and scaling one function called mother wavelet. The basics of wavelet analysis can be found in Mallat (36). Some of the applications of WT involve ERP component separation and measurement, time-varying filtering for denoising single trial ERPs, isolation of specific ERP and EEG rhythms, hearing threshold estimation via auditory brain stem-evoked response measurements, scale-specific topographic analysis, and data compression [referred in (37)]. WT is especially useful for evaluation of time-locked phenomena and their distinction from the non time-locked events. As the examples may indicate, distinction of both kinds of components in AEP (38) and reconstruction of a single AEP based on discrimination between background and evoked activity parameterized by means of WT (39). Multiresolution analysis, offered by WT, provides the measure of EEG energy at each decomposition scale. This property was used to achieve spatial enhancement of ERP to bring out topographic features that might not be seen without processing (40). The assessment of complexity of the energy distribution in different frequency subbands may be evaluated in terms of wavelet entropy (41). This measure was used, for example, to follow EEG evolution after hypoxic-ischemic injury (42). WT was also used for automatic detection of arousals during sleep (43). A wide range of biomedical applications of wavelets together with basic theory are described, for example, in (44).

Time and frequency resolution in WTs are subject to certain restrictions that lead to poor frequency resolution at high frequencies. The representation depends also on the setting of the time window, which makes WT mostly suitable to the evaluation of time-locked signals such as EP, but less appropriate for detecting structures appearing more or less randomly in the signal. This problem has been approached by application of time-shift and frequency-shift invariant time-frequency distributions from the Cohen class. However, significant cross terms are present in these distributions, and sophisticated mathematics has to be applied to diminish their contribution. Another drawback for EEG applications may stem from the fact that, as continuous functions of time and frequency, those distributions do not provide direct parameterization of signal structures.

These drawbacks are absent in the adaptive time-frequency approximations, which decompose the signal into waveforms of well-defined frequency, time occurrence, time span, and amplitude. Such an iterative algorithm—matching pursuit (MP)—was introduced by Mallat and Zhang in 1993 (45). In Fig. 9 time-frequency energy distribution of an epileptic EEG signal, obtained by means of the MP algorithm, is presented. MP parameterization makes possible statistical evaluation of EEG features and automatic detection of desired signal structures (46). Application of MP to the detection and parameterization of sleep spindles and slow waves is shown in Fig. 5, where

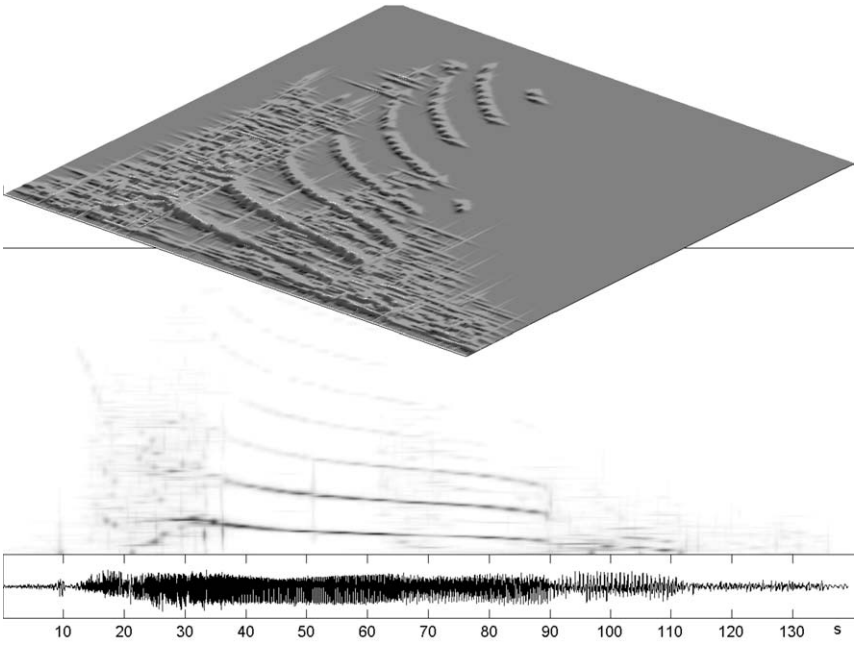

Figure 9. Time-frequency representations of EEG energy density during an epileptic seizure, obtained by means of MP method. Upper plot in 3-D, lower—the same in 2-D, below—EEG trace (scale in seconds).

certain features of these structures are presented in time together with hypnogram.

Parameterization by means of time-frequency features may serve also as an input to the artificial neural networks (ANN), usually with the aim of classification, discrimination, or feature extraction. ANN are constructed from artificial neurons (or units), which produce the output depending on the sum of weighted inputs from other units. Weights are modified in the process of learning. The most popular type of ANN applied for post-processing of the EEG signals are networks with one or more hidden layers of neurons (a hidden layer is a layer between input and output layer) and the supervised learning based on "back-propagation of errors" (47). This type of network was used, for example, for sleep stage scoring (48). Performance of ANN depends heavily on the input parameters, which was demonstrated in many papers. For example, in Trejo and Shensa (49), it was found that prediction of human performance from EGG parameterized by means WT coefficients gives better results than application as input parameters to ANN raw data or components found by PCA. The training of the abovementioned ANN with back propagation is based on "supervised learning," which means that the desired output is known. The unsupervised networks are based on competition between units. The procedures of unsupervised learning minimize the sum of two factors: the cost of code and the cost of reconstruction (50). Learning vector quantizer (51) belongs to this type of network. Its version, improved in respect to enhancing informative features, by updating weights in each step was used, for example, for EEG classification during externally-paced hand movements (52).

12. LOCALIZATION OF CORTICAL SOURCES OF EEG ACTIVITY

The determination of geometry and orientation of cortical sources of EEG is a complex problem. Electrical activity propagates along neuronal tracts and by volume conduction. Potentials measured by scalp electrodes are attenuated by media of different conductivity and complicated geometry (cerebrospinal fluid, skull, skin), which results in a decrease of their amplitude by over an order of magnitude. However, the major problem in localization of the sources of EEG activity stems from the fact that different configurations of sources can generate the same distribution of potentials on the scalp. Therefore, a unique solution of the EEG inverse problem can be obtained only by introducing extra *a priori* assumptions. Usually, one or several dipole sources are assumed and their positions and orientation are estimated by an iterative fit to the measured field [e.g., (53)]. The number of dipole sources is an open question; therefore, linear solutions based on distributed source models become more popular. However, in this case additional constrains on the solution are also needed, like, for example, Laplacian-weighted minimum norm of the solution [LORETA (54)]. In any of these cases, the solution space is usually *a priori* restricted to physiologically plausible locations. As a result of the nonuniqueness and high sensitivity to noise of the solution, results must be interpreted with care. For a recent review, see, for example, (55).

13. SPECIFIC CLINICAL APPLICATIONS

For particular medical applications, specific methods of EEG analysis were designed. An example may be the assessment of "drug profiles." The method relies on estimation of spectral power in basic frequency bands before

and after drug application and finding the significance of changes by means of statistical tests. A drug profile is constructed by plotting the results of a test (commonly in form of t-value of Student test) for frequency bands δ, θ, $\alpha 1$, $\alpha 2$, $\beta 1$, and $\beta 2$. The method is based on observation that drugs of similar profile give similar effects. More recently, nonparametric tests came into use and the shifts of spectral peaks are considered as well (56). An interesting approach is the combination of pharmaco-EEG with pharmacokinetics, by finding a relation between EEG features and pharmacodynamical models (57).

The analysis of overnight sleep is a very tedious and time-consuming procedure; therefore, many attempts were made to automate the procedure of hypnogram construction [listed, for example, in (58)] as well as the automatic identification of arousals, for example, (43). Some authors (48) reported quite good performance of their systems [e.g., the system of sleep scoring based on assessment of EEG spectral power in frequency bands, their ratios and parameters derived from EMG and EOG signals, followed by classification with the use of ANN (multilayer perceptron) achieved an average agreement rate of 82%, whereas the interexpert agreement was 87.5%]. The current tendencies in sleep EEG analysis are directed toward more continuous description of sleep going beyond R&K rules and assessment of sleep microstructure. Major progress may be achieved via incorporating recognition of transient structures into analysis, such as sleep spindles and K complexes, and consideration of wave amplitude and wave incidence separately, not only in terms of spectral power (59). The approach that offers possibilities of description of phasic and tonic features of EEG in the framework of one formalism is matching pursuit (46).

The analysis of epileptic activity serves for localization of epileptic focus, monitoring of interictal activity, prediction of seizure, and characterization of epileptic discharges. The analysis of seizures evolution is used for their classification, which offers the possibility of an application of appropriate treatment [e.g., (60)]. An example of the evolution of seizure is shown in Fig. 9. For localization of the epileptic focus on the basis of EEG, the inverse problem has to be solved. Taking into account its nonuniqueness and other limitations mentioned above, when the removal of the part of brain is considered, the localization requires confirmation by means of imaging techniques, such as CAT or MRI, and verification by analysis of EEG from subdural and implanted electrodes (60). A variety of methods for detection of epileptiform activity in the EEG have been implemented by means of expert systems [e.g., (61,62)], some of which are available commercially (63). A growing interest in the forecasting of epileptic seizures also exists. Seizure prediction times from minutes to hours have been reported [for a recent review, see (64)]. However, some of the claimed results have been severely challenged by appropriate statistical analysis (65,66).

14. COMPUTER-ASSISTED EEG DIAGNOSIS

Computer-assisted diagnosis usually consists of two steps: feature extraction and classification. As a primary feature in the amplitude domain mean, variance and higher-order moments can be used; in the frequency domain, spectral intensities in different frequency bands and their ratios are mostly applied.

One of the first automatic diagnostic methods (67) was based on the observation that an increased amount of slow pathological EEG activity might be analogous to the slow activity seen in the immature EEG. For each electrode, maturity calculated on the basis of spectral features was compared with the actual maturity. A significant discrepancy was considered an abnormality. In another diagnostic system (1), the ratio of slow and fast EEG activity as well as the degree of asymmetry between homologous derivations were taken into account.

The most extended diagnostic system, called Neurometrics (68), is based on standardized data acquisition techniques and EEG and ERP feature extraction. A neurometric test battery includes spontaneous EEG spectral intensities in frequency bands and their ratios and similarity of signals from homologous derivations. ERP are quantified in terms of amplitudes and latencies or by means of application of principal component analysis. In the last approach, the signals from different derivations are represented as linear combinations of some basic waveforms multiplied by weighting factors. In Neurometrics, each parameter is subjected to a transformation, such that the difference between individual index and the group mean value is divided by the standard deviation of the whole sample. In this way, the metric is created reflecting the relative probability of finding the given value within a normal reference group. The next steps of diagnostic procedure involve application of multivariate statistical methods such as factor analysis, cluster analysis, and discriminant analysis. Profiles of neurometric features that deviate from age-matched normals have been obtained for patients suffering from cognitive disorders, psychiatric illnesses, and neurological dysfunctions.

The computerized EEG monitoring in the intensive care neurological units involves measurement and assessment of several signals apart from EEG (e.g., ERP, ECG, heart rate variability, respiration, intracranial pression, and others depending on the injury). Physiological signal analysis can be combined with other diagnostic techniques [e.g., ultrasound (69)]. Advances in computerized EEG monitoring in neurological intensive care unit are described in (70).

Design of contemporary computer-assisted diagnosis (CAD) systems is usually based on computation of spectral parameters followed by artificial intelligence methods. In (71), the frequency components of EEG were converted into pseudo-linguistic facts via fuzzification. The EEG features were extracted by expert systems applying symbolic rules formulated by neurologist. The results were presented as linguistic terms, numerical values, and maps of temporal extent. In (72), the procedures involved in the diagnosis consisted of the following steps: (1) real-time

processing and compression of EEG and VEP, (2) brain mapping of spectral powers, (3) classifier design, (4) automatic detection of morphologies through ANN, (5) signal analysis through fuzzy modeling, and (6) a knowledge-based approach to classifier design. In the automatic system for classification of adult EEG (73), single epochs of EEG were classified by ANN. Time and space correlations of outputs from ANN were evaluated by an expert system, which generated a final report in the form of a medical diagnosis.

15. FUTURE OF ELECTROENCEPHALOGRAPHY

EEG, for many years, has been an important diagnostic tool, and more recent investigations have proven its significance for the understanding of information processing by the functional brain. At present, the topographical techniques, such as positon emission tomography (PET) or functional nuclear magnetic resonance (fMRI), are widely used for the diagnosis of pathologic neurological states and in brain research. However, these methods give information about the absorption of certain substances in specific structures or about the metabolism rate or glucose consumption, not directly about the brain electrical activity. Although their spatial localization properties are good, their time resolution is much lower than EEG. Moreover, in the information processing by brain, EEG rhythms have a different specific role, which cannot be distinguished by imaging techniques. The highest information content is usually connected with high-frequency rhythms (especially gamma) generated by small neuron pools, which makes the information carried by them even less accessible to the imaging techniques. Therefore, these techniques are not likely to replace EEG, which is a totally noninvasive and low-cost technique capable of providing information about relationships between cortical sites and the time evolution of brain processes.

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