Evoked Potentials Studies of Visual Information Processing

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INTRODUCTION

Sensory and perceptual processes of the human mind have been extensively studied in the past by psychophysical methods. Modern neurosciences offer several anatomical and physiological methods to complement such studies by analyzing the neurophysiological correlates of sensory information processing (Kandel et al., 2000). In animal experiments, neuronal mechanisms are investigated using invasive biochemical, anatomical, and neurophysiological methods that tag activity and processes within various structures of the nervous system. For the examination of human subjects, in general only noninvasive procedures can be used. Because human information processing takes place in fractions of a second, one of the most feasible methods constitutes the recording of brain electrical activity. The strengths of electrophysiological methods lie in their very high time resolution (in the order of milliseconds) and their sensitivity to detect functional changes of global brain states and of nervous activity. The high temporal resolution as well as their noninvasive nature constitute a significant advantage of these methods over brain imaging techniques (computer topography (CT), positron emission tomography (PET), or functional magnetic resonance imaging (fMRI)), and evoked brain activity data reveal steps in sensory information processing that occur very rapidly. Comparison of imaging and neurophysiological methods shows that there is a reasonable but imperfect correlation between electrophysiological data and hemodynamic responses measured by fMRI (George et al., 1995).

For the study of perception and cognition, measures with very high temporal resolution are needed. This is reflected by the fact that brain mechanisms related to perception are fast (note that motor reaction to visual stimuli occurs in a fraction of a second), and that individual steps in information processing are associated with rapid changes of the spatiotemporal characteristics of spontaneous and evoked electrical brain activity. In addition, the binding of stimulus features by the cooperation of distinct neural assemblies has been proposed to be mediated through high-frequency oscillation and its coherence of neuronal activation in different parts of the brain (Singer, 1999).

The present chapter illustrates how the recording of brain electrical activity in combination with knowledge of the human visual system may be employed to study information processing in healthy volun-
teers as well as in patients with selective visual deficiency. Data are presented on different experimental questions related to human visual perception, including contrast and stereoscopic vision as well as perceptual learning.

Psychophysical procedures are inherently subjective because the dependent variable consists of the verbal response or motor reaction to a physical stimulus of the subject under study. Thus, the subject’s willingness and ability to cooperate in the examination determines the result of the experiment. We also draw attention to the fact that psychophysical results always reflect the final outcome of the complete chain of information processing involving sensory transduction in specialized receptor organs (Corey and Roper, 1992), subcortical and cortical processes, as well as higher, cognitive strategies. This mostly prevents the identification and direct interpretation of behavioral data in terms of isolated steps of sensory processing.

Electrophysiological recordings constitute a supplement to such psychophysical methods, whereby the electrical activity of large neuronal populations is obtained noninvasively via electroencephalograms (EEGs) or evoked and event-related potentials; these may be used to quantify neuronal correlates of perceptual and cognitive processes and relate them to anatomical structures and functional systems of the human central nervous system.

**NEUROPHYSIOLOGICAL BASES OF EVOKED ELECTRICAL BRAIN ACTIVITY**

Neurons communicate by transmitting to their neighbors membrane potential changes in their synaptic endings, and they are able to connect different structures by sending over long distance in the brain information in the form of frequency-modulated action potentials of constant amplitude. In animal experiments, it is possible to record such activity directly inside of neurons or in their vicinity, whereas human studies have to rely on recordings from the intact skull. Due to the fact that scalp-recorded activity has amplitudes in the order of only microvolts ($\mu V$), for technical reasons it was not until about 70 years ago that EEG recordings became possible (Berger, 1929). For the interpretation of such data it is important to keep in mind that we are dealing with mass activity originating from large neuronal populations, spreading by volume conduction to the scalp. The electrodes commonly used are very large (about 10 mm in diameter) as compared to the dimension of individual neurons (about 20 $\mu$m in diameter), which implies that the area of a single electrode corresponds to that of about 250,000 neurons. The spatial integration of electrical nervous activity is even larger considering the fact that activity simultaneously originating in distant neuronal structures is always picked up by the recording electrodes (Skrandies et al., 1978).

In contrast to the spontaneous EEG of relatively large amplitude, stimulus-related brain activity is much weaker, and may be revealed only by some processing of the data. More than 100 years ago sensory evoked potentials had been recorded by the English physiologist Caton, (1875) directly from the cortical surface of rabbit and monkey brains, whereas the recording of human evoked potentials became feasible only after the advent of electronic and computerized signal-processing capabilities in the 1950s and 1960s.

Evoked potentials are systematic changes of the EEG induced by incoming information to the brain. Every sensory stimulus elicits electrical activity that is projected by selective and specialized afferent fiber systems to the corresponding cortical sensory areas, where it induces changes of the ongoing electrical activity. These changes depend on (1) the function state of the brain (information processing is different during various sleep stages and in differ-
ent states of wakefulness), (2) the specific meaning and importance of a given stimulus (attention and cognitive set of the subject determine the way stimuli are processed), and (3) the physical stimulus parameters and sensory thresholds of the organism (which also influence the subject’s sensory capability to perceive stimuli).

A single sensory stimulus evokes brain activity of only very small amplitude; although the ongoing EEG has amplitudes in the order of up to 150 µV, evoked brain activity reaches amplitudes between only 0.1 and 20 µV, and such small changes cannot be detected in the spontaneous EEG. Signal averaging enables identification of evoked activity: the same stimulus is presented repeatedly, and typically EEG segments of 10–1000 msec in length, following each stimulus presentation, are averaged. Stimulus-related brain activity looks similar in repeated trials, whereas the spontaneous EEG shows a randomized amplitude distribution over time.

Figure 1 illustrates how visual evoked potentials (VEPs) are obtained by averaging. From animal experiments it is known that neurons in the mammalian visual cortex can be activated optimally by contrast changes. In order to obtain the data illustrated in Fig. 1, at time 0 msec the contrast of a checkerboard pattern is reversed, and the EEG segment following stimulation is recorded for an epoch of 1000 msec. This procedure is repeated at a rate of 2 Hz, thus two stimuli occur during the recording epoch. The contrast reversal elicits an occipitally positive component with a latency of about 100 msec that, however, cannot be seen in the raw EEG. With the averaging of only a few trials it is obvious that large, independent potential fluctuations occur with positive and negative polarity at random (see upper two curves in Fig. 1); with further averaging their mean value tends toward 0 µV. On the other hand, all stimulus-related, time-locked VEP activity shows consistent polarities over the recording epoch, and a stable potential configuration emerges after summation of several single potentials. This can be seen for both contrast reversals that occur every 500 msec (stimulus onset is indicated in Fig. 1 by the solid vertical lines at 0 and 500 msec). The averaging of 32 single potentials yields a VEP waveform with a consistent positive component with a latency of about 100 msec (indicated by dashed lines in Fig. 1), and additional stimulus presentations result in

![Figure 1](image-url)
a further decrease in variability of the recorded signal. Evoked components are commonly denoted by their relative polarity (positive, P; negative, N) followed by the number of milliseconds of their approximate latency. Thus, Fig. 1 displays the so-called P100 component of the VEP.

The latencies and amplitudes of evoked potential components as well as the number of stimulus presentations needed to obtain a stable evoked brain response are dependent on the physical stimulus parameters as well as on the sensory modality: the amplitudes of the so-called brain stem auditory evoked potentials are in the order of 0.2–1.0 µV, thus 1500–2000 single evoked responses have to be used (Jewett et al., 1970). The small amplitudes are due to the fact that the neuronal elements activated are located in the brain stem structures of the auditory pathway, and thus are far away from the recording electrodes on the scalp. Along a similar line, fewer cortical neurons are selectively sensitive to visual horizontally disparate stimuli than they are to contrast changes, and 300–600 trials are needed to obtain a VEP elicited by stereoscopic stimuli (see later discussion on stereoscopic perception).

Evoked brain activity consists of a sequence of components that are interpreted to reflect steps in information processing; these must be determined by quantitative methods (Lehmann and Skrandies, 1980; Skrandies, 1987). Such components occur at times of high neural activity accompanied by strong electrical fields, and large potential differences are seen in the recorded wave forms. The main parameters extracted from evoked brain activity are component latencies (time between stimulus presentation and the occurrence of a given component indicating neural processing times), amplitude (strength of the evoked electrical field, indicating the degree of synchronous neuronal activation), and amplitude topography, which may give some indication of the neuronal populations involved in the processing of a given stimulus.

It is important to note that mapping of electrical activity does not make it possible directly to draw conclusions on the exact neuroanatomical locations of the intracranial sources. Neuronal mass activity produces electrical fields that spread via volume conduction throughout the brain, and these can be recorded at locations distant from the generating source. This has been shown in a study on various stages of the cat visual system, whereby single unit activity and field potentials were compared and the spread of electrical activity was evident throughout the brain (Skrandies et al., 1978). Thus, model source computations on scalp-recorded data always have to rest on certain explicit (and sometimes implicit) assumptions concerning the number, location, and spatial extent of dipoles as well as the homogeneity and geometry of the intracranial media in order to arrive at physiologically meaningful solutions (Koles, 1998). It is also obvious that the “inverse problem” of how to determine the sources of potentials in a conductive medium, when the scalp potential field is given, has no unique solution (Von Helmholtz, 1853). The computation of equivalent dipoles thus must be regarded as a further step of data reduction. The multidimensional scalp data space consisting of potential measurements from many electrode locations may be explained or modeled by an equivalent dipole data space with typically fewer dimensions. It is evident that such a data reduction has to be performed for each poststimulus time point separately, whereby the solution reflects the instantaneous source configuration.

As will be shown in the next section, direct interpretations of scalp potential fields in terms of intracranial neuronal generator locations may be misleading. This is due to the fact that the inverse problem, and source localizations, should mainly be
viewed as models that explain the scalp-recorded activity.

Visually elicited activity may be recorded noninvasively, both at the level of the retina as electroretinogram (ERG) and from the visual cortex as visual evoked potential. Here the focus is concentrated on VEP activity, and the reader is referred elsewhere for a more detailed description of electroretinographical methods in basic research and in clinical settings (Armington, 1974; Heckenlively and Arden, 1991). Skrandies and Leipert (1988) give some instructive examples on how the combination of cortical and retinal electrophysiological recordings allows the topological identification and diagnosis of the causes of visual field defects in neuroophthalmologic patients.

**MULTICHANNEL RECORDING AND TOPOGRAPHIC MAPPING**

EEG activity derives from an electrical field, the characteristics of which vary with time and space. Thus, the position of recording electrodes on the scalp determines the pattern of the recorded activity; multichannel recordings of EEGs and evoked potentials enable topographical analysis of the electrical fields of the brain as they are reconstructed from many spatial sampling points. [For details of topographical analysis of EEG data, see also Skrandies (2002) and Appendix E, this volume.]

Figure 2 illustrates the scalp distribution of evoked potential fields between 60 and 190 msec obtained from 30 electrodes, with contrast reversing stimuli presented to different retinal areas. The upper row in Fig. 2 shows maps of activity evoked by stimuli presented to the left hemiretina; the bottom map series shows activity elicited by visual stimuli presented to the right retinal half. The maps in the middle row illustrate the activity evoked when the same stimulus was foveated by the subject, and one can see that the major positive component that occurs at a latency of 110 msec shows a symmetrical distribution over the occipital areas. When lateralized stimuli are presented to the subject, it is obvious that the evoked potential fields show a strong lateralization of activity depending on retinal stimulus location. In humans, the retinal projections to the visual cortex are very orderly, resulting in a retinotopic cortical representation of the visual field. Due to the decussation of the ganglion cell fibers originating from the nasal retina in the optic chiasm, each visual half-field projects to the contralateral visual cortex. Thus, with lateralized

**FIGURE 2**

Topographical distribution of potential fields between 60 and 190 msec at 10-msec intervals evoked by contrast reversal stimuli presented to different retinal areas. Recordings were obtained simultaneously from 30 electrodes distributed over the head (note head scheme in inset). Checkerboard reversal stimuli were presented to the left or right hemiretina or with central fixation of the subject. In all map series a major positive component occurs with a latency of 110 msec with a symmetrical occipital distribution for central stimuli, and with a lateralized distribution for lateral stimuli. Equipotential lines in steps of 2 μV; hatched areas are negative with respect to the average reference.
stimulation, neurons are activated in the visual cortex ipsilateral to the retinal half that receives the stimulus. Inspection of the potential distributions in Fig. 2 reveals, however, that the evoked potential data appear to show a different picture: with lateral half-field stimulation we see an occipital positive component occurring between 100 and 120 msec after stimulation that is largest over the contralateral hemisphere (maps series in Fig. 2, top and bottom). This effect is called “paradoxical lateralization” of the VEP. From earlier work it is known that visual stimuli presented in the lateral half-fields yield a complex pattern of asymmetric distributions of evoked potential components on the scalp: ipsilateral and contralateral component locations have been described, and the direction and amount of scalp potential lateralization appears to depend critically on the physical stimulus parameters (Skrandies and Lehman, 1982). Of course, the lateralization of evoked potential components is different from hemispheric specialization effects.

One aim of electrophysiological recordings of human brain activity is the identification of the underlying sources in the brain. Information is processed in circumscribed areas of the central nervous system, and spontaneous activity also originates from specific brain structures. Thus, it appears of consequence to try to explain the topography of scalp distribution patterns in terms of anatomical localization of neuronal generators. To arrive at valid interpretations of scalp-recorded data is no trivial task: a fundamental and severe complication constitutes the so-called “inverse” problem that cannot be uniquely solved. Any given surface distribution of electrical activity can be explained by an endless variety of intracranial neural source distributions that produce an identical surface map. Thus, there is no unique numerical solution when model sources are determined, but knowledge of the anatomy and

FIGURE 3 Original and reconstructed potential fields evoked by stimuli in the left or right visual field at component latency (110 msec for left, 105 msec for right visual field stimuli). Original maps represent the original potential distribution; the model maps are the surface distribution computed from the model dipoles. The great similarity between the recomputed and original potential fields indicates that the model dipoles are able to explain most of the variance in the data (more than 95% for each data set). The head schemes with the results of model dipole computations are shown from above or from the left side. Dots mark the locations of the dipole, the lines indicate dipole orientation and strength. Recordings are in 30 channels, with electrodes evenly distributed between the inion and 25% of the nasion–inion distance (see scheme in Fig. 2).
physiology of brain systems allows deduction of a meaningful source localization (see below and Fig. 3). We note that this still implies that model sources are determined and this aspect needs to be considered when interpreting evoked potential or EEG data (Skrandies, 2002).

Data such as those illustrated in Fig. 2 indicate that the scalp locations of strongest electrical activity do not necessarily coincide with the intracranial localization of the neuronal generators, and most attention should be drawn to the areas where steep potential gradients occur. This will now be illustrated with results from dipole location computations. With mathematical approaches it is possible to compute the electric potential distribution on the surface of a homogeneous conducting sphere surrounded by air, which is due to a point current dipole inside the sphere (cf. Pascual et al., 1990). In addition, it appears reasonable to assume the head to be represented best by a concentric three-shell model (Ary et al., 1981). Other methods for localization of sources of electrical brain activity consider more complex anatomical (realistic head model) and physiological (distributed sources) information, as is illustrated by the merging of data from imaging methods and electrophysiological data (Fuchs et al., 1998; George et al., 1995; Koles, 1998; Pascual-Marqui et al., 1994; Skrandies, 2002).

The results of such a source localization computation for lateralized visual evoked potential fields are given in Fig. 3. In order to control for positional errors, prior to computation all electrode locations have been quantified by digitizing their positions in three dimensions on the subject’s head. This information, along with the positional information on the major anatomical landmarks of the head, was used for computation of best-fit dipole localizations. Figure 3 illustrates the dipole source location of a component occurring between 105 and 110 msec latency after the presentation of a visual stimulus in the left or right visual half-field. Component latency was determined by the computation of maximal field strength as the mean standard deviation within the field at each time point [i.e., global field power (GFP)] (Lehmann and Skrandies, 1980; Skrandies, 1987) (see also Appendix E, this volume).

The evoked potential fields at component latency [110 msec for stimuli presented in the left visual field (i.e., on the right hemiretina; upper part of Fig. 3), 105 msec for stimulation of the right visual field (i.e., on the left hemiretina; lower part of Fig. 3)] are illustrated in the maps on the left side of Fig. 3. As seen before, lateral visual stimuli result in a “paradoxical” lateralization, with potential maxima occurring contralateral to the retinal half stimulated. The results of the dipole computation are given as source localizations in the schematic head as seen from above or from the left side. Despite the lateralization of high peaks of activity over the contralateral hemisphere, the model sources are located in the hemisphere ipsilateral to the hemiretina stimulated. This is in line with the anatomy of the visual cortex whereby the retinal projections arrive in the calcarine fissure in the medial part of the ipsilateral occipital cortex. Electrodes over the contralateral hemisphere, however, appear to be located optimally to record most of the activity originating from the calcarine cortex. This observation has been confirmed by intracranial recordings in human patients (Lehmann et al., 1982), and it also explains why the retinal extension of the stimulus determines the amount of lateralization of the evoked brain activity (Skrandies and Lehmann, 1982).

We must stress the point that such dipole computations result in a model that best explains the electrical field recorded on the scalp, but due to the inverse problem discussed above, there is no unique solution for such computations. Anatomical locations of the neuronal sources determined may be quite different
if the same data have to be fit by more than one dipole or if different assumptions about conductivity and head geometry are made. On the other hand, the “model” maps computed from the dipole source solution (the so-called forward solution) are very similar to the measured data of our example: for both data sets illustrated in Fig. 3, more than 95% of the variance is explained. This indicates that the data reduction achieved by the model dipole computation yields reasonable results. It is important to keep in mind that the absolute locations of the potential maxima or minima in the field do not necessarily reflect the location of the underlying generators (this fact has led to confusion in the EEG literature, and for visual evoked activity this phenomenon became known as “paradoxical lateralization”). Rather, the location of steepest potential gradients in the scalp fields is a more adequate parameter, indicating the intracranial source locations. This is evident when the potential distribution maps and the location of the model dipoles are inspected in Fig. 3.

STEADY-STATE VEPs: INFLUENCE OF STIMULATION FREQUENCY

The data illustrated in Fig. 1 and 2 were elicited by a checkerboard pattern reversing in contrast at a rate of 2 reversals/sec.
and two responses occur in 1 sec. With increasing stimulation frequency the brain responses follow the reversal rates because each single stimulus elicits time-locked brain activity, and subsequent components overlap. This is shown in Fig. 4, where VEP activity was recorded while a checkerboard stimulus was reversed in contrast at 6, 8, 10, 12, or 14 reversals/sec.

All VEP wave forms are highly correlated with the stimulation frequency: e.g., for 6 reversals/sec three components occur within 500 msec, and 8 reversals/sec elicit four components, etc. This means that every contrast reversal is followed by evoked activity in the visual cortex. Such potentials are also called “steady-state” VEPs because it is assumed that repetitive stimulation results in a continuous stream of steady responses. It is also obvious that different frequencies yield brain responses of different strengths. Note that amplitudes are largest with the stimulus changing at 6 reversals/sec, and there is some amplitude tuning for the higher frequencies, with a relative maximum occurring for a stimulation frequency of 10 reversals/sec. Frequency analysis may be used to quantify amplitudes in given frequency bands and also to detect brain responses in noisy signals. Conventionally, this is done by computing a fast Fourier transform (FFT) on the VEP amplitudes, resulting in a description of the data in the frequency domain. As is evident from the wave forms in Fig. 4, low stimulation rates evoke time-locked activity as can be determined by visual inspection of the VEPs for frequencies up to a rate of 12 reversals/sec. On the other hand, it looks like there is no stimulus-related activity when the subject observes a checkerboard pattern changing at 14 reversals/sec.

The results of a frequency analysis, however, reveal that also with 14 reversals/sec significant stimulus-related VEP activity may be detected (see spectra in Fig. 4). Although its amplitude is rather small and the VEP wave form is largely dominated by lower frequencies, there occurs a clear peak at 14 Hz when the power spectra resulting in a frequency analysis are consulted (see Fig. 4, right side). Thus, prior knowledge of the temporal course of stimulation allows one to detect brain activity related to the processing of visual input.

Stimulation with high temporal frequencies may also be employed in order to study the time resolution and refractory periods of the human visual system. With double-flash stimulation (two flashes occurring at intervals in the order of milliseconds) Skrandies and Raile (1989) demonstrated that both retinal and cortical activity may be recorded with such stimuli. Most interestingly, even when the subject was not able to perceive two flashes, the evoked neuronal activity showed two responses. In addition, there were significant differences of retinal and cortical structures in temporal resolution capabilities: with intervals below 40 msec only very few subjects displayed a VEP response to the second flash, whereas the electroretinogram yielded two separate responses to a double flash even with an interval of only 10 msec. Differences between retinal and cortical processing are further supported by the fact that there appears to exist no direct relationship between the amplitudes and latencies of retinal and cortical potentials (Skrandies and Raile, 1989) indicating that knowledge of electrophysiological parameters in the retina does not allow prediction of how cortical potentials will be influenced by the variation of stimulus parameters.

### COGNITIVE AND AFFECTIVE PROCESSING OF THE BRAIN

Cognitive effects also affect evoked brain activity, which depends on the information processing during a task. Factors such as attention, motivation, or
expectancy as well as the occurrence probability of stimuli determine the pattern of electrical brain activity. The presentation of task-relevant information yields so-called endogenous components, commonly occurring with large latencies of more than 300 msec. In general, such components are elicited only when the stimulus is relevant for a task and the subject attends to the stimuli. An identical stimulus presented without task relevancy is not followed by this kind of activity. These endogenous components are interpreted to reflect higher, cognitive information-processing steps (see also Gazzaniga et al., 1998; Picton, 1988; Skrandies, 1995).

One may find that attentional processes also influence earlier components. In a study on visual information processing the randomized presentation of relevant and irrelevant alphanumeric and geometric stimuli yielded significant differences in evoked components at a latency of only about 100 msec, in addition to the expected effects occurring at much longer latencies (Skrandies et al., 1984). This indicates that rather early information-processing steps, probably in primary visual cortical areas, are influenced when the subject is involved in a pattern discrimination task [see Skrandies (1983) for a more detailed description]. Such data are in line with the report by Zani and Proverbio (1995), who illustrated the effect of selective attention to the size of checks (squares) on early VEP components.

In addition, there are systematic changes in the scalp topography of event-related brain activity during processing of language stimuli (Skrandies, 1998). According to the “semantic differential technique” the affective meaning of words can be quantified in statistically defined, independent dimensions, in which every word is uniquely located in three dimensions—evaluation (good/bad), potency (strong/weak), and activity (active–passive). These dimensions are very stable and culture independent (Osgood et al., 1975). It is important to note that visual processing of words yields a scalp topography of the P100 component which is globally similar to checkerboard evoked brain activity. With more detailed topographical analysis, however, small but significant differences appeared when the locations of the positive and negative centers of gravity (so-called centroids; for details see Appendix E) were compared (Skrandies, 1998).

When brain activity evoked by different semantic word classes was analyzed, significant effects were not restricted to late “cognitive” components, but brain activity at early latencies (corresponding to the P100 component) was affected by semantic meaning of the stimuli. These data show how visually evoked brain activity is modulated by the meaning of the stimuli at early processing stages (see Skrandies, 1998). In a similar way, it has been illustrated that attention affects early steps of visual processing (Skrandies et al., 1984). Thus, the influence of attention and cognitive parameters on activation of the visual cortex can be studied electrophysiologically by recordings of VEP activity.

Similarly, there are effects on brain electrical activity that accompany learning processes. From psychophysical experiments it is known that performance of a number of perceptual tasks improves as a result of training, not only during the ontogenetic development in early childhood but also in adults, reflected by perceptual improvements in sensory discrimination ability (Fiorentini and Berardi, 1981; Gibson, 1953). Similarly, neurophysiological studies on the cortical plasticity in adult animals have established that the representation of sensory functions in cortical areas is not hard wired, and it can change as a function of repeated stimulus processing. Selective deafferentiation is the most drastic alteration of adequate sensory input: the interruption of peripheral somatosensory afferences is followed by an extensive rewiring of cortical projections in the somatosensory cerebral cortex.
Such modifications were also found in animals trained for perceptual discrimination, whereby functional changes of cortical mechanisms have been documented with invasive neurophysiological methods; there is a correlation between functional changes observed in single-unit responses and sensory discrimination performance in adult monkeys observed with somatosensory stimuli (Recanzone et al., 1992) as well as in auditory frequency-discrimination tasks (Recanzone et al., 1993). For the mammalian visual system, functional changes in receptive field organization of cortical neuronal assemblies were demonstrated (Gilbert and Wiesel, 1992).

Electrophysiological correlates of improved discrimination performance of special visual stimuli have been reported by Skrandies and Fahle (1994) and by Skrandies et al. (2001). The human visual system is able to resolve stimuli with an accuracy that is much better than the spacing of individual photoreceptors in the retina: the small offset of line stimuli (so-called vernier targets) in the order of only a few seconds of arc may be detected by normal human subjects, yielding much higher than usual visual acuity coined (“hyperacuity”) (see overview in Westheimer, 1982). The repeated presentation of such visual vernier targets during an experimental session is accompanied by a significant improvement in sensory thresholds within less than half an hour of training. This learning is stimulus specific, based on the demonstration that there is no transfer of improved performance when the orientation of the stimuli is changed by 90° (Poggio et al., 1992). Thus, there are no attention effects, and the subject does not learn simply to adjust to the experimental procedure, but rather very specific information-processing strategies improve by training. In different populations of healthy adults, Skrandies and Fahle (1994) and Skrandies et al. (1996) consistently found that the mean performance improved significantly within about half an hour of passive training. Such improvements in performance derived from psychophysical testing are paralleled by significant alterations of electrical brain activity. Analysis of potential distributions recorded over the occipital areas of the subjects during the learning phase revealed highly significant changes. These effects were reflected by differences in the topography of the scalp potential distributions, with short latencies below 100 msec as well as at latencies extending to over 500 msec.

Figure 5 illustrates the mean potential fields of 10 subjects at 250 msec latency evoked by the first or second block of 600 presentations of vertical or horizontal vernier targets. Note the very small amplitude of the brain electrical response to such weak stimuli. This is commonly observed also with three-dimensional visual stimuli that selectively activate only a small population of neurons in the human visual cortex (see below). From Fig. 5 it is obvious that for both stimulus orientations the scalp potential fields that are elicited after learning are very different from those evoked by the same stimulus before learning. Before the training the potential fields are shallow, and display only little activity. After training a strong negative component over the occipital areas can be seen. The direct statistical comparisons computed as paired t-tests between maps turn out to be highly significant, indicating the occurrence of different electrical brain activity after learning (see significance probability maps illustrated in Fig. 5). These differences cannot be explained by a different time course of evoked activity in the two conditions, as has been shown in a number of different studies (Skrandies and Fahle, 1994; Skrandies et al., 1996, 2001). Learning of a vertical vernier target and learning of a horizontal target are both followed by similar electrophysiological changes, although differences in electrical activity,
depending on the orientation of grating stimuli, have been reported (Skrandies, 1984). Similarly, in our psychophysical experiments we could verify that improvements in performance over time are independent of the orientation of the stimulus (Skrandies and Fahle, 1994; Skrandies et al., 1996, 2001). These results suggest that after training intracranial neuronal generator populations were activated in a different way by an identical visual stimulus. It is important that in both psychophysical and electrophysiological experiments significant effects of perceptual learning were obtained with a similar time course. The high correlation between the change in perceptual performance and the change of stimulus-related brain potential topography as a function of practice, as well as the spatiotemporal pattern of neuronal activation with steep gradients over the primary visual cortex, corroborates the notion that perceptual learning occurs at an “early” level of visual processing. This interpretation is in line with the fact that neurons in the striate cortex respond to the presentation of vernier offset stimuli (Swindale and Cynader, 1986).

In summary, significant effects of perceptual learning can be obtained in both psychophysical and electrophysiological experiments with a similar time course—within about half an hour. The covariation of the subjective sensory and neurophysiological results illustrates that more efficient perceptual processing is paralleled by activation changes, mainly over the primary visual cortex, suggesting that implicit learning may occur at a relatively early level of perceptual processing. The neurophysiological data recorded noninvasively from large neuronal assemblies of human subjects simultaneously during perceptual processing reflect the dynamic changes going on at the cortical level (Darian-Smith and Gilbert, 1995).

Similar learning takes place with three-dimensional perception. Random-dot stere-
ograms (RDSs) have been used in studies for many years (Julesz, 1971; Bergua and Skrandies, 2000), and these stimuli contain only binocular horizontal disparity as depth cue to be extracted by the visual system. Three-dimensional information contained and hidden in RDSs is not easy to see. Similar stimuli are the so-called autostereograms, printed in the well-known “Magic-Eye” books; in these it is obvious that naive observers must learn to perceive a three-dimensional structure. With RDS stimuli most normal subjects also need several seconds or even longer to identify stereoscopic targets, and this response time drops significantly with practice (O'Toole and Kersten, 1992). Skrandies and Jedynak (1999) have shown in a combined psychophysical and electrophysiological study that more than half of the 16 subjects tested learned to see stereoscopic targets after 8 min of training. It is important to note that significant improvements in sensory discrimination occur even after viewing only stimuli below perceptual threshold. These observations are in line with previous studies on subliminal perception and implicit learning in normal subjects (Berry and Dienes, 1993) and “blind sight” in brain-damaged patients (Weiskrantz et al., 1974; Zihl, 1980), which also suggests that perceptual processing and learning are possible without conscious awareness. On a cortical level, this learning was accompanied by topographic changes in the electrophysiological pattern of activation of neural assemblies in the visual cortex, where the center of activity shifted toward the right hemisphere. Subjects who did not improve in perception displayed no such effects (Skrandies and Jedynak, 1999).

STEREOSCOPIC PERCEPTION AND EVOKED POTENTIALS: PHYSIOLOGICAL BASIS AND CLINICAL APPLICATION

Binocular and depth perception have been examined for many years and are being studied today by employing computer-generated random-dot stereograms. A historical account of the invention and development of random-dot stimuli has been given by Bergua and Skrandies (2000).

Three-dimensional depth perception is based in part on the fact that our two eyes see the environment from slightly different viewpoints, and depth information is extracted from the horizontal disparity of visual stimuli on the two retinas. Slight differences in the image viewpoints—horizontal disparity—are the crucial cue for depth perception. Because the input into the two eyes remains separated up to the level of the visual cortex (Bishop, 1973; Gonzalez and Peres, 1998), evoked brain activity generated exclusively by cortical structures may be investigated when random-dot stereograms (Julesz, 1971) are presented binocularly. Such RDS stimuli do not contain any contrast information, and can be used to investigate three-dimensional vision in isolation. Commonly, such stimuli are presented dynamically at high frequency by modern computer graphics (Skrandies, 2001). The perception of these stereograms depends on the fusion of two nonidentical, horizontally disparate inputs in the visual cortex, and under monocular viewing conditions a dynamic RDS (dRDS) stimulus cannot be perceived stereoscopically. The neuronal correlates of these processes are cortical neurons selectively responsive to disparate binocular stimuli; these as have been found in the monkey visual cortex (Hubel and Wiesel, 1970; Von der Heydt et al., 1981).

For experimental studies of human vision, the use of dRDSs offers the possibility to investigate selectively cortical processing of visual information. With random-dot displays any desired three-dimensional form can be created: e.g., a three-dimensional checkerboard pattern is produced when each eye sees a different array of randomly arranged dots, and one
of the patterns is horizontally displaced in such a way that the area of each individual check square contains crossed binocular disparity. After binocular fusion, these areas will stand out in front of the plane of fixation, and a study participant will perceive a checkerboard pattern hovering in front of the monitor. The time-locked averaging of electrical brain activity is triggered by the sudden change in horizontal disparity, but independent stimulation of the two eyes may be achieved by employing polarizing foils or anaglyphs (red and green dots in combination with red/green goggles), or by liquid crystal diode shutter glasses. With such glasses, dRDSs are presented as monocular half-images alternating at the refresh rate of the monitor, and the glasses are electronically synchronized with the monitor frequency so that every second image is seen by one eye only. For practical application, the different methods yield very similar perceptual effects, they are employed only in order to route independent information to the left and the right eye.

Figure 6 illustrates evoked potentials recorded from a healthy young adult. Checkerboard reversal stimuli with contrast borders were presented either monocularly to the left and right eyes (lowest two curves) or binocularly (second curve). It is obvious that differences in component latencies can be seen when VEPs evoked by monocular and binocular stimulation are compared: stimulation of both the left and right eyes yields latencies of 113 msec, whereas binocularly evoked brain activity displays a component latency of only 103 msec. Such binocular summation effects have been described before, illustrating that latencies or amplitudes of the evoked potential are significantly different when binocular and monocular conditions are compared (e.g., Nakayama et al., 1982; Skrandies, 1993). The physiological correlate for such findings is the fact that many neurons of the mammalian visual cortex are influenced by input from both eyes (Gonzalea and Perez, 1998), and vision with two eyes and monocular vision result in different perceptions. Binocular fusion of disparate retinal images yields stereopsis (see below), and vision with two eyes enlarges the visual field. In psychophysical experiments it was shown that with binocular stimuli higher contrast sensitivity is obtained, as compared with monocular targets (Campbell and Green, 1965).

Figure 6 also shows stereoscopic VEPs that were elicited by the presentation of a three-dimensional checkerboard pattern: red/green anaglyph dynamic RDS patterns that were generated every 20 msec by special hardware were presented on a color monitor. By using red/green spectacles, each eye saw only a portion of the dots displayed, and the green pattern was horizontally displaced in such a way that the subject could perceive a checkerboard pattern, etc.
pattern standing in front of the plane of the monitor. Disparities were changed locally every 256 msec by 13.8 min of visual angle, resulting in the percept of a three-dimensional checkerboard pattern that stood in front of the monitor and reversed in depth. Stereoscopic evoked activity yields evoked components with latencies very similar to those due to contrast evoked brain activity, whereas stereoscopically elicited amplitudes were significantly smaller. This is evident in Fig. 6, and has been described repeatedly (Skrandies, 1986, 1991, 2001; Skrandies and Vomberg, 1985), suggesting that the afferent binocular information flow to the human visual cortex is of similar velocity for processing of both dynamic RDS patterns and contrast borders. On the other hand, three-dimensional stimuli are significantly less effective in exciting many visual neurons synchronously, which is in line with the assumption that there are many more neurons sensitive to contrast changes than there are neurons selectively sensitive to binocular disparate stimuli. In addition, topographic comparisons of stereoscopic and contrast evoked potential fields suggest that disparate retinal stimuli are processed preferentially by neuronal populations outside area 17 (Skrandies, 1986, 1991, 1997; Skrandies and Vomberg, 1985), which is consistent with results obtained with single-unit recordings in cats and monkeys (Hubel and Wiesel, 1970; Von der Heydt, 1981).

Within certain physiological limits, increasing disparities lead to the perception of increasing depth, and one would expect some optimal disparity range when depth perception is strongest. Thus, stereoscopic evoked brain activity also depends on the horizontal disparity of the RDS stimulus, and significant effects of horizontal disparities on brain electrical activity are observed (Skrandies, 1997).

Figure 7A illustrates the topographical data recorded in 30 channels over the occipital areas with dynamic RDS stimuli of different disparities, ranging from 7 to 24.5 min of arc. Stimulation frequency was 6 Hz, and stimulus-locked brain activity was obtained with all disparity values. The maps in Fig. 7A are the responses occurring at stimulation frequency. With large or small disparities, potential field strength was rather small, whereas the largest responses were obtained with intermediate disparities, as is evident from the fewer field lines in Fig. 7A. This observation illustrates that there is a functional disparity tuning of cortical activation: low and high disparities yield less synchronized neural activity as compared to intermediate disparities. This tuning of response strength is in line with studies on single neurons in the monkey visual cortex (Gonzalez and Perez, 1998; Hubel and Wiesel, 1970). In addition, significant differences were observed in dRDS evoked brain activity when central and lateral stimulus locations were compared. With lateral stimuli (extending from the fovea to 17.1° eccentricity), maximal amplitudes were obtained at larger disparities than with central stimuli (Fig. 7B): with RDS stimuli presented to foveal areas, the largest amplitudes occurred with mean disparities of 10.5 min of arc, whereas with lateral stimuli, sensitivity was largest with stimuli of 14 min of arc (Skrandies, 1997). These observations indicate that more peripheral and lateral areas are less sensitive to disparity information, supporting data on disparity thresholds for fusion where for patent and qualitative stereopsis as well as stereo, thresholds increase with retinal eccentricity (Ogle, 1962).

Further analysis of the data also reveals that there are not only differences between central and eccentric stimulation, but that there are also pronounced differences between brain activity evoked with stereo stimuli presented in the left or right visual field (Fig. 7B). Stimuli located in the right visual field show a tuning function with a clear response peak at 14 min of arc disparity. Neuronal response strength is
significantly reduced for higher and lower disparities, as is reflected by smaller amplitudes of brain electrical activity. Surprisingly, with stimuli presented in the left visual field the brain responses lack this tuning function: here all horizontal disparities appear to be processed in a similar way, and there is no peak in the tuning curve. In a population of 22 test subjects there was no preference for a certain disparity of the RDS stimuli, and an analysis of variance confirmed a significant interaction between visual field location and disparity. These results are independent of the location of the recording site, because recording electrodes over the left and right hemispheres yield very similar results (Skrandies, 1997). The lack of disparity tuning of VEP responses with stimuli in the left visual field is explained by high intersubject variability of amplitudes in this stimulus condition. In the case of large-amplitude variation between subjects, the tuning effect is expected to disappear. Thus, the basic difference between the processing of disparity information in the left and right visual fields may be explained by the smaller variation and higher consistency of brain activity elicited by three-dimensional stimuli presented to foveal areas or parafoveal areas extending toward the right visual field, indicating differences in global processing of three-dimensional information.

Knowledge of the influence of the horizontal disparity of VEP activity may be useful for the clinical application of recordings of stereoscopically evoked brain activity. In psychophysical and electrophysiological experiments, we compared patients with selective disturbance of stereoscopic vision and healthy young adults (Vomberg and Skrandies, 1985; Skrandies, 1995, 2001). It is important to
note that meaningful comparisons are possible only with patients who have normal visual acuity in both eyes and who possess other normal visual functions (color vision, visual fields, contrast sensitivity). It is comprehensible that these are rare cases because the patients have no subjective symptoms and experience only very little disturbance.

The data displayed in Fig. 8 illustrate evoked potentials recorded from a subject with microstrabism. The conventional VEPs elicited by contrast reversal stimulation of the left and right eyes or binocularly, show amplitudes and latencies in the normal range. As in the healthy subject, with binocular stimuli, significantly shorter component latencies (108 msec) are observed as compared with monocular stimulation (115 msec). However, with dRDS stimuli, quite a different picture emerges: when a stereogram with a horizontal disparity of 13.8 min of visual angle is presented, the major VEP component displays a reduced amplitude as well as a latency prolongation by more than 20 msec, resulting in a component latency of about 140 msec. These data suggest that there is some deficiency that affects only stereovision in this patient, leaving the processing of contrast information intact. This is in agreement with the fact that this patient had increased psychophysical thresholds for three-dimensional stimuli.

With an increase of horizontal disparity ("more depth"), the pathological VEP activity may become normal: a dRDS pattern with a horizontal disparity of 27.6 min of visual angle elicits brain activity with normal component latencies (113 msec) and amplitudes that are similar to those of the healthy subject (compare the upper curves of Figs. 6 and 8).

Related electrophysiological results have been described by Vomberg and Skrandies (1985) and Skrandies (1995, 2001) in groups of patients with various degrees of stereovision deficiency but normal binocular visual acuity: there is a high correlation between disparity thresholds that were determined psychophysically and electrophysiologically in a group of patients with various degrees of stereovision deficiency but normal binocular visual acuity.

Such results indicate that the recording of brain activity evoked by three-dimensional stimuli may be employed to objectively determine stereovision capability. Another application is the monitoring of visual development in infants: similar to many other sensory functions, depth perception is no innate capacity but has to be learned in the first months of life. This has also been demonstrated in evoked potential studies in which, with contrast stimuli, evoked brain activity is recordable in neonates; using RDS stimuli, stimulus-related brain activity is elicited only after about 4 months of age. The critical period of stereovision development as determined electrophysiologically is in the
order of 10 and 19 weeks of age, which is somewhat earlier than when it is determined by behavioral methods (Petrig et al., 1981).

CLINICAL APPLICATIONS IN NEUROLOGY AND OPHTHALMOLOGY

The classical application of VEP measurements for clinical purposes is its contribution to the diagnosis of multiple sclerosis (MS). The main characteristic of this disease is the patchy demyelination of afferent and efferent nerve fibers distributed all over the nervous system, and the patients have neurological symptoms that cannot be explained by a single lesion. Myelin is an insulating sheath, found on most axons, that increases conduction velocity (cf. Kandel et al., 2000), thus, electrophysiologically, latency prolongations are expected when demyelination occurs. In many patients the visual system is affected at an early state of the disease, and one finds patients with pathological VEP results who, however, do not display any subjective visual symptoms (i.e., they have normal visual acuity and visual fields). An optic neuritis occurs frequently at a very early stage of the disease, which in general is followed by a recovery after several weeks, whereas other symptoms—hemipaesthesia, ataxia, and sensory disturbances—may be seen only after some years. The diagnosis of MS is warranted only if several independent lesions can be quantified, or if several repeated attacks of similar neurological symptoms occur over time. Thus, with pathological VEP measurements clinically silent lesions can be detected in patients with no visual symptoms, and this may contribute to a final diagnosis of MS. For more information on pathophysiological and clinical details of MS the reader is referred to Bauer et al., (1980) and McKhann (1982).

Other applications of VEP measurements in ophthalmology and neurology comprise the documentation of visual development in infants (as discussed in the section on stereoscopic vision) as well as the topologic localization of disturbances in the visual system (Heckenlively and Arden, 1991). The combined recordings of VEP and ERG activity allow localization of lesions in the afferent visual pathway in patients with visual field defects. Skrandies and Leipert (1988) could demonstrate a significant relationship between pathological electrical activity and the site of the lesion in a group of neuro-ophthalmological patients. After lesions of the optic nerve or optic tract, ERG changes appear in parallel to a retrograde degeneration of the axons of the retinal ganglion cells. On the other hand, in adult patients with cortical lesions, no electrophysiological sign of subsequent retinal alterations can be found. This has also been demonstrated in controlled lesion experiments performed on adult cats (see Skrandies and Leipert, 1988). In summary, such data illustrate the topodiagnostic possibilities of the combination of various electrophysiological recordings in patients with defective vision. Due to their noninvasive nature and their sensitivity to functional (and not only structural and anatomical) changes, these methods are commonly applied for a wide variety of diagnostic questions.

CONCLUSION

Classical psychophysics allows study of integrative, subjective aspects of sensory information processing, but electrophysiological experiments give us tools for the assessment of neuronal mechanisms at various levels of the central nervous system. In addition to the visual processes described in this chapter, various sensory modalities may be investigated with only minimal active cooperation of the subject, and primary sensory evoked brain activity
is largely independent of cognitive processing strategies.

High temporal resolution inherent in electrophysiological recordings helps to reveal steps in information processing occurring in fractions of a second. For functional analyses of sensory processes this is a significant advantage over brain imaging techniques such as computer tomography, positron emission tomography, or magnetic resonance imaging, the strengths of which are the exact anatomical three-dimensional identification of structures of the central nervous system. For MRI, substantial improvements in time resolution are in reach, as reports on “functional MRI” suggest (cf., Belliveau et al., 1991; Frackowiak et al., 1997). However, the direct relationship between neuronal activation and local hemodynamic changes that occur on a much cruder time scale still remains unclear (George et al., 1995). Although it has been demonstrated that functions of the human visual cortex may be successfully studied by fMRI (Wandell, 1999), due to the huge cost of the equipment and the technical operating expense, however, one may predict that in most cases the access to such techniques will be restricted to medical centers specialized for clinical diagnosis, and in general it will not be available on a routine basis for workers in the fields of sensory physiology or experimental psychology. On the other hand, electrophysiological recording of brain electrical activity is relatively easy to perform, and it has widespread applications in the fields of human basic and clinical neurophysiology as well as in cognitive neuroscience (Gazzanigga et al., 1998).

The noninvasive recording of evoked potentials constitutes a powerful supplement to psychophysical testing, and it may reveal steps of information processing with a high resolution in the time domain. As has been illustrated in this chapter, electrophysiological measures may also be employed for functionally localizing certain effects in the central nervous system, as is also evident from the clinical applications of auditory brain stem potentials, electroretinography, and visual evoked brain activity. On the other hand, it is important to keep in mind that direct interpretations of electrical brain activity in terms of absolute anatomical localization of neuronal generator populations are not warranted. Careful experimental planning as well as profound knowledge on the anatomical and neurophysiological bases of perceptual processes are mandatory in order to arrive at a meaningful interpretation of the recorded data. Thus, a combination of psychophysical and electrophysiological methods in controlled experiments holds the promise for further insight into the mechanisms of sensory information processing in the human brain in the future.

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References


