Acta Neurobiol. Exp. 2000, 60: 467-478

Expectation of an important event affects responses to irrelevant stimuli of different modalities

Andrzej Michalski

Department of Neurophysiology, Nencki Institute of Experimental Biology,
3 Pasteur St., 02-093 Warsaw, Poland, Email: michan@nencki.gov.pl

Abstract. Periodic alterations of event-related potentials (ERPs) were studied during "oddball" tasks. Sequences of randomly intermixed frequent (non-target) and rare (target) stimuli were presented. In visual experiments, these were flashes of light of two different colors. In auditory tests there were two tones of different frequencies. The instruction was to keep a mental count of each target stimulus. To study the alterations of the "state of the brain" produced by target detection, responses to non-targets immediately following targets were compared with responses to an eighth subsequent non-target stimulus. To evaluate the effect of such "brain states" on responses to stimuli of a different modality, additional visual stimuli (probes) were delivered after both auditory and visual "oddball" stimuli. It was found that responses to the eighth presentation of non-target stimulus were preceded by significant negative shift of recorded potential. This shift was smaller before the responses to non-targets immediately following the presentation of target stimuli. The difference was significant both in auditory and visual tests. Responses to "oddball" stimuli were little affected: only the reduction of P200 peaks in "after target" responses was significant in visual tests. Responses to probes showed stronger effects: when visual probes followed visual "oddball" stimuli, all three components measured (N100, P130 and P200) were shifted positively in responses to eighth presentations of non-targets. When visual probes were presented in auditory tests, only the amplitude of the N100 component was significantly affected.

Key words: sequential effect, "oddball" task, probes

INTRODUCTION

An extensively studied problem in brain physiology is the relationship between the brain's response and the physical parameters of the stimuli that evoke a response. A great number of experiments, from behavioral observations to measurements of electrical potentials, indicated that identical stimuli seldom produced identical responses. It is generally assumed that a specific response results from an interaction of the incoming stimulus and the "brain state" at the time of stimulus arrival. It is obviously very difficult to precisely define "brain state" but several attempts have been made in simplified models. For example, it has been found that electrical potentials evoked by neutral stimuli in humans were systematically altered by factors such as emotions and stress (Michalski 1998, 1999). Momentary maps of brain electrical fields displayed repetitive patterns that could be suggested as markers of "brain microstates" (Lehmann et al. 1994, Kondakor et al. 1995). It was found that these spontaneous microstates were correlated with alterations of electrical responses evoked by external stimuli.

An interesting model of periodically changing "brain state" is offered by "oddball" paradigm, commonly used to evoke a P300 wave in scalp-recorded potential (Desmedt et al. 1965, Sutton et al. 1965). In this paradigm, infrequent target stimuli are randomly interleaved with more frequent non-target signals. Subjects are either asked to produce motor responses to target events or to count them mentally and report their number at the end of the experiment. Non-target stimuli are ignored. In the great majority of experiments aimed at the analysis of the P300 component all non-target responses were averaged together and compared with the averaged response to target stimuli. However, in the now classical experiment, Squires and co-authors (1976) found alterations of responses to stimuli, depending on their position in a sequence of targets and non-targets. In particular, there were differences in responses to non-targets immediately following the presentation of target stimuli and responses to non-targets preceded by the presentation of a number of non-targets. These alterations were further studied by Hirata and Lehmann (1990) and Starr and co-authors (1995, 1997). It was reported that the amplitude of the N100 component was reduced in responses to non-targets that directly followed target stimuli (Hirata and Lehmann 1990, Starr et al. 1997). This wave gradually increased in amplitude with subsequent presentations of non-targets. The positive P200 component was larger in responses to non-targets presented immediately after targets and then decreased gradually with the number of non-targets in a sequence (Starr et al. 1997). The duration of the P200 component increased with the increasing number of subsequent non-targets, extending even to the latency region where P300 to targets would occur (Starr et al. 1995, 1997). These elongated P200 components were followed by a negative, late, slow wave of increasing amplitude (Starr et al. 1997). Systematic alterations were found also in the slow, negative potential shifts that preceded stimulus presentation (McCarthy and Donchin 1976, Squires et al. 1976, Hermanutz et al. 1981, Sams et al. 1984, Verleger, 1987, Hirata and Lechmann 1990, Starr et al. 1995, 1997). These shifts, very small in responses to non-targets immediately following targets, increased with subsequent non-target presentations. But there were also inconsistencies between the reports: Starr and co-authors (1995) found no significant differences in N100 or P200 amplitudes. Moreover, most of the sequential alterations were found when subjects were asked to press the button in response to target stimuli. When the task was to keep a mental count of the targets, sequential effects were much less clear (Starr et al. 1995, 1997). Finally, all the data concerning periodic modulation of responses in the "oddball" tests were collected in auditory experiments. Nothing is known about the behavior of other sensory systems.

More detailed knowledge of how incoming stimuli and their classification (relevant vs. meaningless) alter the "brain state" and how this "brain state" affects the responses to subsequent stimuli can be very important for our understanding of the brain as an information processor.

The aim of the present experiment was to gather the data that should help to answer the following questions:

1. To what extent is a motor act necessary in producing the sequential effects seen in other ERP studies?
2. Do these effects look similar if they are evoked by visual as opposed to auditory stimuli?
3. How do the "brain states" generated in the "oddball" paradigm affect the other, completely unattended, stimuli?
4. Are the effects modality specific? If stimuli of one modality are used to manipulate the "brain state", how this "brain state" alters the responses to stimuli of different modality?

To answer these questions, the present study used the probe technique introduced by Rockstroh and co-authors (1992, 1993) for the analysis of cortical responsiveness during slow potentials of positive and negative polarity. Additional stimuli (probes) were delivered at various intervals after initial "oddball" stimuli. The neurophysiological state of the cortex was inferred from the parameters of the potentials evoked by these probes. In the present experiment, probes offered the possibility of testing the transfer of sequential effects between different stimulus modalities. The probes also represented the completely ignored stimuli, whereas both target and non-target "oddball" stimuli had to be attended to in order to differentiate between them.

METHODS

Data were collected from 12 volunteers of both sexes (9 females and 3 males), aged 27-48 years. Informed consent was obtained from all participants.

EEG signals were recorded with four disc electrodes glued at Fz, Cz, Pz and Oz positions, referenced to linked mastoids and supplemented by vertical and horizontal EOG recording. Software (Elmiko Paperless EEG system) rejected EEG epochs if EOG amplitude exceeded 40 μV. Rejected epochs were replaced with the new ones. Signals were sampled with 2048 Hz frequency, 12 bit resolution, digitally filtered 0.16-35 Hz and reduced to 256 Hz by averaging the adjacent points.

In visual experiments, flashes of centrally located yellow and red squares were used as stimuli. Squares, 2 deg x 2 deg of visual angle, were formed with spatially overlapping arrays of light emitting (LED) diodes of both colors. Subjects were asked to fixate the center of the arrays. Luminosity was 10 cd/m^2 against 1 cd/m^2 background. They were switched on for 100 ms. In auditory experiments, tones (80 db, 100 ms duration) of 1,000 Hz and 2,000 Hz were presented by earphones. Tones were produced by driving the earphones with a sinusoidal signal.

The experimental paradigm is shown in Fig. 1. Each row of the figure represents a 2 s long epoch i.e., the time when data were stored. There was a 0.2 s break between the epochs. Each epoch consisted of a 1 s long prestimulus recording after which an "oddball" stimulus was presented. In visual experiment (left column), it was either the red square (non-target) or yellow square (target). In the auditory experiment (right column), it was either the 2,000 Hz tone (non-target) or 1,000 Hz tone (target). Targets and non-targets were presented in random order but targets were less frequent. The probability of occurrence of target stimulus was 0.12. Subjects were asked to mentally count the target stimuli and report their number at the end of the recordings. Data were rejected if the counting error was bigger than 20%. Non-targets were ignored. Within each epoch, with a specified delay after target or non-target, an additional probe stimulus was delivered. This was always the green square of the same spatial location, size, luminosity and duration as the other visual stimuli. Subjects were instructed to ignore the probes. In the visual experiment, probes and the initial "oddball" stimuli were of the same modality. In the auditory experiment, probes were in the visual modality. After probe presentation, the recording continued till the end of the two seconds long epoch. Standard equipment for the analysis of "oddball" data was modified in such a way that responses to the first non-target after each target were averaged in one channel and responses to the eighth non-target after a target were averaged in the other channel. Averaging continued until 50 good repetitions were collected in the second channel. Both averaged waveforms also contained averaged responses to probes.

Four blocks of trials were completed with each subject:

1. visual "oddball" stimuli with visual probe delivered 400 ms after each visual stimulus,
2. visual "oddball" stimuli with visual probe delivered 600 ms after each visual stimulus (not shown in Fig. 1),
3. auditory "oddball" stimuli with visual probe delivered 400 ms after each auditory stimulus,
4. auditory "oddball" stimuli with visual probe delivered 600 ms after each auditory stimulus (not shown in Fig. 1).

The order of these blocks was counterbalanced between subjects.

In responses to visual stimuli, amplitudes and latencies of three components were measured, both in initial responses to "oddball" stimuli and in responses to probes:

1. the earliest measurable negative component with a mean latency of 95 ms (N100),
2. positive wave with a mean latency of 129 ms (P130),
3. positive component with a mean latency of 211 ms (P200).

Two components were measured in responses to auditory stimuli:

1. large negative component with a mean latency of 93 ms (N100),
2. positive component with a mean latency of 185 ms (P200).

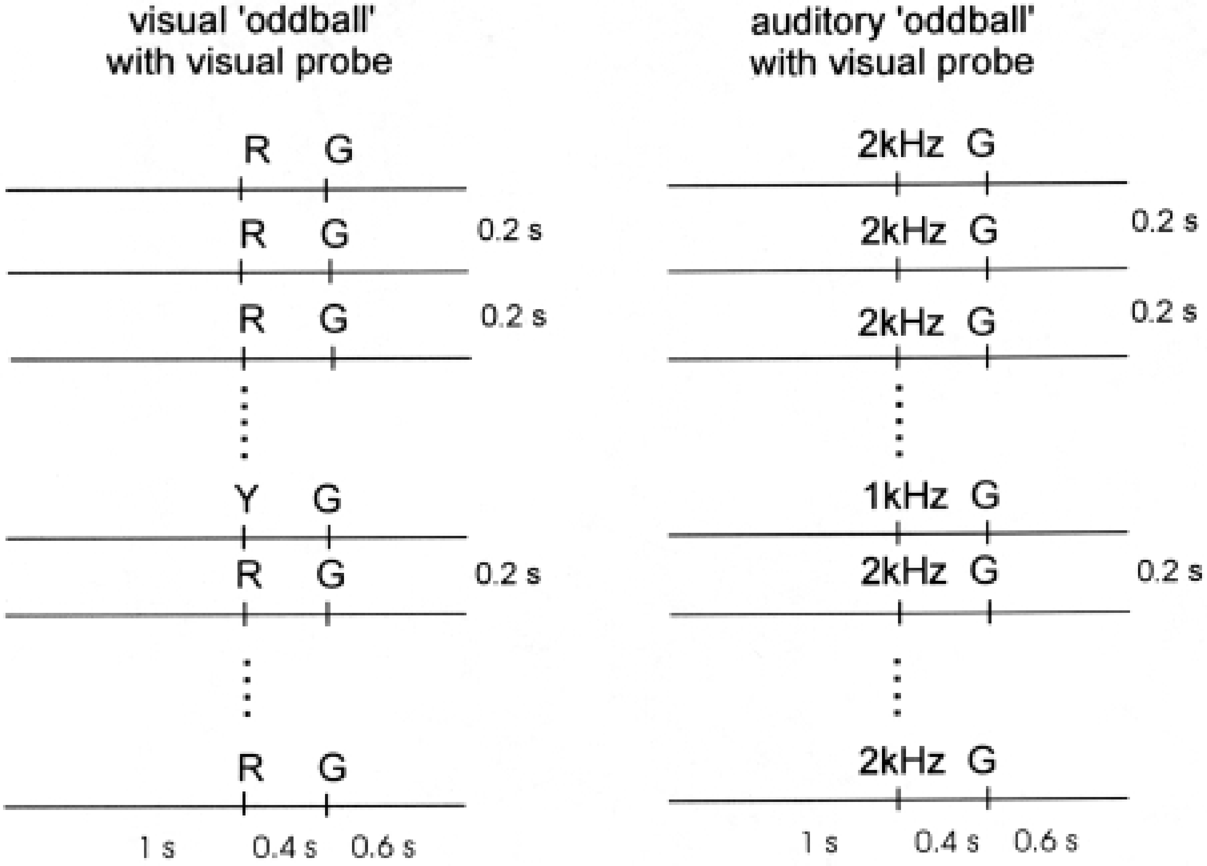

Fig. 1. Graphic illustration of the experimental paradigm. Horizontal lines represent the epochs during which data were collected. In the visual experiment (left column), yellow squares (Y) were presented among the more frequent red squares (R). At a specified delay, both were followed by the presentation of green squares (G). In the auditory experiment (right column), 1 kHz tones were presented among the more frequent 2 kHz tones. Auditory stimuli were followed by the presentation of green squares (G), the same as in the visual experiment. Subjects were asked to count mentally the Y squares or 1 kHz tones. For the full description see the method section.

Components were measured using a cursor on a computer screen. Data were transferred to SYSTAT program for multi-factor analysis of variance (ANOVA). To provide compatibility with previous experiments (Starr et al. 1995, 1997), amplitudes were defined relative to the averaged pre-stimulus level. This level was measured 250 ms - 500 ms before the onset of the "oddball" stimuli. Part of the recording immediately preceding the stimulus onset was not used for this measurements due to the expected pre-stimulus voltage shifts (Hirata and Lehmann 1990, Starr et al. 1995, 1997). The latencies of peaks were defined from the largest excursions of specific components.

In addition, grand-averaged waveforms were computed by averaging data for all subjects, in each experimental condition.

RESULTS

Figure 2 shows the grand-averaged responses to non-target stimuli immediately following targets and to the eighth presentations of the same non-target stimulus. Responses to "oddball" stimuli are followed by responses to probes delivered 400 ms and 600 ms later. "Oddball" stimuli were either visual or auditory. Probes were always visual. Figure 2 indicates that sequential alterations observed without motor responses to targets are rather weak and can not be easily seen on grand-averaged traces.

Visual "oddball" stimuli with visual probes

Amplitudes and latencies of every component were separately analyzed with identical, three-way ANOVAs (elec-

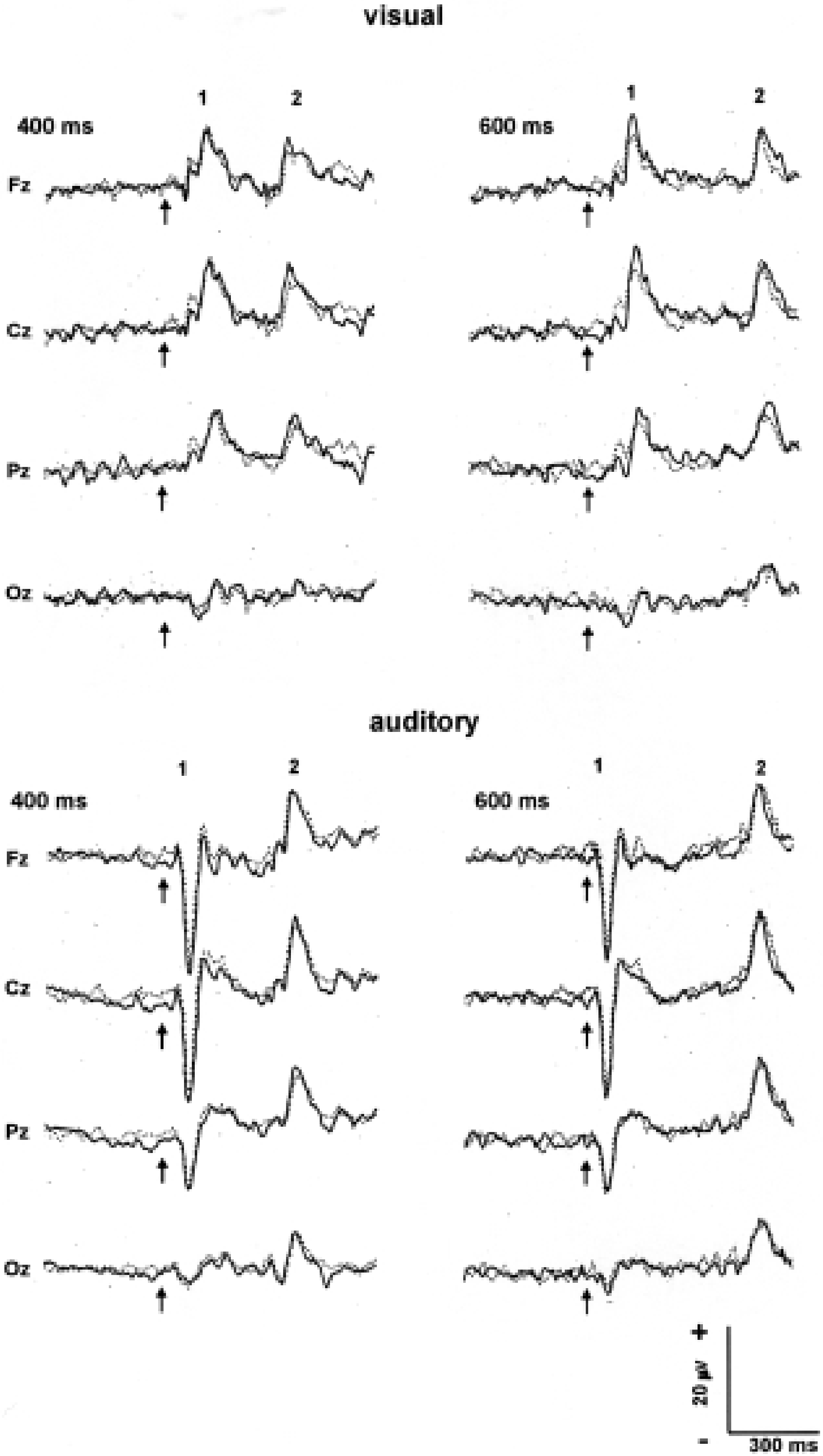

Fig. 2. Grand-averaged responses to non-target stimuli presented as first (dotted line) and eighth (solid line) non-targets after targets. Upper block, potentials recorded in visual "oddball" experiments in which both target and non-target stimuli were visual. These were followed by visual probes presented 400 ms or 600 ms later, as indicated above the traces. Lower block, potentials recorded in auditory "oddball" experiments in which both target and non-target stimuli were auditory. These were followed by visual probes. Arrows indicate the onset of the initial non-target, "oddball" stimuli. Numbers label the responses to non-target stimuli (1) and responses to probes (2).

trode x delay x sequence). The delay variable indexed the 400 ms and 600 ms delay with which probe stimulus was delivered. Delay could not affect the early "oddball" responses, but it was used in this analysis in order to check for uncontrolled differences between the recording conditions. The sequence variable indexed the responses to the first and the eighth non-target after a target stimulus.

RESPONSES TO "ODDBALL", NON-TARGET STIMULI

Amplitudes of the N100 components differed significantly only between the electrodes ($F_{3,168}$ = 3.894, P=0.01). Bonferroni tests revealed that Oz waves were different from Cz (P=0.038) and Fz (P=0.015) potentials. Latencies of the N100 component did not show any significant effects.

Amplitudes and latencies of the P130 component differed only between the electrodes ($F_{3,168}$ = 62.789, P<0.001 for amplitudes and $F_{3,143}$ = 13.366, P<0.001 for latencies). Bonferroni tests showed that amplitudes and latencies recorded with Oz electrode differed from all the others (P<0.001 in all cases). The P130 component was selected for analysis in spite of the fact that Oz recordings showed a negative rather than positive deflection within its latency range. This was done because the grand-averaged curves (Fig. 2) indicated that the P130 component could be affected by stimulus sequence. The combination of the highly significant effect of the electrode (ANOVA) and the clear difference between Oz and all the other recordings (Bonferroni) most likely reflected this polarity reversal.

Significant effects of stimulus sequence were found for the P200 components. This wave was smaller in responses to non-targets immediately following targets than in responses to the eighth subsequent non-target ($F_{1,165}$ = 8.045, P=0.005). The mean amplitude of the P200 component was 9.57 μV (SD = 7.2) in "after target" responses and 12.43 μV (SD = 7.7) in later responses. Amplitudes of the P200 components also differed between the electrodes ($F_{3,165}$ = 22.5, P<0.001). Bonferroni test showed that Oz recordings differed from all the others (P<0.001 in all cases). Pz recordings also differed from Cz recordings (P=0.022). Latencies of P200 components did not show any significant effects. Since earlier reports indicated that the duration of the P200 wave was altered by stimulus sequence (Starr et al. 1995, 1997), the width of this component was measured at its half-height and analyzed with the same ANOVA. No significant differences were found.

RESPONSES TO PROBES

Amplitudes of the N100 components were significantly affected by stimulus sequence ($F_{1,164}$ = 11.301, P=0.001). In addition, there was a significant interaction between the effects of the sequence and the delay ($F_{1,164}$ = 9.573, P=0.002). When the data for each delay were analyzed separately with two way ANOWA (sequence x electrode), a highly significant effect of stimulus sequence was found among responses to probes presented with 400 ms delay ($F_{1,80}$ = 21.217, P<0.001). The mean amplitude of the N100 component in responses immediately following targets was - 6 μV (SD = 2.9). In responses following the eighth non-targets it was -1.6 μV (SD = 6.3). When probe stimuli were delivered with 600 ms delay, the effect of the stimulus sequence was insignificant. Amplitudes of the N100 components also differed significantly between the electrodes ($F_{2,164}$ = 8.432, P<0.001). Bonferroni tests revealed that this component was significantly smaller (less negative) in Oz than at any other recording site (P=0.002 in all cases). Latencies of the N100 component did not show any significant differences.

A significant effect of stimulus sequence was found also on the amplitudes of the P130 component ($F_{1,164}$ = 6.037, P=0.015). The mean amplitude of this component was -0.35 μV (SD = 5.5) in "after target" responses and +1.1 μV (SD = 5.8) in responses following the eighth non-target. The effect did not depend on probe delay. Both amplitudes and latencies of the P130 components differed between the electrodes ($F_{3,164}$ = 6.037, P=0.015 for amplitudes and $F_{3,131}$ = 9.636 P<0.001 for latencies). Bonferroni test showed that amplitudes and latencies of Oz waves differed from all the others (P<0.001 in all cases).

Finally, stimulus sequence affected the amplitudes of the P200 components ($F_{1,164}$ = 17.943, P<0.001). Mean P200 amplitude was 9.04 μV (SD = 6.2) in "after target" responses and 12.67 μV (SD = 6.4) in the eighth responses. The effect of the delay was of borderline significance (P=0.059). Amplitudes of the P200 components differed significantly between the electrodes ($F_{3,164}$ = 17.943, P<0.001). Oz amplitudes were smaller (less positive) than all the others (Bonferroni, P<0.001 in all cases). No significant effects were found among P200 latencies.

Sequential alterations of probe responses are summarized in Fig. 3 that shows the mean amplitudes of all three components of these responses as a function of stimulus sequence.

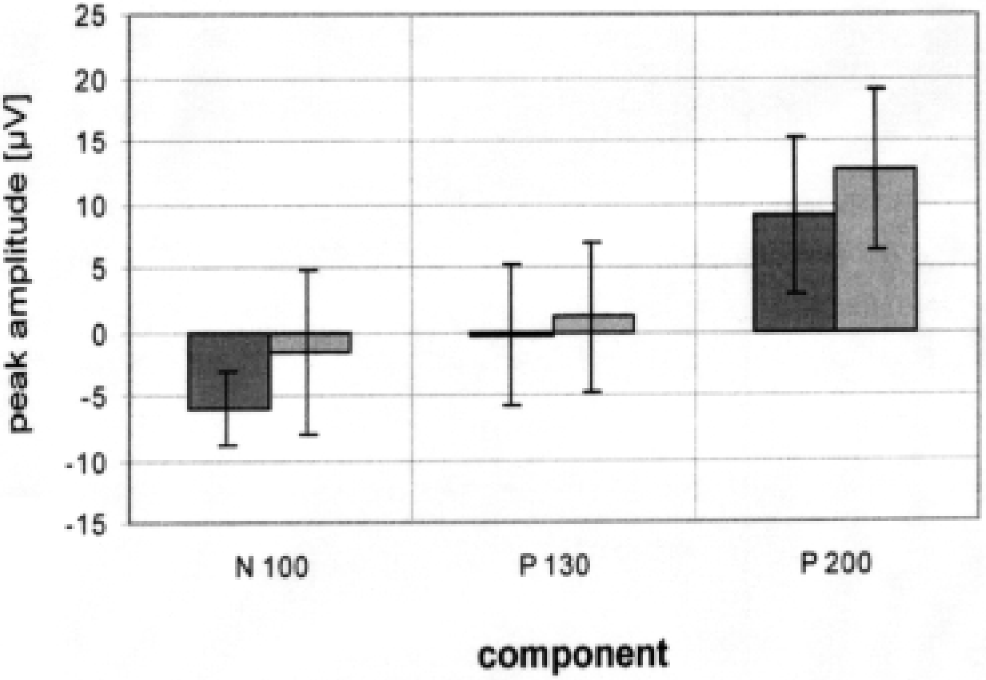

Fig. 3. Mean peak amplitudes of the three components (N100, P130, P200) of responses to visual probes presented after visual "oddball" stimuli. Dark gray bars, components of responses to probes that followed the first non-targets after targets. Light gray bars, components of responses to probes that followed the eighth non-targets after targets. Standard deviation markers are added on top of the bars.

Auditory "oddball" stimuli with visual probes

Responses to visual probes were measured the same way as they were in the visual experiment. Amplitudes and latencies of specific components of both modalities were analyzed with identical three-way ANOVAs (electrode x delay x sequence). Oz potentials were also recorded in this experiment, because they were useful for the analysis of responses to visual probes. In the case of auditory "oddball" responses, Oz electrodes recorded only small, probably volume conducted signal.

RESPONSES TO "ODDBALL", NON-TARGET STIMULI

No significant effects of stimulus sequence on the parameters of the auditory non-target responses were found. Amplitudes of both N100 and P200 components differed only between the electrodes ($F_{3,176}$ = 49.732, $P<0.001$ for N100 and $F_{3,176}$ = 9.746, $P<0.001$ for P200). The N100 component, recorded from the Pz electrode, was significantly smaller than the same component recorded from Cz or Fz electrodes (Bonferroni, $P<0.001$ in both cases). Also, the N100 wave was significantly smaller in Oz recordings than in any other channel ($P<0.001$ in all cases). Amplitudes of the P200 component differed between the Pz and Cz electrodes (P=0.01). Again, Oz recordings differed from Cz and Fz ($P<0.001$ in both cases). Latencies of the N100 component differed only between the electrodes ($F_{3,156}$ = 3.609, P=0.015). Oz latencies were significantly different than all the others (P=0.024 in all cases). Latencies of the P200 component did not show any significant effects. There were also no significant alterations of the width of this component, measured at its half-height.

RESPONSES TO PROBES

The effect of stimulus sequence on the amplitudes of the N100 component in responses to visual probes was insignificant. However, there was a significant interaction between the effects of sequence and electrode ($F_{3,176}$ = 7.239, $P<0.001$). To test this effect further, amplitudes recorded with each electrode were separately analyzed with two-way ANOVAs (sequence x delay). The effect of sequence was significant in Fz recordings ($F_{1,144}$ = 13.66, $P<0.001$). It was insignificant in Cz recordings. It was significant again in Pz ($F_{1,144}$ = 4.62, P =0.0037) and in Oz recordings ($F_{1,144}$ = 4.383, P=0.042). Thus, the strongest effect of the sequence was found in Fz recordings. The mean amplitude of the N100 component recorded at the Fz electrode was - 6.08 μV (SD = 4.0) in eighth responses and -1.21 μV (SD= 5.3) in "after target" responses. The N100 component also differed between the electrodes ($F_{3,176}$ = 4.06, P=0.008). Bonferroni tests showed that it was significantly larger at the Oz than at the Fz electrode (P= 0.007). Latencies of the N100 component did not show any significant differences.

No significant effects of stimulus sequence on either amplitudes or latencies of the P130 and P200 components were found. Amplitudes of both components differed significantly only among the electrodes ($F_{3,176}$ = 49.92, P<0.001 for P130; $F_{3,176}$ = 15.42, P<0.001 for P200). In both cases, Bonferroni tests showed that Oz amplitudes differed significantly from all the others (P<0.001 in all cases). Latencies of the P130 component differed between the electrodes ($F_{3,166}$ = 9.528, P<0.001). Again, Bonferroni tests showed that Oz latencies differed from all the others (P<0.001 in all cases). Latencies of the P200 component did not show any significant differences.

Pre-stimulus potentials

Pre-stimulus potential level was measured by averaging the values within the 150 ms wide time window immediately preceding the presentation of the "oddball" stimulus. Potentials were analyzed with a three-way ANOVA (modality x sequence x electrode). The effect of stimulus modality was insignificant. In contrast, the effect of stimulus sequence was highly significant ($F_{1,334}$ = 15.472, P=0.01). Averaged potential levels preceding the presentation of the first non-target after target stimulus was - 0.511 μV (SD = 2.4). Averaged potential preceding eighth non-target in the sequence was -1.479 μV (SD = 2.3). Potential levels differed between the electrodes ($F_{3,344}$ = 3.818, P=0.01). Figure 4 shows the mean values of pre-stimulus potential, recorded in the visual and auditory experiments, as a function of recording electrode and stimulus position in a sequence. Interestingly, Fig. 4 indicates that responses to the first non-targets after targets were preceded by a slight negative potential shift. This effect, however, was insignificant. Pre-stimulus shifts were small in Oz recordings. Their maximum amplitudes were recorded at Pz and Cz locations. At Fz, the shifts were smaller but still bigger than those recorded at Oz. The difference between potential levels preceding responses to the first and the eighth non-target was significant only at Pz ($F_{1,86}$ = 6.656, P=0.012) and Cz recordings ($F_{1,86}$ = 6.588, P=0.012).

DISCUSSION

Responses to "oddball" stimuli

The present experiment revealed significant negative shifts preceding non-target responses in spite of the fact that no motor responses to target stimuli were required. In earlier reports, such shifts were evident only when subject were asked to press the button in response to target stimuli (Starr et al. 1995, 1997). With mental count, negative deflections were always much smaller. In some experiments they reached the level of significance (Starr et al. 1995), in the others they were insignificant (Starr et al. 1997). In the present experiment, pre-stimulus potentials were significant, in spite of the fact that a much shorter time constant was used. Starr and co-authors used the exceptionally long time constant of 16 s. The filter presently used was equivalent to a 1 s time constant. The difference in time constant can explain the relatively small shifts in the grand-averaged curves (compare Fig. 2 in this paper with Fig. 1 in Starr et al. 1995).

The presence of pre-stimulus shifts in potentials recorded without motor responses did not exclude the possibility that these shifts belong to the family of preparatory potentials for which the expectation of motor activity is essential (Starr et al 1995, 1997). Subtle activation of muscles of the face, tongue and larynx may be present during silent counting (Hardyck and Petrinovich 1970). It is also possible that mental counting involves motor preparation even though no movement is actually produced. Alternatively, pre-stimulus negative shifts can belong to the family of potentials that do not depend on motor activity, such as contingent negative variation (CNV), which are generated when one stimulus forewarns the subject that the subsequent event is imminent (Walter et al. 1964, Ruchkin et al. 1986). In the "oddball" paradigm each non-target stimulus can be treated as a warning signal that the next stimulus may require a response. The expectancy that the next stimulus will actually be a target would increase with an increasing number of subsequent non-targets. At present, it is not possible to resolve the problem of which mechanism is

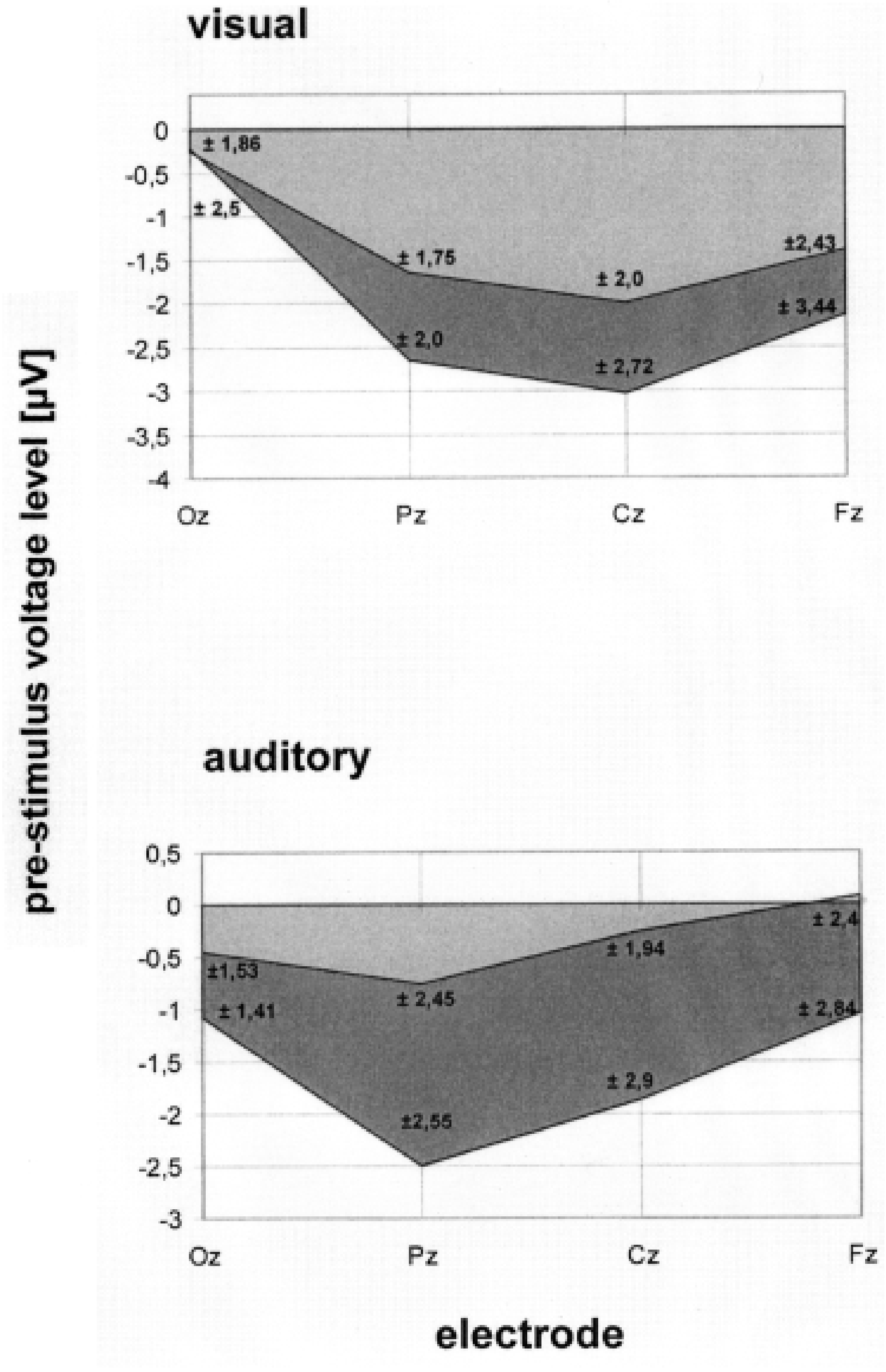

Fig. 4. Averaged voltage levels measured within 150 ms immediately preceding the onset of non-target stimuli. Upper graph, visual tests; lower graph, auditory tests. Voltage levels are shown as a function of the recording electrode. Light gray area, voltage levels preceding the first non-targets after targets. Dark gray area, voltage levels preceding the eighth non-targets after targets. Standard deviations are given with numbers.

responsible for the generation of pre-stimulus shifts. But, even at this stage of research, the possibility of pre-stimulus shifts should be considered while measuring evoked potential amplitudes. It is a common practice to measure the amplitude in reference to the average prestimulus level even if experimental procedures such as the "oddball" are used. It would be safer to exclude the segment mostly contaminated with pre-stimulus shifts.

In the present experiment, alterations of the auditory N100 component did not reach the level of statistical significance. Alterations of the visual N100 and P130 components were also insignificant. No earlier data on sequential effects on visual responses are available. The reports on the auditory N100 component, in experiments with mental counting, have been inconsistent. Hermanutz and co-authors (1981) reported that the amplitude of this component increased as a function of the number of immediately preceding non-targets. Hirata and Lehmann (1990) found similar difference between responses to non-targets immediately preceding and immediately following targets. However, Sams and colleagues (1984) and Starr and co-authors (1995, 1997) found no changes in this component.

In the present experiment, alterations of the auditory P200 responses were insignificant. A significant effect was found in visual tests, in which the P200 component was reduced in responses immediately following targets. It was enlarged in the eighth responses. The existing data on the alterations of the P200 component are limited to the auditory system. They also show inconsistencies. Starr and co-authors (1995) found that, in a mental counting condition, the auditory P200 component was unaffected by stimulus sequence. Later reports from the same laboratory, however, described bigger P200 amplitudes in responses immediately following than in responses immediately preceding targets (Starr et al. 1997). In the experiments of Hirata and Lehmann (1990), maximal amplitudes of the P200 components did not show the sequential effects but there was a significant difference in their locations. The difference between the sequential effects on P200 components in the auditory and visual systems, found in the present experiment, should be treated with caution. More experiments are needed to evaluate whether or not it is genuine.

The lack of sequential effects on latencies of both the N100 and P200 components, found in the present experiment, is in keeping with earlier data of Starr and co-authors. (1995, 1997). But Hirata and Lehmann (1990) found reduced P200 latencies in responses to non-targets following targets.

Responses to probes

The present experiment showed stronger sequential effects on responses to probes than on responses to non-target stimuli. The important difference between these two types of stimuli was that non-targets had to attract some attention, simply because they had to be distinguished from targets, whereas probes could be truly ignored. Probe stimuli accompanied all the target and non-target responses thus, they could not be treated as rare or novel. It seems rather that the mechanism responsible for sequential changes of "oddball" responses affected also responses to the other, completely meaningless stimuli.

Sequential effects on probes were stronger when probes and "oddball" stimuli were of the same modality. The strongest sequential effects were found among visual probes that followed visual "oddball" stimuli. The pattern of changes of these responses was rather regular. Peak values of all three components (N100, P130 and P200) were more negative in "after target" responses than later in the sequence. The entire waveform was shifted towards negative potentials immediately after a target and then it became more positive. The effect of the delay with which the probes were delivered after the initial "oddball" stimuli was significant among N100 amplitudes: their sequential alterations were significant only if the delay was short. The effect of the delay was insignificant among P130 amplitudes, but it was of borderline significance among P200 components.

In conditions in which visual probes followed an auditory "oddball" stimuli, the sequential effects on probe responses were much weaker. In the entire population of responses none of their parameters showed the significant alterations. Significant effects were found among N100 amplitudes recorded with Fz, Cz and Oz electrodes, when data from these electrodes were analyzed separately. However, the direction of changes was opposite to that recorded in the visual "oddball" task: amplitudes became more negative in the eighth responses. Can the interactions between two potentials differ so dramatically when they are produced by stimuli of the same or different modalities? Probes have never been used before in studies of sequential effects. Moreover there are no earlier reports on such effects in the visual system. Thus, present data need to be verified in the other experiments. But the observed differences are not impossible to explain. Surface recorded waveforms evoked with visual and auditory stimuli were produced by activity of very different assemblies of neurons, located in different cortical regions. Obviously, interactions between assemblies belonging to the same and different modality can be very different. On the other hand, electrical activity underlying such "high level" processes as the expectation of an important stimulus can be rather widespread, encompassing regions of the cortex far from specific visual or auditory areas. For example, the P300 potential, specific for the detection of relevant stimuli, reaches its maximum in the midline Pz and Cz recordings in both visual and auditory conditions (for review see Donchin 1988, Verleger 1988). In the present experiment, these "high level" processes were triggered by visual or auditory stimulation but probes were always visual. It can not be excluded that, in the case of visual "oddball" stimuli, visual probes also interacted with late reminders of specific - therefore localized - visual response to non-targets.

Processes that could produce the observed effects

As in the case of most ERP data, the interpretation of the present results in terms of underlying neuronal mechanisms or cognitive functions is difficult. However, the following points can be mentioned:

1. It is assumed (Colon et al. 1983) that evoked potential components within the latency range 100-200 ms represent the activity from intercortical neurons. Components recorded with 100 ms latency can also originate from presynaptic activity of afferent thalamocortical fibers. These responses are often regarded as more local and specific than 200 ms waves. However, it was shown that visual P200 waves were re-generated in a number of cortical fields (Simson et al. 1976). Thus, even this component probably represent the information processing in specific cortical area.
2. The analysis of the potential level preceding specific responses indicated, that this level could be correlated with cortical responsiveness: response amplitudes increased when they were evoked at the time of more negative potential (Rockstroh et al. 1992, 1993).
3. There is the potential component that is fairly specific to "oddball" paradigm: the P300 wave in response to target stimulus. There is still no agreement concerning the interpretation of this potential. It was linked with such brain functions as updating the "internal model" in subject's brain that was necessary after the important information had been received (Donchin and Coles 1988). Alternatively, it was suggested that P300 potential marked the resolution of expectancy when the awaited event was detected (Verleger 1988). It was also proposed that P300 wave reflected the inhibitory input of prefrontal cortex to the activating reticular formation (Desmedt 1980). More recently, P300 potential was linked with the mechanisms of regulation of cortical thresholds and responsiveness (Rockstroh et al. 1992). In spite of these differences, there seems to be a general agreement that P300 potential accompanies the detection of the meaningful or at least rare stimulus in a train of meaningless information.

Present data, together with the earlier results, show that important events that evoke P300 potential also produce the alterations in the "state" of cortical networks that last for tens of seconds or even minutes. These "states" affects the local, cortical processing of the other stimuli even if they are completely irrelevant, do not participate in target / non-target differentiation or have the different modality.

Present results support the earlier findings that motor responses to target stimuli produce stronger effects but they also show that the alterations of the "brain state" can be detected without motor responses. Taking into account the discussion above, it seems that the clear presence of negative shifts of prestimulus voltage in the absence of motor responses to targets should prevail and present findings should rather be linked with the results of experiments in which the expectancy was experimentally modeled and contingent negative variation of prestimulus potential was recorded (Walter et al. 1964, Ruchkin et al. 1986).

Attention is the other mechanism that could contribute to observed changes. The N100 component of auditory evoked potential was shown to increase in amplitude when attention was directed to the stimulus (Hillyard et al. 1973) The increasing attention in the period between targets should result in gradual increase of N100 to subsequent non-targets. This effect, however was not observed in the present study.

The results of the present experiment show how difficult the interpretation of electrical responses can be when the "state of the brain" is completely unknown, for example when the data were obtained from anaesthetized animals. On the other hand, if the problem of sufficient control of stimulus relevance in animal experiments is solved, more detailed information about the neuronal mechanisms underlying the observed alterations of evoked potentials will most likely be gained.

ACKNOWLEDGEMENTS

I thank Magda Studzińska M. Sci. and Rafał Milner M. Sci. for help in data collection and analysis. The technical assistance of Mrs. Halina Szeliga is gratefully acknowledged. This research was supported by statutory grant of the Nencki Institute.

REFERENCES

Colon E., Visser S., de Weerd J., Zonneveldt A. (1983) Evoked potential manual. A practical guide to clinical applications. Martinus Nijhoff Publishers, Boston.

Desmedt J.E., Debecker J., Manil J. (1965) Mise en évidence d,un signe électrique cérébral associé á la détection parle sujet d,un stimulus sensoriel tactile. Bulletin de l,Academie Royale de Médecine de Belgique 5: 887-936.

Desmedt J.E. (1980) P300 in serial tasks: an essential post-decision closure mechanism. Prog. Brain Res. 54: 682-686

Donchin E., Coles M.G.H. (1988) Is the P300 component a manifestation of context updating? Behav. Brain Sci. 11: 357-374.

Hardyck C.D., Petrinovich L.F. (1970) Subvocal speech and comprehension level as a function of difficulty level of reading material. J. Verb. Learn. Verb. Behav. 9: 647-652.

Hermanutz M., Cohen R., Sommer W. (1981) The effects of serial order in long sequences of auditory stimuli on event-related potentials. Psychophysiology 18: 415-423.

Hillyard S.A., Hink R.F., Schwent V.L., Picton T.W. (1973) Electrical signs of selective attention in the human brain. Science 182: 177-180

Hirata K., Lehmann D. (1990) N1 and P2 of frequent and rare event-related potentials show effects and after-effects of the attended target in the oddball-paradigm. Int. J. Psychophysiol. 9: 293-301.

Kondakor I., Pascual-Marqui R.D., Michel C.M., Lehmann D. (1995) Event-related potential map differences depend on the prestimulus microstates. J. Med. Eng. Technol. 19:66-69.

Lehmann D., Michel C.M., Pal I., Pascual-Marqui R.D. (1994) Event-related potential maps depend on prestimulus brain electric microstate map. Int. J. Neurosci. 74: 239-248.

McCarthy G., Donchin E. (1976) The effects of temporal and event uncertainty in determining the waveforms of the auditory event related potential (ERP). Psychophysiology 13: 581-590.

Michalski A. (1998) Novel environment as a stress-inducing factor. An event-related potentials study. Acta Neurobiol. Exp. 58: 199-205.

Michalski A. (1999) The effect of accomplishment and failure on P300 potentials evoked by neutral stimuli. Neuropsychologia 37: 413-420.

Rockstroh B., Müller M., Cohen R., Elbert T. (1992) Probing the functional brain state during P300-evocation. J. Psychophysiol. 6: 175-184.

Rockstroh B., Müller M., Wagner M., Cohen R., Elbert T. (1993) "Probing" the nature of the CNV. Electroencephalogr. Clin. Neurophysiol. 87: 235-241.

Ruchkin D.S., Sutton S., Mahaffey D., Glaser J. (1986) Terminal CNV in the absence of motor response. Electroencephalogr. Clin. Neurophysiol. 63: 445-463.

Sams M., Alho K., Nätanen R. (1984) Short-term habituation and dis-habituation of the mismatch negativity of the ERP. Psychophysiology 21: 434-441.

Simson R., Vaughan H.G., Ritter W. (1976) The scalp topography of potentials associated with missing visual or auditory stimuli. Electroencephalogr. Clin. Neurophysiol. 40: 33-42

Squires K.C., Wickens C., Squires N.K., Donchin E. (1976) The effect of stimulus sequence on the waveform of the cortical event-related potential. Science 193: 1142-1146.

Starr A., Sandroni P., Michalewski H.J. (1995) Readiness to respond in a target detection task: pre- and post-stimulus event-related potentials in normal subjects. Electroencephalogr. Clin. Neurophysiol. 96: 76-92.

Starr A., Aguinaldo T., Roe M., Michalewski H.J. (1997) Sequential changes of auditory processing during target detection: motor responding versus mental counting. Electroencephalogr. Clin. Neurophysiol. 105: 201-212.

Sutton S., Braren M., Zubin J., John E.R. (1965) Evoked-potential correlates of stimulus uncertainty. Science 150: 1187-1188.

Verleger R. (1987) Sequential effects on P3 in a counting task: a partial replication. Biol. Psychiatr. 26: 221-246.

Verleger R. (1988) Event-related potentials and cognition: A critique of the context updating hypothesis and an alternative interpretation of P3. Behav. Brain Res. 11: 343-356.

Walter W.G., Cooper R., Aldridge V.J., McCallum W.C., Winter A.L. (1964) Contingent negative variation: an electric sign of sensorimotor association and expectancy in the human brain. Nature 203: 380-384.

Received 14 March 2000, accepted 20 September 2000