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Interactions between P300 and passive probe responses differ in different visual cortical areas

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Abstract. The regulation of firing thresholds of cortical neurons was suggested as one of the mechanisms underlying the generation of the P300 component in the human event-related potential. According to this hypothesis, the detection of an important stimulus produced the widespread inhibition of "irrelevant" networks, interrupting their ongoing activity and facilitating the analysis of selected information. In the present experiment, the responsiveness of visual cortex was evaluated during the P300 potential by using additional, probing stimuli. Large separation of the cortical visual fields permitted separate analysis of the input and more advanced stages of processing. Responses were recorded from Fz, Cz, Pz and Oz scalp sites. P300 waves were evoked by visual, mentally counted stimuli in a standard "odd-ball" procedure. Visual probes were delivered 200, 300, 400, 500, 700 and 1000 ms later. No responses to the probes were required. Significant suppression of responses to the probes delivered less than 400 ms after target stimuli was found in Oz and Pz but not in Cz or Fz . The suppression was not proportional to the voltage levels from which probe responses started. In Fz and Cz, latencies of probe responses were elongated if probes were delivered less than 400 ms after target stimuli. The results suggest that probe responses suppressed by the P300 potential in occipital and parietal cortex may be restored in frontal areas. In these areas the P300 potential could delay probe responses instead of suppressing them.

Key words: visual event-related potentials, meaningful stimuli, excitability of different cortical fields

INTRODUCTION

The positive polarity of the P300 component of the event-related potential is puzzling. A number of experiments have shown that this wave is the most prominent evoked potential that is sensitive to psychological variables (Donchin and Cohen 1967, Squires et al. 1975, Johnson and Donchin 1978, Desmedt and Debecker 1979a,b, Polich 1987). Donchin and co-authors (1988) related the P300 wave to the process of "context update" or the updating of an internal model in the subject's brain that was required when external situation had changed significantly. Verleger (1988) suggested that P300 reflected the "context closure" that occurred when the meaningful, awaited stimulus had been detected. Because processes involve the modification of memory traces, they should be linked with excitatory activity. But simultaneous recordings from single neurons and from the surface of the skull indicated that the surface positive waves originated mainly from the hyperpolarization of apical dendrites of cortical cells. Thus they should correspond to periods of reduced cortical excitability (Caspers et al. 1980, Creutzfeldt 1983, Speckmann et al. 1984). Of course, the putative excitatory phenomena could be masked by stronger inhibitory processes. But what could be the physiological role of such strong inhibition? Desmedt and Debecker suggested that the P300 potential reflected an inhibitory input of prefrontal cortex to the activating reticular formation (Desmedt and Debecker 1979a,b, Desmedt 1980). Alternatively, Elbert and Rockstroh suggested that this potential reflected a threshold regulation mechanism in the cortex (Elbert and Rockstroh 1987, Elbert 1993). The present experiment was designed to test the latter hypothesis.

According to threshold regulation theory, cortical response to incoming stimuli consists of the activation of "relevant" neurons that is accompanied by the elevation of thresholds, or the inhibition of the large numbers of unrelated cells. This inhibition was stronger if the important, meaningful stimulus had been detected. Elbert and Rockstroh's (1987) hypothesis is interesting because it pertains to the principles of neuronal network operation rather than to the psychological meaning of the P300 potential. It does not contradict the other theories (Donchin and Coles 1988, Verleger 1988) but it leads to a number of conclusions that can be experimentally tested. The alterations in cortical responsiveness can be tested by measuring the responses to a third "probing" stimulus presented before, during or after the P300 potential. It has already been demonstrated that responses to auditory "probing" stimuli were attenuated during a P300 potential evoked in an auditory "odd-ball" experiment (Rockstroh et al. 1992). The experiment proved to be difficult. The use of probe stimuli in conjunction with a P300 evoking, "odd-ball" paradigm resulted in the competition for brain processing resources that reduced the P300 waves (Israel et al. 1980, Wickens et al. 1983, Polich 1989). Strong suppression could be due to the fact that subjects were asked to produce motor responses to probes. Probably these difficulties cause the authors to change the method and use the steady-state responses, SSR (Stapells et al. 1987, Makeig and Inlow 1993, Tobimatsu et al. 1996). Subsequent experiments demonstrated that the amplitude of an auditory SSR was reduced and its phase advanced in parallel to P300 potential (Rockstroch et al. 1996). However, the alterations were small and could only be seen when motor responses to target stimuli were required.

If the P300 potential indeed reflects the complex cortical activity that involves the excitation of specific neurons and the inhibition of the rest of the network, then the marked differences in patterns of responding and inhibited neurons can be expected in different cortical fields. Differences could be produced by several factors. The proportion of responding and inhibited cells most likely does not stay constant at the different levels of information processing. The assemblies of responding cells can be enlarged in the higher cortical areas as the result of divergent connections. At the highest level, the final classification of the stimulus can be conveyed by excitation of a small set of highly specialized neurons. Finally, as suggested by Elbert and Rockstroh (1987), there may be differences in threshold regulation loops operating in frontal and posterior areas.

In the present experiment, an attempt was made to demonstrate the differences in the interactions between P300 and probe responses in different cortical fields. In contrast to previous experiments, the visual system was used due to the much larger separation of its cortical fields and their specific organization with a posterior input field and progressive anterior shift of the fields involved in more advanced processing. To ensure that probe responses would reach the higher areas, discrete probes were used. It was feared that SSR responses could be "filtered out" at the higher levels of information processing. Fortunately, the preliminary experiments (Michalski, unpublished data) showed that discrete stimuli could be used as probes, even if they did not require

any responses from the subjects (passive probes). The best pronounced components of potentials evoked by such probes were identified as P200 waves. Earlier experiments (Simson et al., 1976) showed that maximum amplitude of the P200 component could be recorded over a large region of the scalp. In some recordings, clearly more than one maximum was visible. Such result indicated that the P200 component was re-generated in several cortical areas thus, representing their local activity. On the other hand, it is well documented that the P300 potential is widespread on the cortical surface and is most likely correlated with the activity of deep structures (Halgren et al. 1998). P300 reaches its maximum at Pz and Cz locations but it is only slightly reduced at Fz. Thus, in the present experiment, the responses to visual probes traveling from the input occipital cortex to frontal fields should pass through the regions where large P300 waves develop.

Scalp recordings inevitably produce the localization problem. That is, it has to be estimated from which region the signal comes and whether or not adjacent electrodes record from different areas. Using the available theoretical data and the results of model testing (Nunez 1981, Niedermeyer and daSilva 1993) it was estimated that four electrodes could be used at the Oz, Pz, Cz and Fz locations. With a typical head size, the distance between the adjacent electrodes was 7.5 cm and the cross-talk between them should be less than 20%. There was a chance that the differences in operation of specific cortical regions would be detected. Simultaneously, this set of electrodes provided the recordings from the primary visual cortex, from the region of higher order visual cortices, from association cortex at the border of visual region and from frontal cortex.

METHODS

Data were collected from 15 volunteers of both sexes (10 females and 5 males), aged 25-48. Informed consent was obtained from all participants.

EEG signals were recorded with disc electrodes glued at Fz, Cz, Pz and Oz positions according to the international "10-20" system. Electrodes were referenced to linked mastoids and supplemented by vertical and horizontal EOG. The software (Elmiko Paperless EEG system) provided for rejection of EEG epochs if EOG amplitude exceeded 40 μV. Rejected epochs were replaced with new ones. Signals were sampled with 2048 Hz frequency, 12 bit resolution, digitally filtered 0.16-30 Hz and reduced to 256 Hz by averaging the adjacent points. Data were stored in epochs containing 250 ms before and 1.5 s after the stimulus onset.

Flashes of spatially overlapped arrays of red and yellow LED diodes (2 deg x 2 deg of visual angle, 10 cd/m^2 luminosity on 1 cd/m^2 background, 100 ms duration) were used as stimuli in an "odd-ball" procedure. The diode array was also visible when the diodes were switched off. Subjects were asked to fixate the center of the array during the recording sessions. Schematic representation of the experimental paradigm is shown in Fig. 1. Red or yellow flashes were presented in random order, every 2.5 s. Yellow (target or "odd-ball") flashes were less frequent than red (non-target). The probability of occurrence of a target stimulus was 0.12. Subjects were asked to mentally count the target flashes and report their number at the end of the recording session. Non-target flashes were ignored. Data were rejected if the error in counting was greater than 20%. Flashes of the third array of green diodes (10 cd/m^2 luminosity, 100 ms duration, located also within the central 2 deg of the visual field)

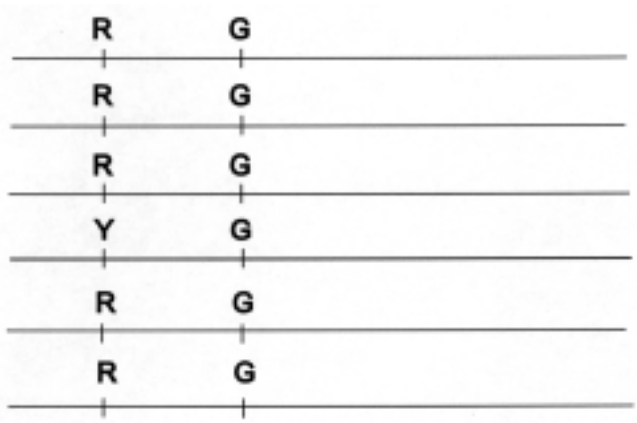

Fig. 1. Schematic illustration of the experimental paradigm. Horizontal lines represent the epochs during which the data were collected. Each epoch lasted 1.75 s. There was a 0.75 s interval between the subsequent epochs. Each epoch started with 0.25 s of pre-stimulus recording. Then a yellow (Y) or red (R) stimulus was presented. Yellow (target) stimuli were less frequent than the red ones (see Methods). The subjects were asked to count mentally the yellow stimuli. Red stimuli were ignored . After a specified delay, both yellow and red stimuli were followed by green probing stimuli (G). The figure shows the recording session in which probes followed the initial Y or R stimuli with the delay of 400 ms. In the experiment, delays of 200 ms, 300 ms, 500 ms, 700 ms and 1000 ms were also used. In these recordings only the position of G stimulus was changed within an epoch of constant length.

were used as probes. Probes were delivered at specified delays after target and non-target stimuli. Subjects were instructed to ignore them.

To ensure the accurate measurement of responses, a minimum of 60 artifact-free target stimulus repetitions were collected in each recording session. These were accompanied by, on average, 440 repetitions of non-target stimuli. Both, target and non-target stimuli were followed by probe stimuli. Probe delay was constant within each recording session. After the recording was completed, responses to target and non-target stimuli were separately averaged. Both responses contained the superimposed responses to probes.

Recordings with probe delays of 200 ms, 300 ms, 400 ms, 500 ms, 700 ms and 1000 ms were obtained from each subject. Interactions between probe responses and P300 waves could be evaluated by comparing responses to probes delivered during and after the P300 potential and by comparing responses to probes delivered with the same delay after target and non-target responses. Amplitudes and latencies of peaks in averaged curves were measured using a cursor on a computer screen and the data were transferred to the SYSTAT program for multi-factor analysis of variance (ANOVA). In addition, the grand-averaged waveforms were computed by averaging data for all subjects in each experimental condition.

RESULTS

Figure 2 shows the grand-averaged potentials evoked by "odd-ball" stimuli (target or non-target) with the superimposed responses to probes. Early components of responses to "odd-ball" stimuli (labeled "1") appear in both target and non-target responses. P300 waves (labeled "2") appear only in responses to target stimuli. Responses to probes (labeled "3") follow the target or non-target responses at the specified delays. Latency analysis indicated that the single wave responses to probes corresponded to P200 components.

Figure 2 indicates that responses to probes presented 400 ms and 500 ms after "odd-ball" stimuli were reduced

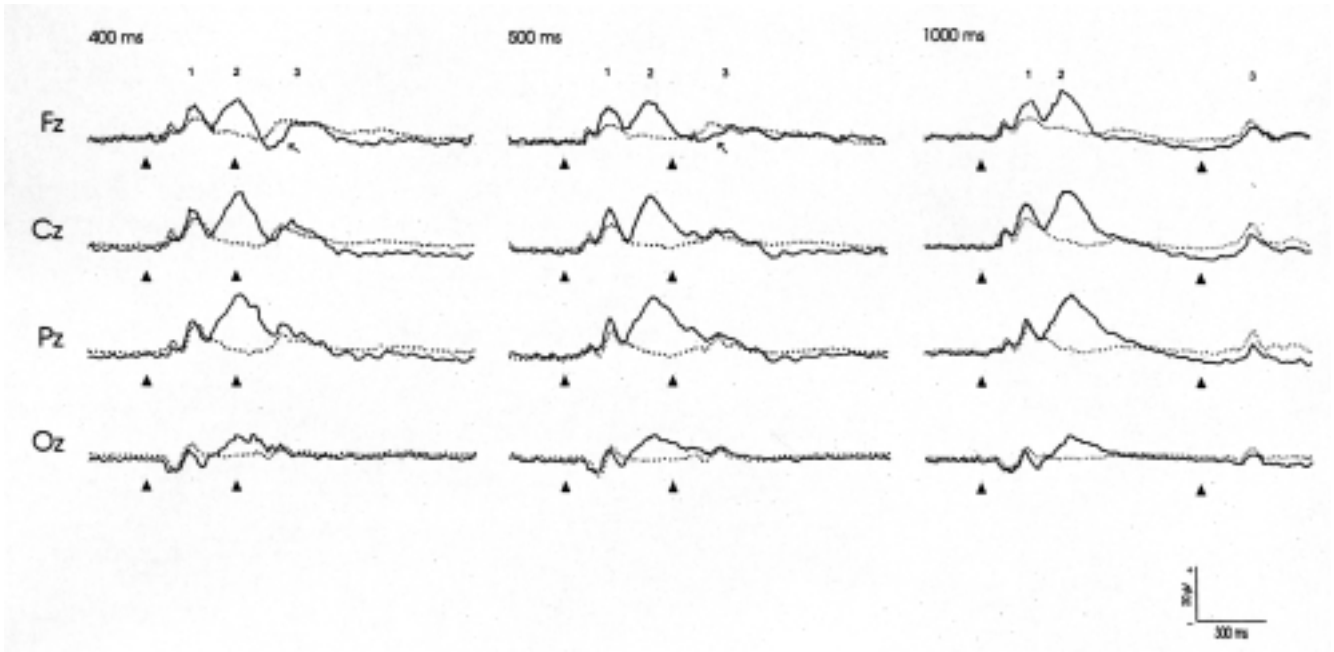

Fig. 2. Grand-averaged responses to visual "odd-ball" stimuli with superimposed responses to visual probes. Solid lines show the responses to target stimuli and dotted lines show the responses to non-target stimuli. The first black triangle indicates the onset of "odd-ball" stimulus. The second black triangle indicates the onset of probe. Probes were presented 400 ms (left column), 500 ms (middle column) and 1000 ms (right column) after the "odd-ball" stimuli. Rows of the figure show the different electrode recordings as indicated on the left margin. ERP components are labeled above the Fz recordings: 1, early responses to "odd-ball" stimuli; 2, P300 waves; 3, responses to probes. Arrows point to the best pronounced differences in latencies of responses to probes presented after target and non-target stimuli.

if the preceding stimulus was the mentally counted target. The reduction was clear in the occipital cortex but in the more frontal areas probe responses seemed to be larger again. Figure 2 also indicates that latencies of these "restored" responses in the frontal area could be elongated (see the regions labeled with arrows).

Amplitudes and latencies of the following peaks were measured and used for statistical analysis:

1. P200 components in responses to target and non-target stimuli,
2. P300 waves in responses to target stimuli,
3. P200 components in responses to probes.

Early responses

The amplitude of the early response was defined as the difference between the P200 peak and the bottom of the preceding negative deflection. Amplitudes were analyzed with a three-way ANOVA (electrode x target x delay). The target variable indexed the target and non-target responses. The delay variable indexed the delay of the probe. Theoretically the delay could not affect the early responses but it was introduced to check if there were any uncontrolled differences between the recordings. The analysis showed that the effect of the delay was clearly insignificant. Early responses to target stimuli were bigger than early responses to non-target stimuli ($F_{1,664} = 93.526$, $P<0.001$). Early responses also differed significantly between the electrodes ($F_{3,664} = 17.133$, $P<0.001$). Bonferroni test revealed that Oz responses were significantly smaller than all the others ($P<0.001$). Pz responses were also significantly smaller than Cz responses ($P<0.001$). The interaction between target and electrode variables was significant ($F_{3,664} = 21.095$, $P<0.001$). This suggested that the effect of mental counting on early responses was different at different electrodes. To test this hypothesis, data from each electrode were analyzed separately with two-way ANOVAs (target x delay). The effect of the delay was always insignificant. The effect of the target was insignificant in Oz recordings and highly significant in the remaining recordings ($F_{1,166} = 18.512$, $P<0.001$ in Pz; $F_{1,166} = 73.597$, $P<0.001$ in Cz; $F_{1,166} = 127.049$, $P<0.001$ in Fz).

P300 components

Clear P300 waves in response to target stimuli were recorded in all subjects. Since the negativity that separated P200 and P300 components in early responses ("1" and "2" in Fig. 2) strongly varied in depth in different subjects, it was found more practical to measure P300 amplitudes from the pre-stimulus level. The largest P300 waves were recorded with Pz (22.5 μV, SD = 7.4) and Cz electrode (22.6 μV, SD = 9.2). In Fz recordings P300 waves were smaller (18.1 μV, SD = 7.1). P300 waves were the smallest, but still easily measurable, in Oz recordings (17.4 μV, SD = 6.6).

P300 amplitudes were analyzed with a two-way ANOVA (electrode x delay). Only the differences between the electrodes were significant ($F_{3,322} = 10.738$, $P<0.001$). Bonferroni test showed that amplitudes recorded with Oz electrode were significantly smaller than amplitudes recorded with Cz ($P<0.001$) and Pz ($P<0.001$) electrodes. Also amplitudes recorded with Fz electrodes were significantly smaller than amplitudes recorded with Cz ($P<0.001$) and Pz ($P<0.003$) electrodes.

Latencies of P300 peaks were analyzed with two-way ANOVA (electrode x delay). All differences and interaction were insignificant.

Since the interactions with probe responses could be affected by the falling time of the P300 wave, time intervals within which the descending slope reached 50% of peak amplitude were measured. Data recorded with the 200 ms delay were excluded from this analysis because the superimposed probe responses made the measurements unreliable. Mean intervals indicated that the decay was faster in frontal electrodes (79 ms in Fz, 83 ms in Cz, 92 ms in Pz and 82 ms in Oz) but these differences analyzed with a two-way ANOVA (delay x electrode) did not reach statistical significance. Interestingly, the effect of the delay was significant ($F_{4,243} = 3.208$, $P<0.014$). Thus, the P300 potential decayed faster with shorter probe delays (75 ms for 300 ms delay; 77 ms for 400 ms delay; 84 ms for 500 ms delay; 97 ms for 700 ms delay; 87 ms for 1000 ms delay). Bonferroni test showed that the decay of P300 potential recorded with 700 ms delay was significantly slower than the decay recorded with probe delays 300 ms ($P<0.015$) and 400 ms ($P<0.04$).

Amplitudes of responses to probes

Amplitudes of responses to probes were measured from the levels immediately preceding the positive-going slopes of their P200 components to the peaks of these components.

Figure 3 shows the mean amplitudes of these responses as a function of probe delay. Probe responses

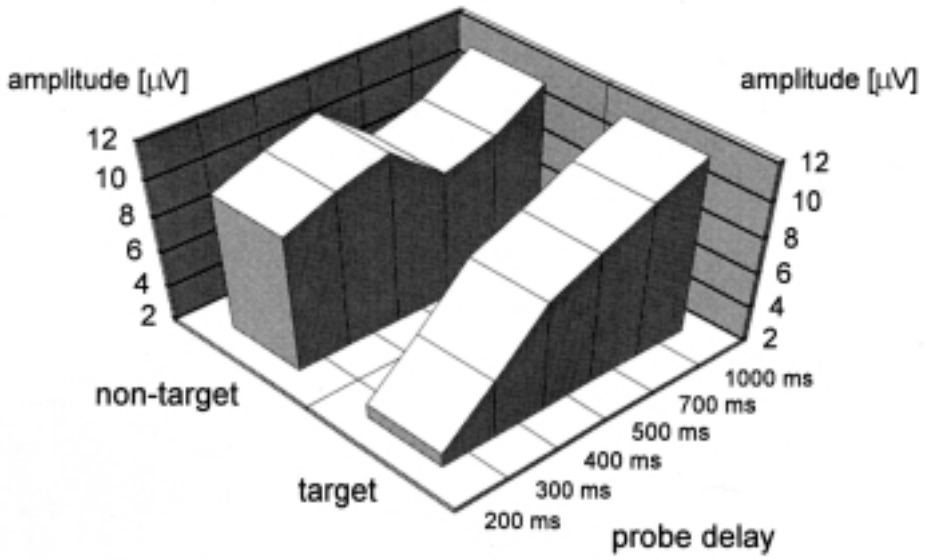

Fig. 3. Mean amplitude of probe response as a function of probe delay after target and non-target stimuli. Amplitudes were measured from the level immediately preceding the P200 component in the probe response to the peak of this component.

following target and non-target stimuli are shown separately. The two distributions are clearly different. Responses to target stimuli reduced probe responses if the probes were presented shortly after the target. Responses to non-target stimuli did not show this effect.

Amplitudes of probe responses were analyzed with a three-way ANOVA (electrode x target x delay). All three variables produced significant effects ($F_{3,664} = 18.689$, $P<0.001$ for the electrodes; $F_{5,664} = 15.117$, $P<0.001$ for the delay; $F_{1,664} = 35.391$, $P<0.001$ for the target). There was also a significant interaction between target and delay variables ($F_{5,664} = 11.403$, $P<0.001$). Thus, as the next step, amplitudes of probe responses evoked after target and non-target stimuli were analyzed separately with a two-way ANOVA (electrode x delay). The reduction of probe responses at short delays after target stimuli was highly significant ($F_{5,332} = 22.688$, $P<0.001$). Bonferroni test showed that responses to probes presented with the 1000 ms delay were significantly different from responses to probes presented with delays shorter than 400 ms ($P<0.006$). Responses to probes presented with the delays longer than 700 ms differed significantly from responses to probes presented with delays shorter than 300 ms ($P<0.001$). Finally, responses recorded 200 ms after a target stimulus differed significantly from all responses recorded later than 400 ms ($P<0.001$). Responses to probes presented after a target stimulus also differed between the electrodes ($F_{3,332} = 9.924$, $P<0.001$). Bonferroni tests showed that responses recorded with Oz electrodes differed significantly from responses recorded with Cz and Pz electrodes ($P<0.006$).

After non-target stimuli, probe responses did not differ significantly as a function of the delay. They only differed between the electrodes ($F_{3,332} = 9.747$, $P<0.001$). Bonferroni tests showed that the amplitudes recorded with Oz electrodes were significantly different from all the others ($P<0.009$).

Figure 4 shows the mean amplitudes of responses to probes presented after target stimuli as a function of probe delay. Amplitudes recorded with different electrodes are shown separately. Responses to probes presented with the 200 ms delay were excluded. These responses showed the strongest suppression and could easily affect the statistical analysis. On the other hand they overlapped heavily with P300 waves and their separation was much more difficult than the separation of responses recorded with the next delay of 300 ms. Figure 4 indicates that the attenuation of probe responses by P300 waves was stronger in posterior electrodes.

Amplitudes of probe responses, recorded with each electrode, were separately analyzed with a two-way ANOVA (target x delay). Significant differences between the amplitudes recorded after target and non-target stimuli were found only in Oz and Pz recordings. ($F_{1,138} = 12.295$, $P<0.001$ in Pz; $F_{1,138} = 3.831$, $P<0.05$ in Oz). In these recordings probe amplitudes also differed significantly with the delay ($F_{4,138} = 3.422$, $P<0.01$ in Pz; $F_{4,138} = 3.073$, $P<0.018$ in Oz). In Pz recordings the interaction between target and delay variables was also significant ($F_{4,138} = 3.075$, $P<0.018$). In Fz and Cz recordings the amplitudes of probe responses recorded after target and non-target stimuli did not differ

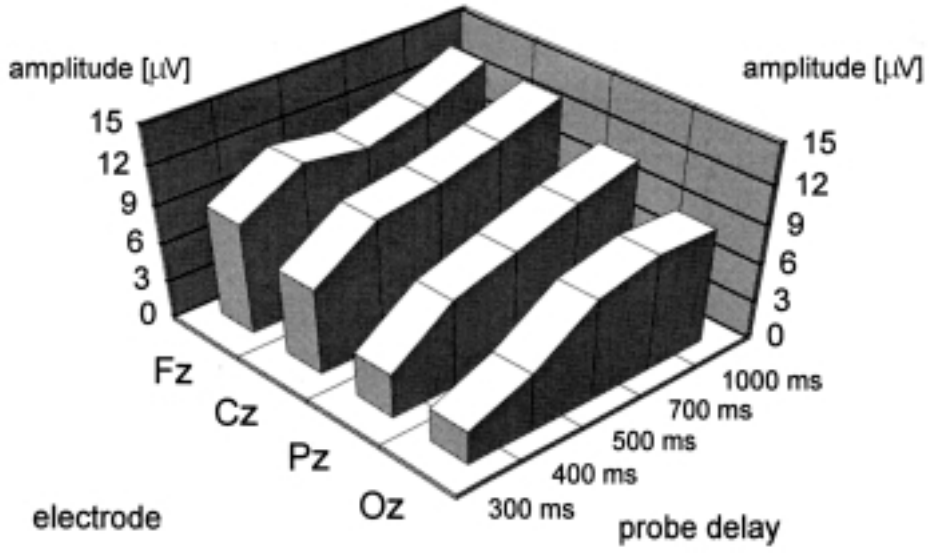

Fig. 4. Mean amplitude of probe P2 response as a function of probe delay after target stimulus. Data from each electrode are shown separately. Responses after non-target stimuli were excluded from this analysis.

significantly. In these recordings the delay also failed to produce significant differences.

Figure 4 could be also analyzed along the orthogonal axis: data for each delay were selected and analyzed separately with a two-way ANOVA (electrode x target). In this analysis data recorded with the shortest delay could not affect the other results, therefore they were included. For the delays shorter or equal to 400 ms, probe amplitudes recorded after target and non-target stimuli differed significantly ($F_{1,112} = 48.645$, $P<0.001$ for 200 ms delay; $F_{1,112} = 28.936$, $P<0.001$ for 300 ms delay; $F_{1,112} = 9.111$, $P<0.003$ for 400 ms delay). For the delays longer than 400 ms amplitudes recorded after target and non-target stimuli did not differ significantly. For the delays shorter or equal to 400 ms, probe amplitudes also differed between the electrodes ($F_{3,112} = 2.787$, $P<0.04$ for 200 ms delay; $F_{3,112} = 6.479$, $P<0.001$ for 300 ms delay; $F_{3,112} = 5.195$ $P<0.002$ for 400 ms delay). Amplitudes recorded with delays of 500 ms and 1000 ms did not differ between the electrodes. The only finding was a statistically significant difference between the electrodes for the amplitudes recorded with 700 ms delay ($F_{3,112} = 4.486$, $P<0.005$)

Latencies of responses to probes

Figure 2 indicates that not only amplitudes but also latencies of probe responses could differ after target and non-target stimuli. The most spectacular differences (labeled with arrows in Fig. 2), suggest that latencies of probe responses presented shortly after target stimuli could be elongated. Interestingly, this elongation seems to be better pronounced in frontal electrodes.

Latencies in the whole population of data were analyzed with a three-way ANOVA (delay x target x electrode). The difference between latencies of probe responses presented after target and non-target stimuli was significant ($F_{1,539} = 24.909$, $P<0.001$). The delay also affected latencies significantly ($F_{5,539} = 8.641$, $P<0.001$). Differences between the electrodes did not reach the level of statistical significance. All the interactions also were insignificant.

As the next step, latencies of probe responses presented after target stimuli were selected. Figure 5 shows these latencies, plotted as a function of the delay and the recording electrode. Responses recorded with the 200 ms delay were again excluded from the analysis due to the low reliability of measurements. Figure 5 shows the rather smooth distribution. Latencies seem to be elongated at short delays but only in frontal and central cortical fields. Latencies of responses to probes presented after target stimuli were analyzed with a two-way ANOVA (delay x electrode). Only the effect of the delay was significant ($F_{5,227} = 2.3$, $P<0.046$). The complementary analysis of the non-target data did not show any significant effects. Latencies of responses presented at specific delays after target stimuli were selected and analyzed separately with one-way ANOVA (electrode). A significant difference between the electrodes was found at the shortest delay of 300 ms ($F_{3,33} = 3.637$, $P<0.023$). For the longer delays, latencies did not differ significantly between the electrodes. The identical analysis of

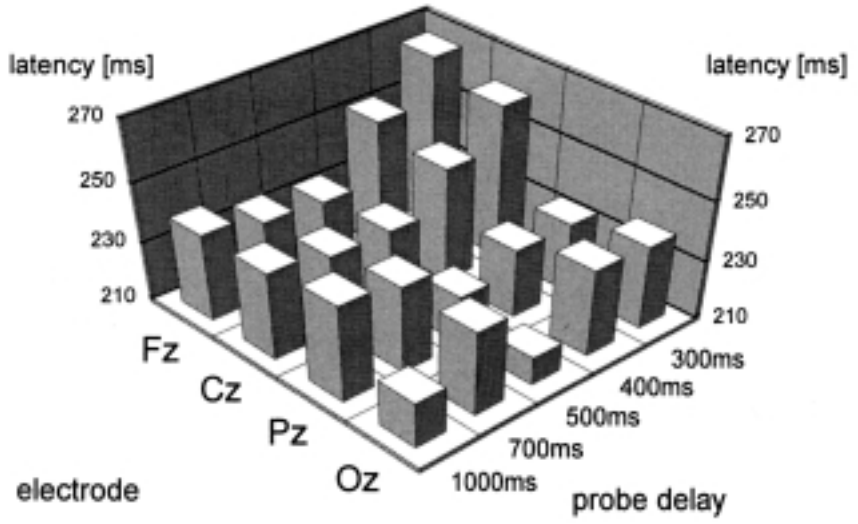

Fig. 5. Probe P2 response latency as a function of probe delay after target stimulus and the recording electrode. Responses after non-target stimuli were excluded.

latencies measured after non-target stimuli did not reveal any significant differences.

Voltage levels from which probe responses started

Figure 6 shows the potential levels immediately preceding responses to probes. Only the recordings in which probes followed target stimuli were included in this analysis. Thus, at short delays, probe responses were superimposed on the falling slopes of the P300 waves. From Fig. 6 it is apparent that, in Pz recordings, probe responses were superimposed on the relatively high levels of positive potential. This was probably due to the fact that Pz electrodes recorded large P300 waves. Mean amplitude of the P300 waves was even slightly higher in Cz recordings. However, Fig. 6 indicates that the positive potentials decayed faster in Cz than in Pz recordings. The fastest decay of positive potentials was recorded with Fz electrode. Interestingly, Fig. 6 indicates that relatively small P300 potentials recorded with Oz electrode decayed slowly. The late negative deflections recorded with Oz electrodes at long latencies were also weaker than negative deflections recorded with the remaining electrodes.

Potential levels immediately preceding responses to probes presented after target stimuli were compared with a two-way ANOVA (delay x electrode). The effects of both variables were highly significant ($F_{3,254}$ = 11.251, P<0.001 for the electrode; $F_{4,254}$ = 16.664, P<0.001 for the delay). Interaction between the delay and the electrode was also significant ($F_{12,254}$ = 2.245, P<0.01).

Data for each electrode were selected and analyzed separately with a one-way ANOVA (delay). In Fz and Oz recordings, potential levels did not differ significantly with the delay. In contrast, in Cz and Pz recordings the effect of the delay was highly significant ($F_{4,67}$ = 6.42, P<0.001 in Cz; $F_{4,65}$ = 13.871, P<0.001 in Pz).

Data for each delay were selected and analyzed separately with a one-way ANOVA (electrode). At 300 ms and 400 ms delays, probe responses recorded with different electrodes started from significantly different voltage levels ($F_{3,51}$ = 7.16, P<0.001 for 300 ms delay and $F_{3,54}$ = 3.475, P<0.022 for 400 ms delay). At 500 ms and 700 ms delays probe responses recorded with all four electrodes started from a similar level. A significant difference appeared again at 1000 ms delay of ($F_{3,52}$ = 4.145, P<0.01). However, Fig. 6 indicates that for this delay, the distribution of voltage levels was different: Oz electrode recorded clearly less negative potential than the other electrodes. This conclusion was supported by a Bonferroni test (P<0.01).

DISCUSSION

Present experiment showed that passive probes could be used to test the functional state of the cortex. Such probes were especially useful in the study of the P300 component because they did not produce the dual task condition. In the present experiment P300 waves were recorded in all subjects. In contrast, when motor responses were required, almost half of the subjects failed to produce this component (Rockstroh et al. 1992). The dual task effect could also be reduced by using SSRs

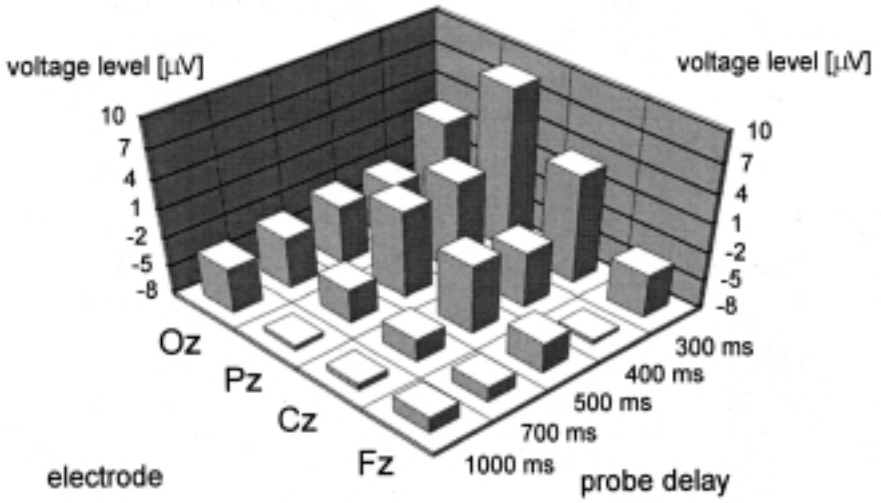

Fig. 6. Voltage level immediately preceding the positive-going slope of probe P2 response as a function of probe delay after target stimuli and the recording electrode. Responses after non-target stimuli were excluded.

(Rockstroh et al. 1996). However, a number of findings indicated that SSR and discrete probe methods may be not directly equivalent. SSR signals were interpreted as a composition of short and middle latency, "automatic" components of evoked potentials (Galambos et al. 1981, Pantev et al. 1993, Tobimatsu et al. 1996). The P200 potential, on the other hand, represents the relatively long latency wave that is probably generated also in the "high" pre-motor areas and could be correlated with "endogenous" processes (Hillyard and Picton 1979). The P200 potential is clearly enhanced in response to target stimuli and showes significant changes due to factors such as pain and stress (Michalski 1998a,b). The notion that steady-state and discrete stimuli may be processed differently was also supported by the finding that attentional modulation of visual SSR and transient responses was expressed in different cortical regions (Gomez et al. 1994, Heinze et al. 1994, Morgan et al. 1996).

The main result of the present experiment was the demonstration of significant differences in the interactions between probe responses and P300 potentials in different cortical areas. Little data about such differences could be found in previous experiments. Rockstroh and co-authors (1992) noted that the strongest attenuation of probe responses was seen in Cz recordings. Since auditory stimulation was used in this experiment, the Cz electrode was located close to the input cortex for this stimulus modality. In contrast, the suppression of auditory SSR signal that was specific to target detection was stronger in frontal areas (Rockstroh et al. 1996). This difference, however, was small and practically disappeared when responses were expressed as a percent reduction from the baseline amplitude.

In the present experiment, responses to passive, discrete probes presented during P300 potentials were strongly inhibited in occipital and parietal fields. Since in these fields the positive "tails" of P300 waves were long, the reduction of probe responses could be due to some kind of ceiling effect. However, the distributions of probe response amplitudes did not indicate a ceiling effect. Responses to probes presented with the 300 ms delay varied between 0 and 32 μV (SD = 6.12). Responses to probes presented with the delay of 400 ms varied between 0 and 23 μV (SD=6.9). For comparison, responses to probes presented with the 1000 ms delay varied between 0 and 23 μV (SD = 5.5). Since the amplitudes were measured from the preceding voltage levels, a ceiling effect should result in a narrower range of amplitudes of short delay responses and smaller maximal values. The fact that the peaks of the probe responses, even superimposed on positive potentials, were clearly lower than P200 peaks in the early responses to "odd-ball" stimuli (see Fig. 2), contradicts the ceiling hypothesis. Finally, regardless of the general attenuation of probe responses during P300 potentials, probe responses were not simply proportional to the preceding voltage levels. The relations were far more complicated:

1. The attenuation of probe responses at short delays after target stimuli was strongest in Oz recordings where the preceding potential levels did not differ significantly as a function of the delay (compare Fig. 4 and Fig. 6).
2. The alterations of potential levels were strongest in Pz recordings but their effect on probe responses was weaker than in Oz.

3. At short delays, the potential levels recorded at Oz and Cz electrodes were similar but probe responses were attenuated much more at Oz then at Cz locations.
4. Figure 4 shows the strongest attenuation of probe responses in the occipital fields and the gradual reduction of this effect in the more frontal regions. Figure 6 indicates that the strongest positive "tails" of the P300 potentials were in Pz recordings. This "tail" becomes weaker in both occipital and frontal cortical fields. Both distributions are rather smooth but they are clearly different.

The complicated pattern of interactions between P300 potentials and probe responses in different cortical areas can be explained on the grounds of the threshold regulation hypothesis (Elbert and Rockstroh 1987, Elbert 1993). Differences could be due to the alterations in sizes or spatial distributions of responding neuronal assemblies and inhibited parts of the network. Alternatively, the results can be explained by invoking different regulatory mechanisms (different feedback loops) operating in specific cortical fields. If the first explanation is accepted, the present results contradict the assumption that probe responses interacted practically only with the inhibited parts of the network. Interactions with both inhibited and excited areas have to be considered. This implies that neuronal assemblies, responding to both P300-evoking stimuli and to probes, were big enough to provide such interactions. On the other hand, the results were not entirely irregular. There was a remarkably smooth transition from the strong inhibitory interactions in the occipital fields to the lack of interactions in frontal areas. It is theoretically possible that the sizes of the responding neuronal assemblies change in such a regular way. Intuitively however, it seems more likely that the effect was due to the different parameters of the threshold regulation loops operating in different cortical fields.

Alterations of responses to probes arising from the different levels of background voltages can be also analyzed in conjunction with the other theoretical concepts, such as the theory of optimal activation (Moruzzi and Magoun 1947, Mangina and Beuzeron-Mangina 1992). According to this theory, there exists an optimal level of physiological activation that provides the best responses to specific stimulation. The theory, developed to explain psychological data, does not contradict the idea of threshold regulation. To the contrary, threshold regulation can be suggested as a putative mechanism providing the optimal level of activation.

In the present experiment, interactions with P300 waves affected not only amplitudes but also latencies of probe responses. The effect looks very convincing in Fig. 2 (regions indicated by arrows). It seems that latencies were actually elongated by preceding P300 waves: probe responses reached their peaks earlier if they were preceded by non-target stimuli. Latency differences were recorded only if probe delays were short enough to provide an interaction with the P300 component. Interestingly, the effect seems to be specific to frontal and central recordings. The distribution of mean latencies, shown in Fig. 5, strongly supports this conclusion. The difference between the latencies of probe responses presented after target and non-target stimuli was highly significant. The delay also affected latencies significantly. However, the difference between the latencies recorded with different electrodes reached the level of statistical significance only when responses after target stimuli were selected and only for the shortest probe delay. Thus, this last effect should be treated with caution. But if there really was a difference between the electrodes, the emerging pattern becomes fascinating. It suggests that information reaching the primary cortex when it is "busy", is delayed in some sort of a buffer and is sent to the higher fields only when they are ready.

At short delays, the amplitudes of probe responses were severely reduced in input occipital areas. But the same responses regained their amplitudes in frontal fields, therefore their strengths had to be restored. The effect of the restoration of attenuated responses at the higher level of information processing has been reported in experiments on responses of single neurons. Reducing the strengths of neuronal responses by cooling did not change the preferred stimulus orientation or the width of orientation tuning in neurons of cat's primary visual cortex (Michalski et al. 1993, 1994). This enabled the restoration of responses to nearly original parameters in the higher visual area 21a that operated at physiological temperature. An attempt to explain the present ERP data with the results of single neuron experiments might be premature but it is not unlikely that similar mechanisms are involved.

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