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Positive shifts of event-related potentials: a state of cortical disfacilitation as reflected by the startle reflex probe

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Summary Cortical positivity as measured by slow event-related potentials is assumed to represent a decreased excitability of cortical networks and suppression of their behavioral-cognitive output. The blink reflex probe is a commonly used defensive electromyographic response whose amplitude was shown to be modulated by emotional and attentional orientation. It was used here as an indicator of cortico-subcortical excitation.

In study 1, 33 healthy subjects took part in a continuous performance test (CPT). Event-related potentials were recorded from 15 standard scalp locations. Acoustic startling noise bursts were delivered during conditions that required either performance of prepared motor responses (Go), inhibition of prepared motor responses (NoGo), or had no motor significance (Irrelevant condition). During the NoGo condition, EEG surface potentials showed a widespread P300-like positivity with a central maximum. Startle responses were inhibited during the NoGo condition as compared to the Irrelevant condition. In study 2 (21 subjects) the same format was used, except that the startle reflex was elicited visually. Startle reflexes again showed smaller magnitude during the NoGo condition, which evoked larger positivity at central sites in comparison to the Irrelevant condition.

The relationship between positivity in the EEG and inhibited startle responses is in line with the hypothesis that positive EEG shifts reflect a state of cortical disfacilitation.

Key words: Event-related potential; P300; Go/NoGo task; Startle reflex; Cortical excitability

Theories of cognitive psychophysiology associate the P300 with "context updating" (Donchin and Coles 1988), "context closure" (Verleger 1988) or "controlled processing" (Rösler 1982). All of these theories are compatible with the assumption that the P300 manifests an inhibitory event (Birbaumer and Elbert 1988). Whereas Rösler (1977) and Verleger (1988) proposed an inhibitory nature of the P300, Donchin and Coles (1988) interpreted the P300 without referring to the underlying physiological nature of the phenomenon. Deecke et al. (1984) are more rigourous in their resolution/relaxation hypothesis which assumes that the P300 positivity constitutes an inhibitory resolution of preceding excitatory negativity. Based on biophysical considerations, Lutzenberger et al. (1987) concluded that slow potentials such as the P300 and other late components of the event-related potentials must have widespread synchronous and primarily cortical sources. Taking into account the highly interwoven cortical networks (Braitenberg and Schüz 1991), consisting mainly of pyramidal neurons, Rockstroh et al. (1989) and Birbaumer et al. (1990) assumed that negative shifts in event-related potentials (ERPs) indicate enhanced excitability of neural networks (a preparatory state for cerebral processing), whereas positive shifts are supposed to reveal decreased excitation (a disfacilitatory state of neural networks).

A relationship between "spontaneously" occurring slow potentials and information processing is supported by studies using the "potential-related event" paradigm (Stamm 1984) and the "brain trigger" paradigm (Bauer 1984). For example, delayed response tasks were solved significantly faster when presented contingent on frontal negative shifts than on frontal positive shifts in slow potentials (Born et al. 1982). Self-generated variations in slow potentials induced via biofeedback confirmed this relationship (e.g., Bir-

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baumer et al. 1981). Additional evidence for the link between negativity and enhanced cortical activation comes from observations made during epileptic seizures. Extreme widespread surface negativity occurs during and before generalized tonic-clonic epileptic seizures which are a consequence of overexcitability of neuronal networks (Elbert et al. 1991). On the other hand, recent studies (Woodward et al. 1991; Rockstroh et al. 1992) have supported a link between positive-going evoked potentials (P300 waves) and cortical disfacilitation or inhibition. In these studies, clicks which required button presses were presented at various time intervals after standard and target stimuli in an oddball paradigm. Slowest reaction times in response to the clicks occurred at the time interval from 300 to 370 msec after target stimuli which evoked maximum positivity in the form of enlarged P300 waves. It was concluded that the enlarged P300 positivity indicated cortical inhibition resulting in delayed responses.

An additional approach which tests the assumed functional significance of positive and negative waves is to use reflexes as a probe for the state of excitability of a neural network. Sudden and intense stimuli of all modalities elicit the startle response, which is a whole body flexor response (Landis and Hurt 1939). The eyeblink is a sensitive part of the startle response. Changes in the amplitude of the polysynaptic blink response reflect changes of excitability at the midbrain and brain-stem level. Higher central processes such as attentional direction (Anthony 1985) or emotional valence (Lang et al. 1990) are capable of altering gains of the neural structures of the reflex path and influencing startle response amplitudes. We expected an additional mechanism capable of startle modulation, namely the processes associated with inhibition of planned actions.

In particular, we assumed that a fronto-central positive shift in the ERP reflects the interruption of response activation processes in a non-specific manner. More pronounced fronto-central positivity has been found during NoGo trials in Go/NoGo tasks (e.g., Pfefferbaum et al. 1985; Kok 1986; Gevins et al. 1989; Jodo and Inoue 1990). In addition De Jong et al. (1990) reported an inhibition of the negative-going lateralized readiness potential when subjects had to withhold a response (stop paradigm). These findings support an association of positive slow potentials with the interruption of specific response activation processes. Whether that inhibition affects response modalities other than those involved in the production or suppression of specific target behaviors is less clear. In the present study, we used the startle probe procedure to test for inhibition associated with scalp positivity, and to evaluate the specificity of that inhibition.

A modified version of the Continuous Performance Test (CPT; Stamm et al. 1982) was used to induce excitatory and inhibitory event-related potentials. Three conditions were employed. Two conditions included preparation of a target response which in one case had to be interrupted (NoGo condition), while in the other case the response had to be performed (Go condition). The third condition involved neither response preparation nor response occurrence and, therefore, was expected to evoke small positivity (Irrelevant condition). In extension of previous studies, the present study used multichannel EEG recording which allows the detailed descriptions of the local distribution of the EEG potentials and their origin. Startle reflexes were elicited during all 3 conditions of the CPT. The question we asked was whether the inhibition thought to be reflected by augmented P300s on NoGo trials would modulate responding in the startle modality.

One problem of our methodology concerned the interpretation of the startle response to the Go condition. Startle delivery could precede or follow the button presses. It is well known that reflex responses including startle responses are facilitated by any response execution (Brunia and Boelhouwer 1988). For that reason, both the conditions which do not involve motor responses (Irrelevant and NoGo condition) are of particular relevance in the present study. Given that surface positive shifts reflect disfacilitation of neural networks, the startle response should be attenuated in the NoGo condition as compared to the Irrelevant condition.

Under the assumption that P300 amplitude reflects disfacilitation of those dendrite pools underlying the respective electrode, inhibition of a motor response such as the startle reflex should be more dependent upon fronto-central positive variations of cortical polarization than the posterior localizations. A closer fronto-central relationship between startle magnitude and positive amplitudes is also supported by the animal literature (Bubser and Koch 1993) which points to a frontal-subcortical pathway of startle modulation as the only established source of cortical modulatory influence on subcortical nuclei that organize the startle response.

In order to exclude interpretations of startle modulation as stimulus modality dependent, a second study was performed using visual startle stimuli as probes.

Study 1

Methods

Subjects

Thirty-seven volunteers (15 women and 22 men; aged from 19 to 37) were paid for their participation in the experiment. Subjects were not included if they reported being on medication. The records of 3 subjects were excluded from the statistical analysis be-

cause no reliable startle response occurred. Data from one subject were lost due to computer failure.

Procedure

The experiment consisted of two series of the CPT, with a 5 min rest period in between. A total of 400 letters were presented on a screen, 200 letters in each series. Five different letters, T, H, Z, O and X were used. Each letter appeared in the center of a video screen for 100 msec and followed the previous one after a fixed inter-stimulus interval of 2 sec. Subjects were instructed to press a button when an "X" appeared but only if it was preceded by an "O." According to their differential meaning, the letter sequences were divided in 3 conditions: (1) Go condition (O–X), (2) NoGo condition (O–non-X), and (3) Irrelevant condition (a letter other than X was presented after a letter other than O). Both series consisted of 50 target sequences (O–X), 50 non-target sequences (O–non-X) and 200 irrelevant letters (T, H, Z). The stimuli were presented in a pseudorandom order.

Eighty startle probes were randomly delivered during both series of the CPT, with a probability of 20%. Each startle probe occurred 450 msec after presentation of a letter. This time point was based on the latencies of the P300 amplitude found in previous studies (Stamm et al. 1982; Roberts et al. 1994). Ten startle stimuli were delivered after presentation of a target sequence (O–X). Another 10 startle stimuli were delivered after a non-target sequence (O–non-X), and 60 startle probes were presented after the occurrence of single irrelevant stimuli.

During the experiment, subjects sat in a reclining chair in a room that had partial electrical shielding. Written descriptions of the CPT emphasized speed as well as accuracy. Subjects could earn a monetary bonus according to their performance. A brief series of practice trials (presentation of 20 letters) was given, which included all CPT conditions and startle probes. Following these practice trials, which were supervised by the experimenter, the CPT commenced.

Stimuli and apparatus

The acoustic startle stimuli consisted of a 50 msec, instantly rising, burst of white noise (0.02–20 kHz), presented binaurally via headphones and generated by a DEC PDP 11/23 computer. Before starting the experimental trials, the intensity was adjusted for each subject and varied in loudness between 85 dB(A) and 95 dB(A). During the experiment, the intensity was kept constant. A second computer (DEC PDP 11/73) controlled stimulus timing and digitized the physiological records. The CPT was presented on a video screen which was located 2 m in front of the subject at eye level. At this distance the display subtended a visual angle of 6°.

Physiological recording and data reduction

The EMG of the right orbicularis oculi muscle was recorded using surface mini-electrodes (Beckman) filled with Beckman electrolyte. The EMG signal was amplified by a Nihon-Kohden amplifier with a 70–500 Hz bandpass. The recording interval commenced when the startle response was detected and lasted for 70 msec. The sampling rate was 2 kHz. EMG records were analyzed off-line according to the "denoising in quadrature" procedure described by Fridlund and Cacioppo (1986). EMG magnitude was calculated as the sum of squares in a window 10–70 msec following startle onset. The logarithm of this score was used in data analysis to normalize the distribution. Trials with an unstable baseline for a 20 msec window after startling noise onset were eliminated. Discarded trials differed only slightly as a function of CPT condition (8.76% Irrelevant vs. 5.71% Go vs. 9.2% NoGo condition).

The EEG was recorded from 15 sites using a commercially available electrode cap with tin electrodes (Electro-Cap International) according to the international 10–20 system. Ag/AgCl electrodes were placed on the mastoids. Electrical impedance was 5 kΩ or less for all electrodes. All channels were recorded with a Cz reference (bandwidth 0.016–35 Hz, sampling rate 100 Hz) and converted off-line to a linked ears reference. Vertical and horizontal eye movements were recorded and trials with excessive eye movements (> 100 μV) were excluded. EOG correction was applied by means of the constant fraction method described by Elbert et al. (1985). All trials including either startle probes or response failures were excluded before averaging.

Stimulus synchronized average event-related potentials were calculated separately for conditions and electrode sites. A baseline-to-peak P300 amplitude was calculated for the maximum positivity between 200 and 500 msec after stimulus onset and referred to a prestimulus baseline. In addition, the mean amplitude shift of the 80 msec before startle onset was calculated. This reflected the cortical positivity just before startle delivery, which is better suited for testing our hypothesis concerning startle modulation rather than the maximum amplitude with its different latencies. To account further for these latency shifts, we calculated the latencies of the maximum positivity in the window from 0 to 500 msec after stimulus onset.

Statistical analysis

In a first analysis, the amplitudes of the late positive components of the EEG were submitted to an ANOVA with 3 within-subject factors. The first factor "condition" consisted of 3 experimental levels, NoGo, Go and Irrelevant conditions. Electrode sites were divided in 3 coronal rows and 5 sagittal rows to detect differences in scalp topography (Ford and Pfefferbaum 1991). The

second factor "anterior-posterior" included 3 levels, frontal (F7, F3, Fz, F4, F8), central (T3, C3, Cz, C4, T4) and parietal (T5, P3, Pz, P4, T6). The third factor "laterality" included 5 levels, these being far-left (F7, T3,T5), mid-left (F3, C3, P3), midline (Fz, Cz, Pz), mid-right (F4, C4, P4) and far-right (F8, T4, T6). Initial results showed no interesting effects of the factor "laterality." Thus, the amplitudes across the sagittal rows were collapsed and the ANOVAs were calculated only with the factors "condition" and "anterior-posterior."

The EMG segments were separated and averaged (Putnam and Roth 1990) according to the 3 conditions of the CPT: (1) NoGo, (2) Irrelevant, and (3) Go conditions. The calculated EMG scores were subjected to an ANOVA containing the within-subjects factor "condition" (with 3 levels) and a second factor "series" (with 2 levels). The "series" factor was introduced to account for habituation effects.

In all ANOVAs, Greenhouse-Geisser epsilon values were applied to correct for lack of sphericities in the covariance matrices involving repeated measures factors with levels exceeding 2. Corrected P values are reported throughout. Contrasts of groups of means were used as post-hoc tests.

In addition, Pearson product-moment correlation coefficients were calculated within each subject between mean startle magnitude on NoGo, Go and Irrelevant trials, and the corresponding mean cortical positivities, separately for every single electrode [1]. For the statistical analysis the correlation coefficients were z-transformed (correlations were restricted to a maximum of 0.7, to avoid inflation of z values). A t test was used to test the mean correlation across all electrodes for significance. In a further analysis, an ANOVA containing the factor "anterior-posterior" was calculated to account for possible topographic specifity of the correlation coefficients.

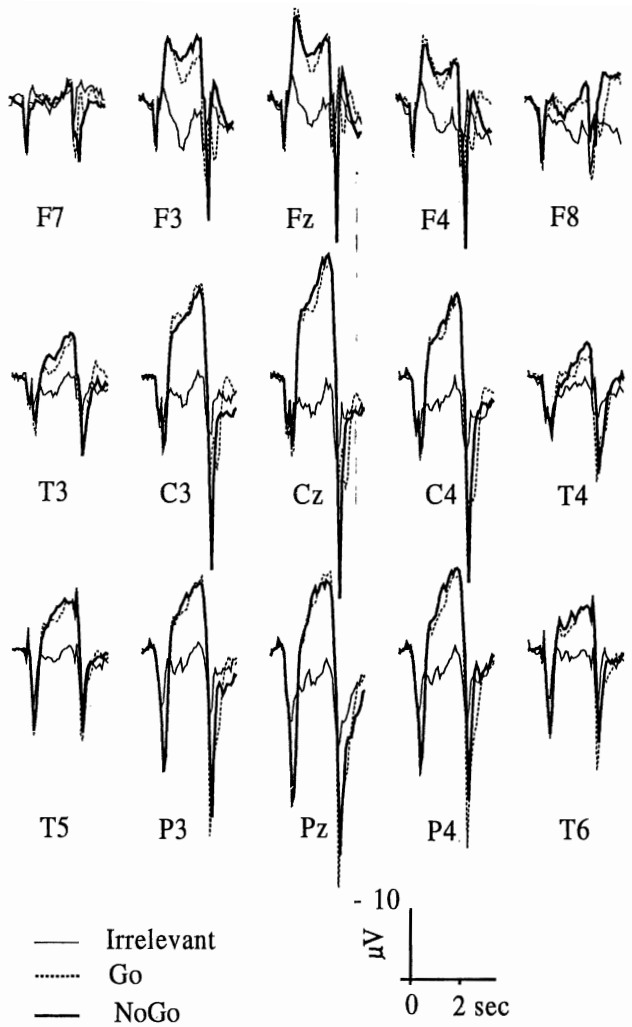

Fig. 1. Grand average wave forms separated for 15 electrodes with (mathematically) linked ears reference, recorded during the Go, NoGo and Irrelevant conditions. Evoked responses to the first (presented at second 0) and second (presented at second 2) letters are depicted.

Results

Reaction time

The mean reaction time to targets was 405 msec (S.D. 84.4). On average, misses occurred on only 0.79 trials (S.D. 1.7) and false alarms on 1.0 trial (S.D. 1.1).

Event-related potentials

Grand average wave forms from the 15 scalp positions and the 3 conditions are presented in Fig. 1. Presentation of S1 elicited in the case of an "O" (Go and NoGo trials) a P300-like wave that was followed by a slow negativity (CNV) as subjects prepared for S2 and a possible button press. A statistical comparison of CNV shifts revealed no difference between Go and NoGo trials (either in terms of a main effect "Go vs. NoGo" or in terms of an interaction "Go vs. NoGo" × "anterior-posterior" (all $Fs < 1.2$, $P > 0.23$)), which was to be expected because subjects were unable to predict the identity of the S2 stimuli (Go or NoGo letter). Obviously, the P300 wave following presentation of S2 is much larger for Go and NoGo stimuli than for Irrelevant stimuli. Go and NoGo trials differed in their fronto-central topography. Fig. 2 illustrates the grand averages for the Fz, Cz and Pz electrodes, with the positive amplitude shift being referred to the pre-S2 baseline. The main effect "anterior-posterior" (F (2, 64) = 34.2, $P < 0.0001$) was due to larger

[1] The rationale for using the trials without startle delivery was that more trials were included in the averaging procedure. However, as startles were delivered pseudorandomly, this was expected to be a reliable estimate of the state of cortical positivity.

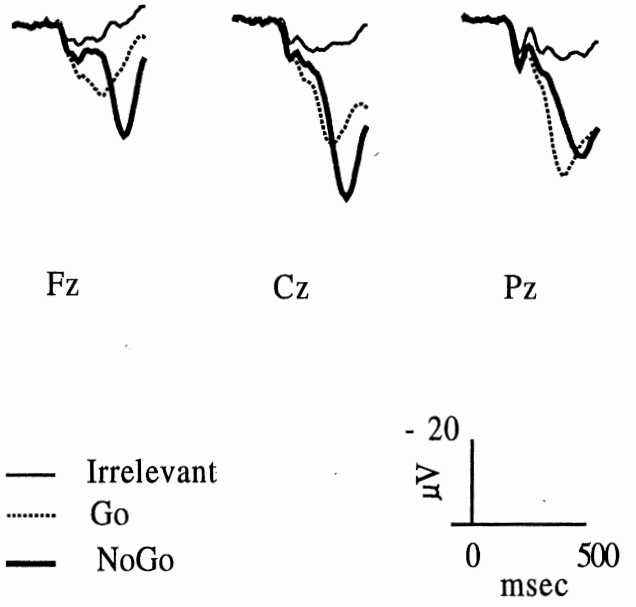

Fig. 2. Average P300 midline wave forms computed with respect to the pre-stimulus baseline on Go, NoGo and Irrelevant trials.

amplitudes centrally and parietally in comparison to frontal sites (both Fs > 53, $P < 0.0001$). The main effect "condition" (F (2, 32) = 79, $P < 0.0001$) was due to larger amplitudes for the NoGo (23.4 μV) and Go (22.7 μV) conditions in comparison to the Irrevelant condition (9.6 μV; both post-hoc Fs > 110), but no difference was found between Go and NoGo amplitudes ($F < 0.5$).

The interaction "condition × anterior-posterior" (F (4, 128) = 29, $P < 0.0001$) is depicted in Fig. 3, where P300s are referred to the pre-S2 baseline (top panel). Go P300 amplitudes had a parietal maximum with decreasing amplitudes at more anterior sites. All post-hoc tests comparing the 3 coronal rows were highly significant (all Fs > 29, $P < 0.0001$). In contrast, the NoGo cues evoked a central row maximum positivity which was significantly larger as compared to the frontal ($F = 132.8$, $P < 0.0001$) or parietal rows ($F = 22.3$, $P < 0.0001$). Amplitudes at parietal sites were significantly larger than at frontal electrodes ($F = 46.2$, $P < 0.0001$) [2].

[2] Close inspection of Fig. 1 revealed also that the NoGo topography resembled the CNV topography, showing a central maximum. To assess the possibility that the NoGo topography was due to a rapid resolution of motor CNV, we recalculated the NoGo P300 with reference to the pre-S1 baseline (Simson et al. 1977). We found the same centro-frontal topographic pattern for NoGo stimuli even after removal of possible CNV influences. Like the pre-S2 baseline, NoGo amplitudes were centrally larger than parietally ($F = 7.6$) and frontally ($F = 39.2$) and parietally more pronounced than frontally ($F = 12.2$). Similar findings have been reported by Roberts et al. (1994).

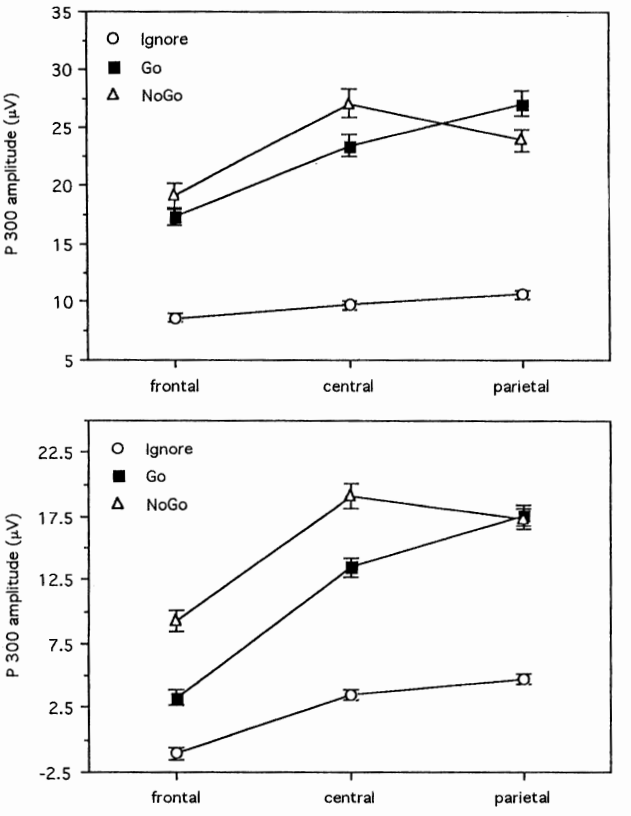

Fig. 3. P300 maximum amplitude on Go, NoGo and Irrelevant trials averaged over frontal, central, and parietal electrodes (top panel). Mean P300 amplitude shift (calculated for values 80 msec before startle onset) averaged over frontal, central and parietal electrodes (bottom panel). Standard errors (+ / − 1) are shown.

Post-hoc tests across conditions revealed that Go stimuli evoked larger parietal P300 amplitudes as compared to NoGo stimuli ($F = 22.6$, $P < 0.0001$). At central ($F = 29.2$, $P < 0.0001$) and frontal ($F = 8.0$, $P = 0.012$) sites, the pattern was reversed: the NoGo stimuli evoked larger P300 amplitudes.

P300 latency

Inspection of Fig. 2 revealed obvious latency differences between conditions. The ANOVA revealed a main effect "condition" (F (2, 64) = 55.6, $P < 0.0001$), indicating that latency was shortest for Irrelevant trials (288 msec), intermediate on Go trials (343 msec) and longest for NoGo cues (398 msec). All possible contrasts had F values higher than 27 ($P < 0.0001$). Latencies also differed along the anterior-posterior axes (F (2, 64) = 51.8, $P < 0.0001$). Latencies were shorter frontally in comparison with central and parietal sites (both Fs > 59). The interaction "condition × anterior-posterior" failed to reach significance (F (4, 128) = 2.3, $P < 0.1$).

Mean amplitude of the positive shift before startle onset

We tried to estimate the functional state of the networks by calculating the mean amplitude shift 80 msec before startle onset, again referred to a pre-S2 baseline. To compare this analysis with the P300 amplitude results, the amplitudes for the anterior-posterior axes are plotted separately for conditions in Fig. 3 (bottom panel). In contrast to the P300 maximum analysis, Go and NoGo trials were not only significantly different from the Irrelevant condition (both Fs > 66), but NoGo amplitudes were significantly larger than Go amplitudes ($F = 11.6$, $P > 0.01$; main effect "condition" F (2, 64) = 70.7, $P < 0.0001$). The main effect "anterior-posterior" (F (2, 64) = 86, $P < 0.0001$) was due to larger mean amplitudes at parietal and central sites in comparison to frontal sites (both Fs > 109). The interaction "condition × anterior-posterior" (F (4, 128) = 37.4, $P < 0.0001$) was due to larger mean amplitudes frontally ($F = 105$) and centrally ($F = 94$) for NoGo stimuli in comparison to Go stimuli but no differences parietally ($F = 0.2$). Go and NoGo stimuli had significantly larger amplitudes frontally, centrally and parietally (all Fs > 55) compared to Irrelevant cues.

In summary, NoGo and Go stimuli had significantly larger amplitudes at every electrode site in comparison to the Irrelevant cues. This effect was more pronounced centrally and parietally. The main difference between Go and NoGo stimuli was attributed to amplitudes that were larger during NoGo trials at frontocentral sites.

Startle responses

The wave forms of the EMG traces after application of the "denoising in quadrature" procedure (Fridlund and Cacioppo 1986) are depicted in Fig. 4 separately for Go, NoGo, and Irrelevant condition. Differences were found which were most pronounced between 50 and 70 msec after noise onset. This is illustrated in Fig. 5 which shows the means of the startle responses for all 3 conditions. The ANOVA confirmed a significant main effect "condition" (F (2, 32) = 5.05, $P = 0.016$) and a highly significant main effect "series" (F (1, 32) = 81, $P < 0.0001$) reflecting the habituation of the startle reflex. The interaction "condition × series" failed to reach significance (F (2, 64) = 2.4, $P = 0.09$). Post-hoc t tests revealed no difference between the reflex magnitude for Irrelevant and Go condition ($F <$ 1), but reduced startle reflex response to the NoGo condition in comparison to the Irrelevant ($F = 9.4$, $P < 0.01$) and Go condition ($F = 5.1$, $P = 0.036$).

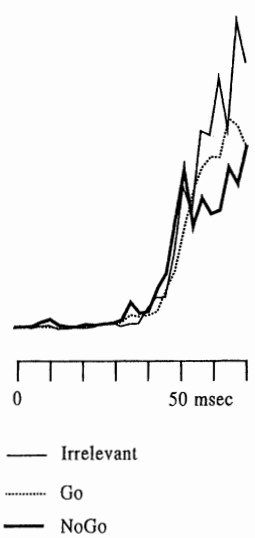

Fig. 4. EMG traces for the Irrelevant, NoGo and Go conditions after application of the "denoising in quadrature" procedure (Fridlund and Cacioppo 1986).

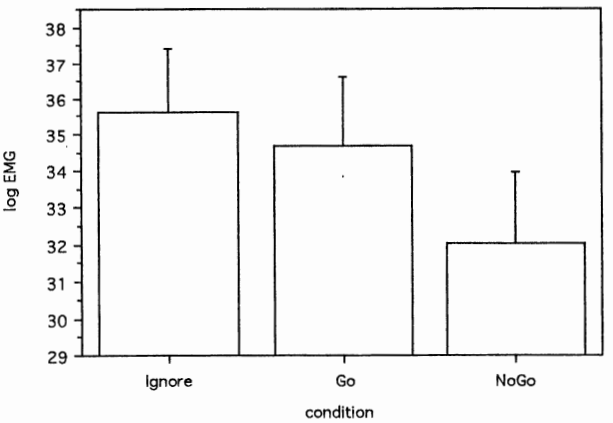

Fig. 5. Startle magnitude to the Ignore, Go and NoGo conditions. The bars indicate between standard errors of the means.

Correlation analysis

Averaging of the correlation coefficients over all electrodes (within-subjects) resulted in a significant overall negative correlation of $r = -0.27$ between cortical positivity and startle magnitude (t (32) = 3.7, $P <$ 0.001) [3]. Thus, more pronounced cortical positivity was associated with smaller startle magnitude. In addition, we tested the correlations along the anterior-posterior axes to look for topographic specificity. Although central electrodes showed highest correlations (mean of -0.3), the parietal (mean of -0.25) and frontal (mean of -0.26) electrodes also showed significant correlation coefficients.

[3] In addition, the same correlation analysis was done with cortical positivities referred to the pre-S1 baseline. A somewhat smaller but still significant correlation of $r = -0.16$ (t (32) = 2.3, $P < 0.03$) was obtained. This points to the view that the actual modulation of cortical excitability was in this context more relevant than the absolute level or amount of cortical positivities.

The Go condition

The reported mean correlation of $r = -0.27$ might be an underestimate of the relationship between startle magnitude and cortical positivity because the startle magnitude during Go trials is also influenced by response execution. Response execution enhances any reflex response for about 100 msec (Brunia and Boelhouwer 1988). Processes of response execution were expected to be less pronounced for slow subjects, these being defined by responses that came after startle delivery.

For descriptive purposes we divided our sample, according to their reaction times, into two groups, and then calculated an ANOVA with the factors "anterior-posterior" and "group." The mean reaction time to the Go letters was 354 msec for fast subjects and 484 msec for slow subjects. A significant main effect "group" (F (1, 31) = 7.7, $P < 0.01$) emerged, indicating a high mean correlation of $r = -0.47$ between startle magnitude and cortical positivity for slow subjects in contrast to an $r = -0.1$ for fast subjects.

Following up this post-hoc group division, we repeated the startle and EEG analyses by adding this "group" factor. There was no significant group effect in the analysis of the mean shift 80 msec before startle onset. In contrast, startle analysis revealed a significant main effect "group" (F (1, 31) = 4.6, $P < 0.05$) and a significant interaction "condition × group" (F = (2, 62) = 4.2, $P < 0.03$). Startle magnitude was generally larger for fast subjects. For fast subjects, the Go condition revealed the largest startle responses. They were significantly larger than in the NoGo condition ($F = 8.7$, $P < 0.01$), but not significantly different from the Irrelevant condition. In contrast, the Go condition revealed an inhibited startle magnitude comparable to the NoGo condition for slow subjects, which was significantly larger than in the Irrelevant condition ($F = 7.7$, $P = 0.02$). In both groups, the NoGo startle magnitude was inhibited compared to the Irrelevant condition ($F = 8.3$, $P = 0.01$ for slow subjects; $F = 15$, $P < 0.001$ in series 1 for fast subjects).

Discussion

We predicted a startle modulation depending on the actual excitability of cortical neuronal networks. Excitability (average firing threshold) is defined here by the polarity and amplitude of late (> 300 msec) event-related potentials. More specifically, startle probes were presented during different conditions of the CPT in order to test the hypothesis of positive shifts being an indicator of reduced excitability of neuronal networks. The attenuated startle response in the NoGo condition supported our hypothesis and was observed in 28 out of 33 subjects in the first series. The fact that startle was modulated by the NoGo P300 indicates that the inhibition brought out by the NoGo requirement was not specific to the target (button press) response.

It could be argued that NoGo stimuli had more relevance and interest as compared to the Irrelevant stimuli: within the Irrelevant condition, subjects already knew that the actual stimuli had no behavioral significance. Much more attention was directed to the NoGo stimuli because the previous "warning stimulus" (O) indicated a subsequent significant event. It is known that interest is an important variable influencing the startle response: when the stimuli which have to be processed and the startle eliciting stimuli share the same modality, increased attention enhances startle responses (Anthony and Graham 1985; Simons and Zelson 1985). In this respect it is noteworthy that in Study 1 acoustic startle stimuli and visual processing stimuli provided a condition of cross-modality. One might therefore argue that startle reduction occurred on NoGo trials, because attention was switched to the modality of the CPT cues (visual) and away from the modality of the startle probe (an acoustic stimulus).

To exclude this alternative account, Study 2 used the visual CPT and elicited the startle reflex from a visual modality. According to the attentional interpretation, visual startle amplitude should be increased during the attentional NoGo condition. According to the prediction of the model proposed here, frontocentral positivity should always be related to startle reduction, independent of stimulus modality.

Study 2

Methods

Twenty-one students (10 females, 11 males) participated in the present experiment. Age ranged from 20 to 24 years. Seven subjects were excluded from all analysis, because they did not show reliable startle responses. This left 14 subjects in the analysis.

Apparatus and physiological recording were identical to Study 1 except that a visual startle probe stimulus was used. This consisted of the simultanous firing of two flash units (modified speed stroboscope, 100 W). The flash units were placed approximately 15 cm apart, 2 m in front of the subject, under the computer monitor where the CPT cues were displayed. The flash units were insulated to prevent any sounds from interfering with the experiment.

Results

Reaction time

The mean reaction time to targets was 376 msec (S.D. 58). A t test comparing the reaction times of the

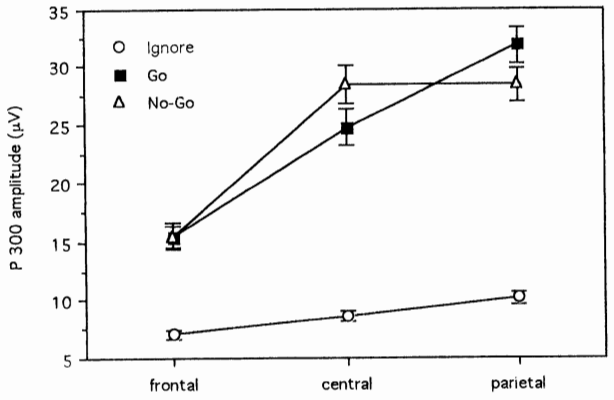

Fig. 6. P300 maximum amplitude (referenced to the pre-stimulus baseline) on Go, NoGo and Irrelevant trials averaged over frontal, central, and parietal electrodes (top panel) in Study 2. Standard errors (+/−1) are shown.

two studies revealed no significant differences between them (F (1, 48) = 1.5, $P > 0.2$).

P300 amplitudes

The comparison of the amplitudes for all 3 conditions along the anterior-posterior axes revealed a close correspondence to the findings in Study 1 as illustrated in Fig. 6. Again, the main effect "anterior-posterior" (F (2, 26) = 33.8, $P < 0.0001$) was due to larger amplitudes at central and parietal sites than at frontal sites (both Fs > 34). The main effect "condition" was highly significant (F (2, 26) = 64, $P < 0.0001$). Post-hoc tests revealed no significant difference between Go and Nogo trials (F < 0.1), but the amplitudes in the Go and NoGo condition were larger than those in the Irrelevant condition (both Fs > 78). The significant interaction "condition × anterior-posterior" (F (4, 52) = 25.2, $P < 0.0001$; see Fig. 6) was due to larger central NoGo P300 amplitudes in comparison to the Go amplitudes ($F = 10.9$, $P < 0.01$), but Go amplitudes were larger at parietal sites than NoGo amplitudes ($F = 9.4$, $P < 0.02$). No difference between Go and NoGo trials was found frontally ($F > 0.1$). All post-hoc tests comparing Go/NoGo trials with the Irrelevant condition were highly significant (all Fs > 56)

Startle reflex

The significant main effect "series" (F (1, 13) = 7.5, $P = 0.016$) revealed the habituation of startle magnitude from the first half of the CPT to the second half. The main effect "condition" (F (2, 26) = 1, $P = 0.38$) was not significant, but the interaction "condition × series" (F (2, 26) = 4.7, $P = 0.027$) revealed startle modulation between conditions for the first half of the CPT only. The startle reflex for the Go condition revealed larger magnitudes in comparison to NoGo ($F = 19.6$, $P < 0.001$) and Ignore stimuli ($F = 5.7$, $P = 0.03$). The comparison of Irrelevant and NoGo startle magnitude revealed smaller startle magnitudes for the NoGo condition, and only approached accepted levels of significance ($F = 4.2$, $P = 0.06$). The relevant comparison of NoGo trials with Irrelevant trials only demonstrated a significant difference for startle attenuation (F (1, 13) = 5.1, $P < 0.05$).

As reported previously (e.g., Bradley et al. 1990), magnitude of the startle to the visual probe was found to be significantly attenuated in comparison to that of the acoustic probe (F (1, 45) = 19.9, $P < 0.0001$). On average, acoustic startle magnitude was about twice as large as that obtained with visual stimuli.

Discussion

Results of study 2 replicate those of the first study. The attenuation of the startle magnitude during cortical positivity is independent of the modality of the startle stimulus. An interpretation of startle modulation on the basis of attentional resource allocation models as proposed by Graham and her associates (Anthony and Graham 1985) seems insufficient to account for the data presented here. Graham's model predicted increased startle amplitude of the same modality due to priming of attentional resources, and reduction of startle magnitude in the case of cross-modal stimulus presentation due to attentional resource competition.

General discussion

In line with previous research, we also found a different topographic pattern between the Go and NoGo P300s (Pfefferbaum et al. 1985; Kok 1986; Jodo et al. 1990), but no general amplitude differences. The positivity elicited by the Go and Irrelevant conditions had a parietal maximum with decreasing amplitudes at central and frontal sites. During the NoGo condition, the positivity was most pronounced at central sites and also present at frontal and parietal sites. Computing event-related covariances, Gevins et al. (1989) reported prominent covariances in the time interval of the P300 between anterior Cz and Fz in Go and NoGo trials. The anterior Cz site led Fz with a short delay in the Go trials and with a long delay in the NoGo trials. Gevins et al. (1989) interpreted the short delay in the Go condition as reflection of control processes for the initiation of response. The widespread centro-frontal positivity in the NoGo condition which required active response inhibition of the preprogrammed motor response (a button press) could be seen as a sign of the differential involvement of the prefrontal cortex, i.e., the interruption of non-specific response activation processes (De Jong et al. 1990; Roberts et al. 1994).

A statistical comparison of the positive shifts revealed an influence of the modality of the probe on the topography of the positive shifts. As revealed by a significant interaction "probe modality" (acoustic or visual) × "anterior-posterior" ($F(2, 90) = 6.9$, $P < 0.01$) frontal positivity was decreased and parietal positivity was increased for the visual probe in comparison to the acoustic probe. This pattern was parietally more pronounced for the Go and NoGo trials than for Irrelevant trials ("probe modality" × "anterior-posterior" × "condition": $F(4, 180) = 4.3$, $P < 0.01$). Thus, the sources generating positive and negative deflections may be more posterior for the visual startle probe. This may be due to the unimodal visual character of probe stimuli and the attention paid to the letters of the CPT. Presentation of stimulus material in the visual modality has been found to produce P300 sources in more posterior directions (e.g., Alho et al. 1992).

Overall the results of both studies are in line with a modality independent association of fronto-central positivity with reduction of motor outflow as measured by EMG responses such as the startle reflex (see also De Jong et al.'s study, 1990, for reaction times). The reported results are also compatible with anatomical and electrophysiological studies in rats (Bubser and Koch 1993) supporting a connection of fronto-cortical regions to subcortical nuclei subserving the organization of the "whole-body" startle response.

To be considered are several alternative explanations of modulations in startle magnitude. One might argue that the present results could be explained in terms of "prepulse inhibition" (Graham 1975). Acoustic and visual startle stimuli were presented 450 msec after a visual stimulus. Graham described an inhibitory effect at this lead interval with discrete, as well as continuous, acoustic lead stimuli (but much stronger effects at shorter intervals). Since this effect is very robust and, at this interval, modality independent (Hoffmann and Ison 1980; Blumenthal and Gescheider 1987), startle amplitudes should have been influenced during all conditions (Go, NoGo, Irrelevant) to a similar degree. The effect of prepulse inhibition therefore cannot explain the condition-dependent startle modulation observed in the present experiment.

Lang et al. (1990) and Bradley et al. (1990) have studied how the startle response is modulated by emotional valence. They found that startle responses were reduced during periods in which their subjects reported positive valence and were facilitated during negative valence. Concerning the present study, an "emotional" explanation is probably not relevant, unless one makes the unlikely assumption that the NoGo condition was less aversive than the Irrelevant condition. Lang's results could also be seen in a more general motor inhibition context. Pleasurable situations may be evolutionarily related to a conservative, "standstill," or diminished response disposition, at least in comparison to aversive flight-fight contexts which require immediate and fast motor readiness. In our experimental situation, we hypothesized that active inhibition of a preprogrammed response was the main reason for startle inhibition and EEG positivity. We speculated that the fronto-central cortical positivity constituted a prerequisite for the motor inhibition (De Jong et al. 1990) and that cortico-fugal disfacilitation attenuated subcortical or brain-stem neuronal pools subserving the startle reflex. Emotional valence is not the critical variable in this context, because valence is just a special case of (non-emotional) response dispositions.

In summary, the presented study supported the hypothesis that positive slow potentials may indicate a disfacilitated state of neuronal networks: during motor response inhibition, surface positivity of the EEG was pronounced and startle reflex responses were decreased. Birbaumer et al.'s (1990) model of the functional role of slow cortical negativities and positivities predicts a disfacilitatory role of local cortical positivities independent of an inhibitory motor response disposition. This generalization requires an experimental approach without motor response requirements and simultaneous presentation of startle probe stimuli. A study of this kind is presently in press (Brody et al. 1993).

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