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SSR-MODULATION DURING SLOW CORTICAL POTENTIALS

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INTRODUCTION

The present series of studies examines the relationship between slow event-related changes in electrical brain activity and higher-frequent activity evoked by a series of stimuli presented in rapid succession (around 40Hz).

The repetitive delivery of brief stimuli at a high enough rate causes event-related responses to individual stimuli to overlap, eliciting a so-called steady-state response (SSR; Galambos et al., 1981; Galambos and Makeig 1988; Makeig, 1989; Makeig, 1993a; Rohrbaugh et al., 1990). The acoustically evoked SSR has been shown to have a primary generator in the auditory cortex (Mäkelä and Hari, 1987; Mäkelä et al., 1990; Hari et al., 1989; Pantev et al., 1991; Pantev at al., in press; Makeig et al., 1992) and to be a "hybrid" of middle latency responses (Galambos et al., 1981). In a series of studies, Makeig (for summary see Makeig and Galambos, 1989; Makeig, 1993a,b) demonstrated systematic and relatively long-lasting variations in the amplitude and phase of the SSR following presentation of foreground auditory stimuli. Perturbations in the amplitude and phase of an ongoing SSR time-locked to a distinct stimulus, such as occasional omissions of a pulse interspersed within the continuous 40-Hz stimulus train, were labeled the "complex event-related potential" (CERP, Makeig, 1985). By varying attentional demands in an oddball paradigm, Makeig (1993) recently demonstrated a characteristic CERP phase advance following rare tones regardless of whether the subject was attending to the stimuli, while an above-baseline peak in SSR amplitude with a 400-msec latency occurred when subjects directed their attention to the target stimuli. Rohrbaugh et al.

(1990) also found a phase[1] advance in the SSR during a 200-msec period following a foreground stimulus in an orienting paradigm. Since this phase advance occurred parallel to the development of a negative slow wave the authors interpreted both phenomena to reflect a transient sensitization during orienting to the foreground stimuli.

In the studies reported here, the relationship between slow brain potentials and the SSR with its stimulus- and task-related perturbations was investigated. The SSR was regarded as a "tool" to explore the functional meaning of slow cortical potentials, such as the P300, the Contingent Negative Variation (CNV) and the Bereitschaftspotential. Elbert and coworkers (Elbert and Rockstroh, 1987; Rockstroh et al., 1989; Elbert, 1992, 1993) have previously suggested that such slow potentials indicate the modulation of excitation and excitability in cortical neuronal networks. This hypothesis is based on a model which may account for certain features observable in neuronal networks: information may be coded by an increase or a decrease in firing rates of neurons; it may equally well be coded through distinct spatial patterns of activation, or most likely by a combination of both (Van der Malsburg and Schneider, 1986), but certainly not through synchronous activation of many or all neuronal elements. Therefore, overexcitation must somehow be controlled by the brain's intrinsic mechanisms, and excitability must be regulated by imposing limits on the dynamic patterns of neural mass action (Elbert, 1993). It is well known that depolarization in the apical dendritic trees of cortical pyramidal cells results in surface negative potentials such as the CNV (Speckmann et al., 1984). These cells are the most likely candidates for enabling and "tuning" cortical excitability. The modulation of excitability, in turn, may be at the basis of attentional mechanisms, reflecting a preparatory state for cerebral processing in the underlying networks (Rockstroh et al. 1989). In contrast, slow positive shifts like the P300 imply a "disfacilitation" of cortical neural networks (Elbert, 1993). This hypothesis has been examined in two previous studies using a "probe" technique (Rockstroh et al., 1992; Rockstroh et al., 1993). In these experiments, occasional probe stimuli were presented during surface-negative potentials induced by a forewarned reaction time paradigm, or during an acoustic oddball paradigm, inducing a P300. Probe-evoked responses (reaction time, probe-evoked potential), indeed, varied with the slow potential shifts induced by the primary task, being facilitated during the development of the CNV but inhibited parallel to the development of the P300 (see also Woodward et al., 1991). It is important to note that both evoked and slower cortical potentials were partially generated within the same cortical regions.

However, a trade-off between the two tasks in dual-task paradigms has been shown to reduce the amplitude of cognitive slow potentials (Strayer and Kramer, 1990), a result which is consistent with the type of regulation described by Elbert & Rockstroh (1987, Elbert, 1993). By using the continuously driven SSR to probe excitability instead of responses to distinct and occasional probe stimuli, the impact of the dual task of responding to probes and responding to warning or oddball stimuli may be circumvented.

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[1] "Phase" refers to the relationship or time interval between the onset of stimuli in the steady state train and the waveform of the SSR, defined as evoked potential bandpass-filtered at the probe stimulus repetition rate.

Results of three experiments, in which the presentation of a continuous train of stimuli (driving an SSR) was combined with an oddball task or a voluntary response task, will be reported. The modulation of SSR-amplitude following target stimuli (brief changes in the frequency of the SSR stimulus train) or following a voluntary button press was considered a measure of the modulation of cortical excitability during the oddball task and the voluntary response task. We hypothesized that if the continuous stimulus train was comparable to probes used in the previous experiments, then the probe train presented to excitable brain regions during the development of a negative-going potential shift in the respective regions should be processed more efficiently. In this case, we should expect a parallel increase in SSR-amplitude, and perhaps even a phase advance signifying an SSR latency reduction. If the train of probes would be presented to less excitable neuronal networks such as during a P300 in the oddball task and the positive-going motor potential complex in the voluntary response task, we might expect a relative suppression of central processing of the probes and, hence, a reduction in SSR amplitude and an accompanying phase retard. If, on the other hand, every stimulus and task, irrespective of their nature and accompanying slow potentials, cause similar perturbations of the SSR amplitude and phase, similar CERP amplitude shifts and/or phase advance would be found in both paradigms, and we must conclude that the time course of the CERP amplitude/phase does not follow the slow potential.

METHODS

Subjects

In all three experiments, healthy, right-handed student volunteers received course credit or monetary compensation for participation. Forty-five male subjects (mean age 22.2 years) participated in Experiment 1, ten subjects (5 male, 5 female, mean age 26.3 years) in Experiment 2, which was comprised of two sessions, and seventeen subjects (7 male, 10 female, mean age 24.8 years) in Experiment 3.

SSR-Generation, Apparatus and Electrophysiological Recordings

A steady-state stimulus train (SSR) was created by presenting 5-msec pulses (Gaussian envelope) of 1000 Hz (65 dB SPL (A)) at a rate of 40 per second in Experiments 1 and 2, and 39.25 per second in Experiment 3, with a zero rise and fall time of the stimuli. The SSR was presented via earphones monaurally to the right ear in Experiments 1 and 2 and binaurally in Experiment 3.

During the experiment the subject sat in a partially electrically shielded, dimly lit and sound-attenuated subject chamber. After being prepared for the physiological recordings, the subject received written instructions informing him/her about the stimuli and the task. The instructions also included a request to avoid blinks and eye or head movements by adopting a relaxed position and fixating a spot on the opposite wall. In order to familiarize the subject with the continuous stimulus train, the first two minutes of the experiment were comprised of only 1000 Hz frequency deviations.

An ASYST program running on an AT 386 computer controlled timing of the experimental stimuli and the storage of electrophysiological responses. Coulbourn Instruments modules were used to produce the acoustic stimuli.

EEG was recorded along the mid-sagittal line (Fz, Cz, Pz) in Experiments 1 and 2, and, in addition, from C3 and C4 in Experiment 3. Recordings were obtained with a DC-amplifier (MES, Munich) using a time constant of 5 seconds in Experiments 1 and 2, and DC in Experiment 3. In all experiments, the reference electrode was affixed to the left earlobe. Nonpolarizable silver-silver/chloride electrodes (ZAK) were used, and Grass EC2 electrolyte served as the conducting agent. The skin under the electrodes was prepared by cleansing with alcohol and rubbing with an abrasive paste (OMNIPREP). The vertical EOG was recorded using Ag/AgCL-electrodes (ZAK) centered about 1 cm above and below the left eye.

Data were filtered with a low-pass filter at 100 Hz and were digitized at a rate of 400 Hz (Experiments 1 and 2) or 312.5 Hz (Experiment 3). In Experiment 3 EMG was recorded by a pair of silver/silver-chloride electrodes (Beckman) placed on the forearm (musculus flexor pollicis longus). After amplification (gain 1000, time constant 0.025 sec) the EMG signal was rectified and integrated with a time constant of 20 msec. The integrated EMG was digitized at the same rate as the EEG recordings (312.5 Hz).

In order to separate SSR and slow potential responses, subject-averages[2] were separately filtered with a 25-Hz high-pass filter (2nd order) and with a low-pass filter of 15-Hz (Experiments 1 and 2) or 8 Hz (Experiment 3), respectively. Perturbations in the SSR time-locked to experimental events were analyzed by complex demodulation using a 5-sec smoothing window. The amplitude of the resulting time series correspond to the peak-to-baseline amplitude of the SSR, and its phase corresponds to the latency shifts of the SSR peaks relative to stimulus onsets[3].

Effects of foreground stimuli and tasks were evaluated by analyses of variance. For within-subject comparison of recording sites, p-values were obtained after adjusting the degrees of freedom by the Greenhouse-Geisser-Epsilon. Means ± standard errors are presented.

EXPERIMENT 1

In the first study, an oddball task was superimposed on the series of 1000-Hz pulses by shifting their frequency for 100 msec at a constant interval of 1.5 sec. Of the total of 1200 frequency-shift events, changes to 2000 Hz on 70% of the trials (840) constituted standard or non-target events, while changes to 500 Hz on 30% of the trials (360) constituted the target stimuli. Thus, the SSR shifted briefly every 1.5

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[2] Prior to data analysis, artifacts were corrected using a computer program (Berg, 1986) that first classified blinks, muscle potentials, drifts or large DC-shifts on the basis of various templates. The influence of eye blinks on the EEG was then corrected using a regression analysis. The artifact correction procedure led to the rejection of five subjects in Experiment 1, two subjects in Experiment 2 and one subject in Experiment 3. For the remaining subjects, data analysis was based on 83.3% of the data in Experiment 1, 83.1% in Experiment 2, and 78.8 % in Experiment 3.

[3] This method can be considered comparable to the moving-average discrete Fourier transform applied by Makeig and Galambos (1989).

sec to either higher or lower frequency tone pulses. The relationship of frequency and standard/ target stimulus was counterbalanced across subjects[4]. Subjects were asked to press a button with their dominant hand as quickly as possible following every target.

Results

The frequency-shift stimulus in the oddball task elicited the expected ERPs including a sequence of N100 and P300 features (see Fig. 1a). As found for other auditory oddball stimuli (Segalowitz and Barnes, 1993), the frontally pronounced N100 reached a later peak and a larger amplitude following targets than following standards , differences being most pronounced at the frontal and central leads ($p < .01$ for all effects). The P300, peaking after 349 msec on average, was largest at the parietal recording in response to targets ($p < .01$ for all effects).

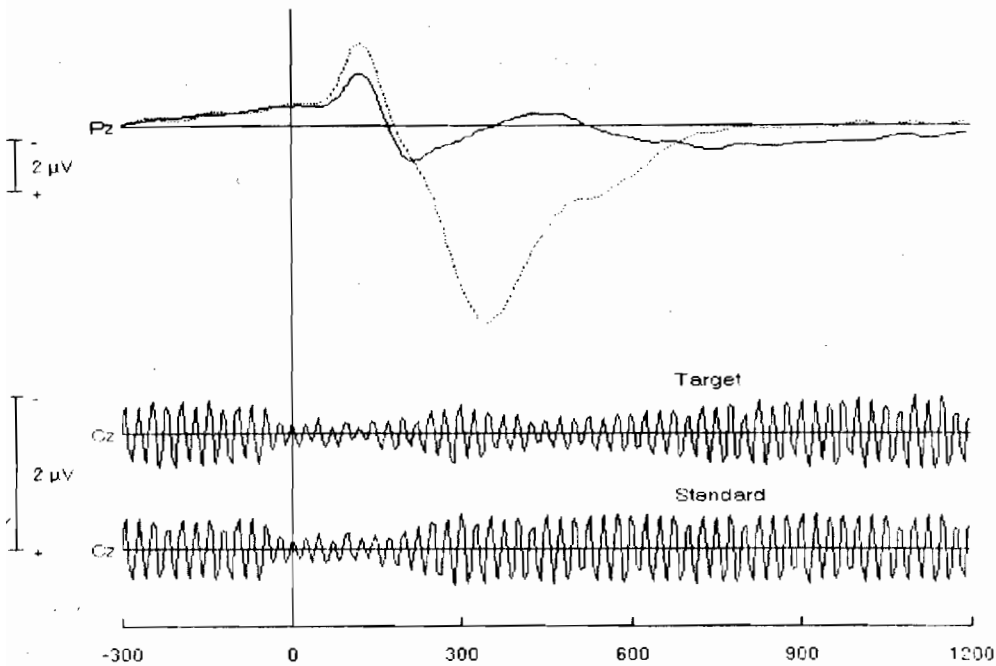

Figure 1A. Top: Grand average of the parietal ERP (in µV, negativity up) to oddball stimuli (targets: dotted line, standards: solid line) during 300 msec prior to and 1.2sec following the stimuli. The vertical line marks the time point of oddball stimulus presentation. Bottom: Examples of SSR perturbation at the central electrode parallel to the ERP, averaged across 12 subjects separately for targets and standards.

[4] No effects were obtained between the subgroups in an ANOVA accounting for the frequency/target relationship.

The 40-Hz stimulus train also drove an SSR[5] with a mean amplitude of 0.51±0.03 μV at Fz, 0.50±0.03 μV at Cz and 0.38±0.02 μV at Pz (baseline-to-peak, $F(2,72)= 63.1$, $p< .001$). Following the oddball stimuli SSR-amplitude was reduced by 0.32±0.02 μV(to 37 % of baseline) at Fz and Cz at 45.4±4.8 msec peak latency [6], and by 0.23±0.02 μV (to 39 %) at Pz (ELECTRODE, $F(2,36)= 66.2$, $p< .01$; see Fig.1a for the evoked responses, and Fig. 1b for the results of the complex demodulation). For the sake of brevity and clarity, this first amplitude reduction during the first 100 msec will hereafter be referred to as R100 . Following the R100, which did not differ between standard and target stimuli, SSR-amplitude increased to above-baseline levels. This amplitude augmentation above baseline near 400 msec (referred to as A300), described by Makeig as a regular feature of the CERP, was significant at all electrodes and under all conditions ($F(1,36)= 168.0$, $p< .001$). A300 was more pronounced following standard than following target stimuli ($F(1,36)= 7.1$, $p< .05$) and was reached earlier at Fz and Cz than at Pz (390±15 msec versus 434±15 msec, $F(2,72)= 6.9$, $p< .01$).

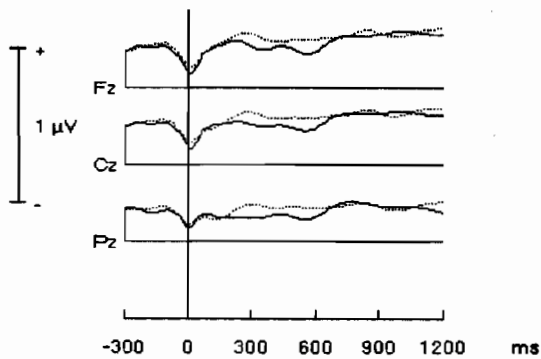

Figure 1B. Modulation of SSR amplitude as determined by complex demodulation, plotted separately for the recording sites and perturbations following targets (solid lines) and standards (dotted lines). Minus signifies amplitude reduction, plus signifies amplitude increase relative to baseline values. Time scale as in Fig.1a.

A second amplitude reduction, R400, ocurred at a mean latency of 422.1±7.6 msec by 0.16±0.02 μV at Fz and Cz and by 0.12±0.01 μV at Pz which corresponded to a reduction to 68% of baseline values at all three electrode sites; $F(2,72)= 34.9$,

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[5] Data of 3 Ss who did not show any measurable synchronisation were not included in the analysis. Reports are based on 37 Ss.

[6] Because of a programming error, the interval between two successive 1000 Hz pulses was increased prior to every oddball stimulus from 25 to 44 msec. Although this delay was not subjectively noticeable, the SSR modulation around the oddball stimuli must have been affected by this "compound" stimulus, and phase shifts could not be analysed. However, effects of stimulus meaning such as differences between target and standard stimuli cannot be attributed to this error, which equally affected both types of stimuli.

$p < .001$. R400 was more pronounced following target than following standard stimuli; $F(1,36) = 1.9$, $p < .01$. The differences between stimulus types were larger at Fz (reduction to 50% and 86% of baseline values, resp.,) and at Cz (reduction to 50% and 84% of baseline levels, resp.) than at Pz (reduction to 55% and 81% resp.; ELECTRODE x STIMULUS; $F(2,72) = 16.9$, $p < .001$; see Fig.1). It is interesting to note that the peak latency of the R400 was shorter at Pz relative to Fz, while the latencies of the R100 exhibited a fronto-parietal gradient ($p < .05$). This shift in latencies suggests some connection of the second minimum with the P300 complex.

Mean SSR amplitude during the time segment 270 to 650 msec confirmed these results for the R400: an amplitude reduction by 0.11 ± 0.01 μV (to 76%) relative to baseline followed target stimuli, while the average amplitude returned to baseline levels following standard stimuli, this difference being more pronounced at Fz and Cz (reduction to 74% of baseline levels) than at Pz (to 80% of baseline levels; ELECTRODE x STIMULUS; $F(2,72) = 23.9$, $p < .01$; STIMULUS; $F(1,36) = 41.4$, $p < .01$).

The first study confirms earlier results: a CERP followed each stimulus, beginning within the first 100 msec, with a fronto-central predominance, and is followed by an augmentation above baseline in amplitude during the subsequent 300-400 msec. Furthermore, another perturbation of SSR-amplitud was observed following target stimuli only. A differentiation of SSR-amplitude by the present stimulus- and task-conditions began with the A300. It could be tempting to associate the following second SSR-amplitude reduction with the target-evoked P300, as it became pronounced in the same latency range. However, with every target-evoked P300 there was also a motor response; thus, either the combination of the two or one of the factors alone could have influenced the SSR near 400 msec following target stimuli. Experiment 2 was designed to separate these contributions, by comparing SSR perturbations when subjects pressed a button to targets, in one condition, or silently counted the targets in another.

EXPERIMENT 2

Under the same experimental conditions as described in Experiment 1, ten subjects participated in two experimental sessions on successive days. In one session their task was to respond with a motor response to every target (as in Experiment 1), whereas in the other session they were asked to silently count the number of targets. The order of these tasks was counterbalanced across subjects. Motivation to count was assured by asking the subject at irregular time intervals during the session for the number of targets counted so far. A frequency change to 500 Hz[7] constituted the target.

[7] In order to evaluate effects of tone frequency on SSR modulation, two of the ten subjects participated in two further sessions, in which a frequency change to 2000 Hz constituted the targets.

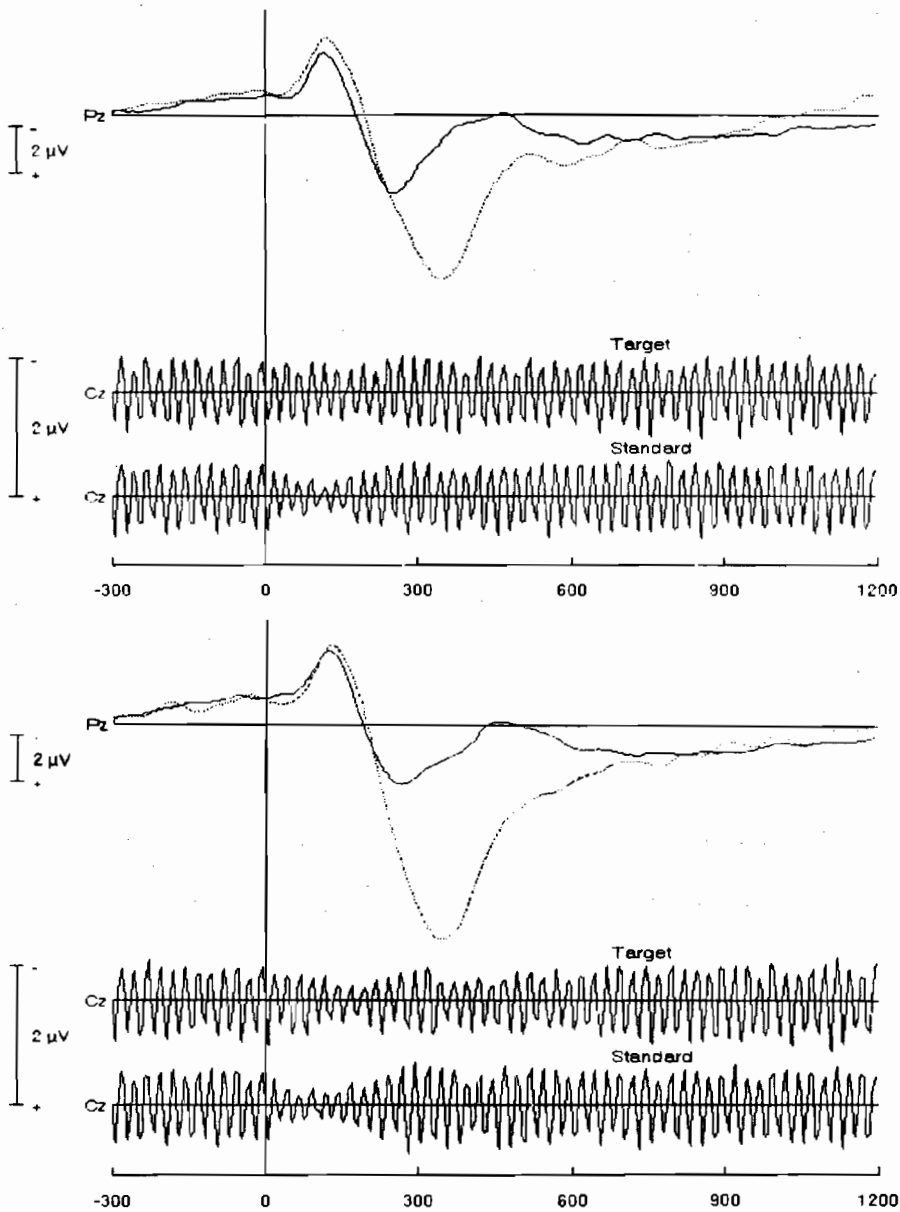

Figure 2A. Grand averages of the parietal ERP (in µV, negativity up) to oddball stimuli (targets: dotted line, standards: solid line) during 300 msec prior to and 1.2sec following the stimuli. Top: session with motor response required to targets, bottom: session in which targets were to be counted. The vertical line marks the time point of oddball stimulus onset. Below each ERP, an example of SSR perturbations at the central electrode is given, averaged across subjects separately for targets and standards.

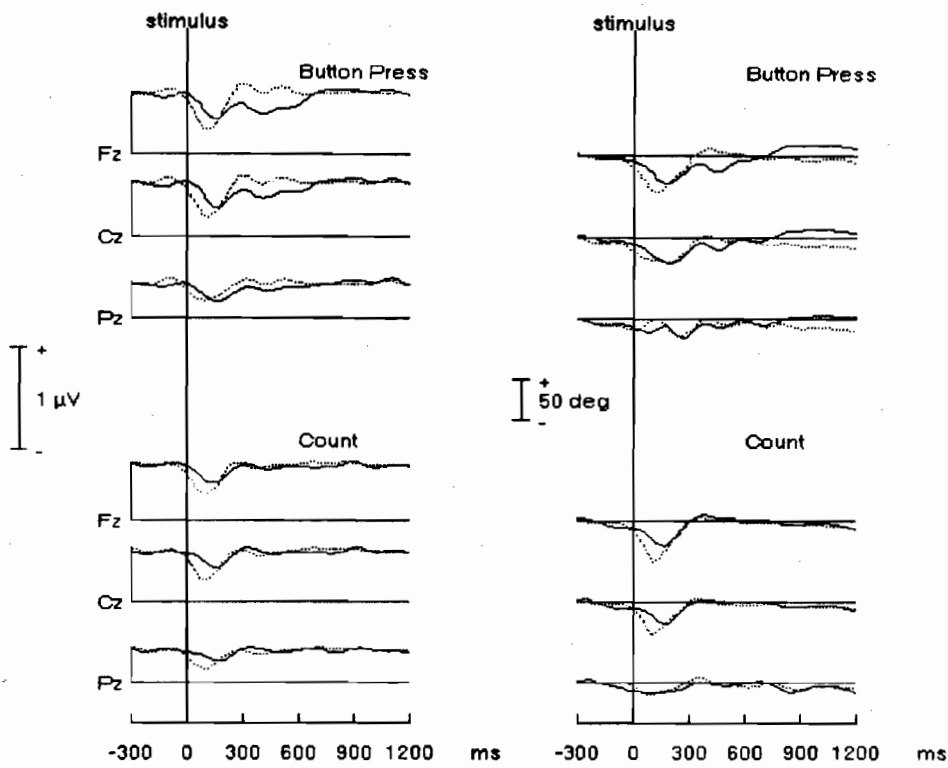

Figure 2B. Modulation of SSR amplitude (left) and phase (right) as determined by complex demodulation, plotted separately for the recording sites, perturbations following targets (solid lines) and standards (dotted lines), and the sessions with a button press required to targets (top) and the session with targets to be counted. Ordinate: Amplitude modulation in µV (minus indicating amplitude reduction) or phase modulation in degrees (minus indicating phase advance relative to baseline). Time scale as in Fig.2a.

Results

As in Experiment 1, subjects[8] developed the expected ERP to the oddball stimuli[9] (see Fig. 2a). While N100 did not differ between tasks or conditions, P300 was larger ($F(1,7)= 19.0$, $p< .01$) and peak amplitude was later ($F(1,7)= 33.7$, $p< .001$) after targets than after standards, in particular under conditions in which subjects indicated target detection by a motor response (STIMULUS x TASK; $F(1,7)= 7.3$, $p< .05$, STIMULUS x ELECTRODE; $F(2,14)= 28.6$, $p< .01$).

As reported for the first study, the 40-Hz stimulus train drove an SSR (mean amplitudes 0.59±0.03 µV at Fz, 0.55±0.03 µV at Cz and 0.37±0.02 µV at Pz, baseline-to-peak, $F(2,7) = 91.3$, $p< .001$). Oddball stimuli elicited an R100 with an average

[8] Data of two subjects, who did not show an SSR were excluded from further analyses, thus, results reported here are based on the data of eight subjects.

[9] including an N100 (mean peak latency 121.31±2.5 msec, mean amplitude -4.82±0.45 µV, frontal maximum, $F(2,14)= 50.5$, $p< .001$) and P300 (latency 325.35±7.3 msec, amplitude 5.16±0.5 µV, centro-parietal dominance, $F(2,14)= 140.3$, $p< .001$.

minimum at 97.6±7 msec (see Fig. 2a) to 52 % of baseline level at Fz, 51% at Cz and 49% at Pz (no significant difference between sites). The peak latency of the R100 was 55 msec later following target relative to standard stimuli; $F(1,7)= 10.9$, $p< .05$. The peak R100 amplitude was more pronounced following standards than targets (ELECTRODE x STIMULUS; $F(2,14)= 4.5$, $p< .05$)[10].

The phase component of the R100 was a phase advance (see Fig.2b) by 48° (of 3.3 msec) at Fz, 42° (2.9 msec) at Cz and 34° (2.4 msec) at Pz, peaking 126.8 msec after the oddball stimulus onset, with a pronounced fronto-parietal gradient ($F(2,14)= 4.8$, $p< .05$) which did not differ between stimulus conditions or tasks.

The A300 (SSR amplitude augmentation) in the latency range of 340 - 410 msec was smaller following targets (2 % of baseline values) and larger following standards (by 17 %) when subjects indicated target detection by button press; smaller differences (17 % versus 16 %) occurred when subjects silently counted the targets (TASK x STIMULUS, $F(1,7)= 5.4$, $p< .06$[11]). A slight phase retard of 11.5° (or 0.8±.01 msec) occurred later following targets (490±17 msec) than following standards (410±13 msec, $F(1,7)= 6.1$, $p< .05$), but was not affected by task.

Figure 2 also shows the presence of an R400 amplitude reduction. For mean SSR amplitude during the time interval 270 to 650 msec following oddball stimulus onset, a TASK x STIMULUS interaction indicates a more pronounced R400 when subjects pressed the button following targets (TASK x STIMULUS, $F(1,7)= 9.2$, $p< .05$[12]). Following target stimuli, mean amplitude at the R400 peak was a reduction to 88% of baseline, the modulation being larger at Fz (reduction to 86%) than at Cz and Pz (reduction to 91%). Following standard stimuli there was no change in mean amplitude from the baseline level for any of the electrodes (ELECTRODE x STIMULUS; $F(2,14)= 8.4$, $p< .01$). The R400 was more pronounced at Fz (to 89 % at Fz) than at Cz (93 %) and Pz (92%) when subjects pressed a button, wheras there was no difference between electrode sites when subjects counted the targets (reduction to 96%, 98%, 94%, resp. , TASK x ELECTRODE, $F(2,14)= 7.8$, $p< .01$). Parallel to the R400, a phase advance was larger (17°, 1.2 msec) in response to targets than in response to standards (10° or 0.7 msec; $F(1,5)= 7.9$, $p< .05$), while no significant task effects could be found. Subsequent to this R400, mean amplitude modulations (650-1450 msec) by stimulus types and tasks were reversed: targets for which a button press was required produced a sustained amplitude augmentation of 5.8%, while an amplitude reduction by 4 % of baseline was observed following standard stimuli. Targets to be counted, however, produced only a slight amplitude

[10] This effect has to be attributed to the tone frequency: When – in two Ss – the target stimulus was a higher frequency (2000 Hz), the relationship between amplitudes to targets and standards was reversed, i.e. the higher tones, whether targets or standards, whether counted or answered with a button press, induced SSR amplitude reductions of about 0.3 μV, lower tones relative to the 1000-Hz stimulus train induced SSR amplitude reductions of about 0.1 μV.

[11] Post-hoc comparisons confirmed the significant stimulus difference under conditions of button press ($t= 2.8$, $p < .05$), and the larger A300 following counted targets ($t=2$ 2.4, $p< .05$), while differences between stimulus types under counting conditions did not reach significance ($t= 0.5$).

[12] Post-hoc t-tests confirmed a significantly larger R400 following a button press relative to targets to be counted ($t= 3.2$, $p< .05$), and relative to standards of both types ($t= 4.1$, $p< .05$), while R400 did not differ significantly between targets and standards under the counting condition.

reduction, while no change relative to baseline levels followed standard stimuli ($F(1,7)= 5.5$, $p< .05$).

The results of this second study closely replicated the findings of Makeig (1993). The interaction of stimulus and task suggests that both motor responding and stimulus processing, with their related slow potentials, may contribute to the observed SSR perturbations. The R100 was equally pronounced at all recording sites (as percent reduction from baseline), suggesting that a common set of generators or equally effective modulation of all generators contributes to the response at all three sites. The R100 was sensitive to physical (tone) frequency but not to psychological (task-related) aspects of the stimuli. The subsequent CERP features (A300 and R400) revealed an impact of stimulus and task relevance.

Experiment 3 was designed to explicitly examine SSR perturbations related to slow potentials that develop prior to and following motor responses. To our knowledge, SSR perturbations parallel to the development of a surface-negative Bereitschaftspotential (BP), the negative motor potential and the positive-going motor potential complex has not been studied previously. As described in the introduction, the slow postive shifts like the P300, or the slow positive changes following a motor response, have been viewed as widespread disfacilitatory responses (Elbert, 1993). A parallel reduction in SSR-amplitude and a phase retard is constistent with this model. The Bereitschaftspotential seems to be restricted to generators in the somatomotor cortex and areas in the frontal lobe (Rockstroh et al., 1989). A facilitation of neuronal activity in these regions should not have much of an effect on the SSR generators in the auditory cortex.

EXPERIMENT 3

In order to elicit movement-related potentials, sixteen right-handed subjects were instructed to press a button with their dominant hand approximately every 10 seconds while the stimulus train was delivered to both ears through headphones at 65 dB (1000 Hz tone frequency, 39.25 Hz stimulation rate). A total of 250 button presses were collected per subject[13].

The course of the slow potential prior to and following the voluntary button presses was described by the following components (named according to Neshige et al., 1988): mean potential during 1.5 - 0.5 sec prior to the button press[14], the Bereitschaftspotential (BP); mean potential during the last 500 msec prior to the button press, the negative slope (NS) of the BP; the negative peak surrounding the button press, the motor potential (MP). Post-response components were described by the maximum positive peak (positive motor potential, PMP), as well as mean potential during the 500 msec interval following the button press (motor potential complex, MPC); mean potential during the interval 0.5 - 2 sec following the button

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[13] Prior to the experimental period, subjects were trained to estimate the time interval to avoid their using a distracting strategy of silently counting to ten between every button press.

[14] In this analysis, components are related to the time point of the button press (closure of the microswitch). Analysis relative to the first EMG response will be reported elsewhere.

press, slow motor potential, MPS). SSR perturbations during similar time intervals were related to these scores.

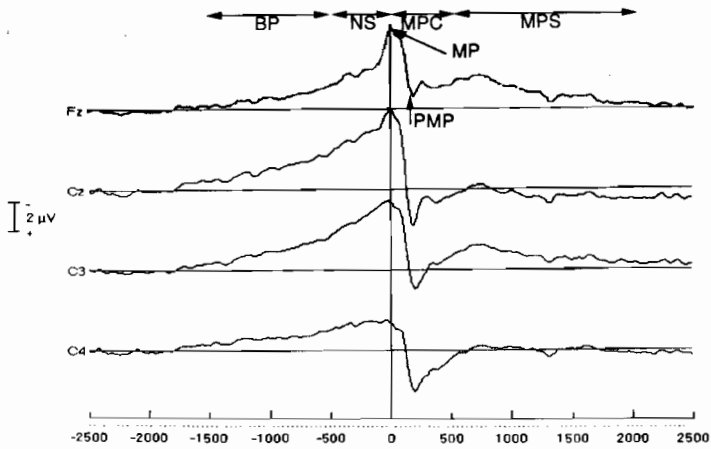

Figure 3A. Top: Grand average of slow potentials 2.5 sec preceding and 2.5 sec following the button press (in µV, negativity up), plotted separately for the frontal and three central recording sites. The vertical line marks the time point of microswitch closure. BP, NS, MP, PMP, MPC, MPS: scores determined to describe the course of the slow potentials (see text).

Results

The ERP revealed a Bereitschaftspotential prior to the voluntary button press in all subjects except one. Mean potential was -1.56±0.2 µV during the interval 1.5 - 0.5 sec prior to the button press (BP), - 3.1±0.3 µV during the last 500 msec before the button press (NS), and -4.3±0.4 µV during the motor potential (MP) at the time point of the button press (mean latency 8.4±5.5 msec relative to the switch closure). For each component, negativity (relative to baseline) was most pronounced at Fz, followed by Cz and C3 (see Fig. 3a)[15]. As expected, the pre-movement negativities (NS and MP) were larger over C3 than C4 ($t(15)= 1.9$, $p< .1$ and 5.1, $p< .01$), i.e., contralateral to the moving hand. Button presses were followed by a positive peak at 161.6±8.5 msec (PMP, mean amplitude +1.85±0.5 µV), followed by a slower positive deflection (MPC). Both post-motor potentials exhibited negative values at the frontal, and positive values at centro-parietal recording sites, with less pronounced amplitudes over the brain areas for which larger pre-response negative shifts had been observed (for the difference C3-C4: $t(15)= 2.3$, $p< .05$). Only the PMP differed

[15] The development of these negative SCPs was confirmed by an ANOVA including baseline values and the three components (COMPONENT x ELECTRODE, $F(12,180)= 16.97$, $p< .001$; COMPONENT: $F(3,45)= 24.4$, $p< .001$; ELECTRODE: $F(4,60)= 13.2$, $p< .001$) as well as by an ANOVA comparing difference values (baseline - BP, NS, and MP: COMPONENT x ELECTRODE: $F(8,120)= 19.2$, $p< .001$; COMPONENT: $F(2,15)= 20.6$, $p< .001$; ELECTRODE: $F(4,60)= 13.2$, $p< .001$). The increase in negativity relative to baseline was 1.2±0.1 µV during the BP, 2.6±0.3 µV during the last 500 msec before the button press and 3.9±0.4 µV during the MP.

significantly from baseline values ($F(1,15)= 6.1$, $p< .05$), while differences between baseline and MPC reached significance only at Fz, Pz and C3 ($F(4,60)= 7.1$, $p< .01$). The post-movement positivities (PMP and MPC) were smaller at C3 than at C4 ($t(15)= 2.3$ and 3.6, $p< .05$).

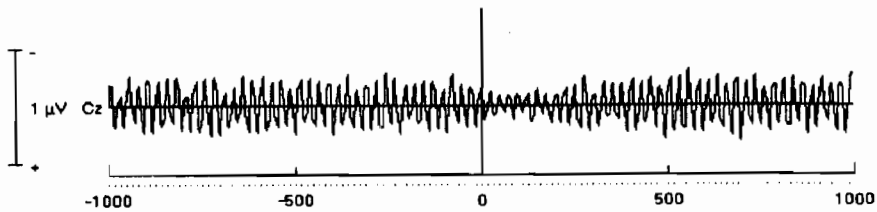

Figure 3B. Example of SSR averaged across 16 subjects driven by the 39.25 Hz stimulus train in µV, from the central recording site during an interval of 1 sec before and 1 sec following the button press (marked by the vertical line).

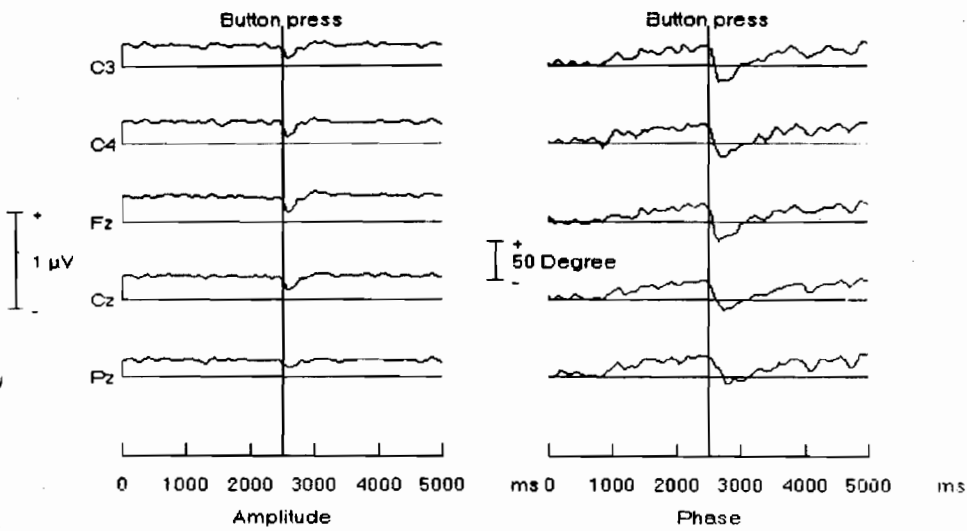

Figure 3C. Modulation of SSR amplitude (left) and phase (right) as determined by complex demodulation, plotted separately for the five recording sites. Ordinate: SSR-amplitude change in µV (minus indicating amplitude reduction) and phase modulation in degrees (minus indicating phase advance relative to baseline). The vertical line marks the time point of switch closure.

All 16 subjects showed SSR-synchronization at 39.25 Hz, SSR amplitude being 0.29±0.03 µV at Fz, 0.27±.02 at Cz and at Pz (0.21±0.02 µV, baseline-to-peak; see Fig. 3b for an example of the central SSR). This gradient was observed not only under baseline conditions but for all response-related time periods ($p< .01$). SSR amplitude

did not change significantly during the period preceding the button press. The button press was followed by a marked reduction in SSR amplitude (R100; see Fig. 3b and c), which was significant for both measures, the peak amplitude change following the button press, and mean amplitude in the 500 msec post-response (parallel to the MPC): Relative to baseline values, SSR amplitudes were reduced to a peak minimum of 46.7 % of baseline after an average latency of 105.0±8.2 msec following the button press ($F(1,15)= 47.9$, $p< .001$ for the R100, $F(1,15)= 13.8$, $p< .01$ for the MPC-related SSR perturbation). Although SSR amplitudes prior to and following the button press were (non-significantly) smaller at C3 than at Cz and C4, amplitude changes from baseline did not differ significantly between recording sites. Following the R100, SSR amplitudes returned to baseline values [16]. (Ten out of the 16 subjects demonstrated an ongoing slow negative shift, i.e., negative MPS relative to baseline.)

CERP phase parallel to the development of the negative slow potential preceding the voluntary movement showed a retard of 1.21±0.5 msec (16.8°) beginning 1.5 sec before the button press and of 1.83±0.5 (25.4° , $p< .01$) msec during the negative slope, resp. (see Fig. 3c). Phase modulation did not differ between recording sites. A phase advance by 1.99±0.6 msec (27.8°, $p< .01$) relative to baseline values at a mean peak latency of 161.6±19.3 msec following the button press vanished during the subsequent 500 msec (no significant difference from baseline for the phase perturbation parallel to the MPC).

In Experiment 3, SSR-amplitude was smaller than the SSR-amplitudes obtained in the preceding experiments. A major difference in the designs for the two experiments was that subjects had to pay attention to the continuous stimulus train in the first two experiments in order to detect changes in tone frequency, while no attention to the stimulus train was required in the last study. Possibly, the boring task of pressing a button for long periods of time may have distracted subjects from attending the stimulus train or may have induced drowsiness, a condition known to affect SSR amplitude (Galambos and Makeig, 1988). The voluntary movement clearly induced a CERP with features in many respects comparable to those described in the previous studies (% amplitude reduction and phase advance). The reduction in SSR amplitude during the execution of a motor response is in line with the results of Böcker et al. (1993), who observed smaller SEP amplitudes to distinct somatosensory probes during the movement (250 msec after the motor response), compared to SEPs to probes prior to the response or following the response at a later point in time. However, the SSR in this experiment is thought to be generated mainly in the auditory and not in the somatomotor cortex. While the size of the phase advance during the CERP is in line with the results obtained in Experiment 2, as well as results reported by Makeig (1993), the phase retard parallel to the development of the negative Bereitschaftspotential contrasts with findings of Rohrbaugh et al. (1990), who described a phase advance parallel to the negative Slow wave following an auditory stimulus, which was attributed to an orienting response.

[16] No significant differences from baseline were found for the mean SSR amplitude during 0.5 - 2 sec following the button press (parallel to the MPS in the SCP) at Cz and Pz, while at Fz, SSR amplitude exceeded the baseline SSR amplitude by 5.1% (BL-MPS x ELECTRODE, $F(4,60)= 6.1$, $p< .01$, ELECTRODE, $F(4,60)= 11.1$, $p< .01$).

DISCUSSION

The series of experiments reported in this chapter clearly demonstrate perturbations of the auditory SSR following auditory stimuli, and particularly in conditions that require stimulus evaluation and motor performance. Under these conditions, auditory stimuli also evoked slow potential shifts typically found in the oddball and in the voluntary response paradigm. As we know of only very few studies (other than Makeig, 1993) systematically exploring the relationship between SSR perturbations and slow potentials, the interpretation of the present results must remain speculative.

In the present experiments, a CERP amplitude reduction and phase advance, relative to SSR baseline – was consistently observed following a foreground stimulus, such as the oddball frequency shifts, but also following voluntary motor responses. This finding replicate results by Makeig (1993). However, varying the stimulus meaning (non-target and target events) provoked an additional SSR perturbation during the time period, during which evaluation of and response to a meaningful stimulus is supposed to take place.

Two hypotheses guided the present series of experiments and provide a framework for discussion of the results: as outlined in the introduction, SSR modulation is an appealing approach to studying the functional meaning of slow potentials. Within the framework of our model (Elbert and Rockstroh, 1987; Elbert, 1993), which considers slow negative potentials to indicate enhanced excitability, and surface positive slow potentials to indicate "disfacilitation" of underlying neuronal networks, the processing of the SSR stimulus train should vary accordingly: if increased excitability corresponds to facilitated input processing, a larger SSR might be expected when negative slow potentials are generated in temporal regions, in the same way as we found evoked responses to occasional probe stimuli to be larger (Rockstroh et al., 1993). If reduced excitability during positive slow potentials corresponds to disfacilitated input processing, smaller SSR amplitudes might be expected during positive slow potentials, such as the P300 and the positive motor potential, in a similar way as we found evoked responses to occasional probes to be smaller during the development of a P300 (Rockstroh et al., 1992) . The present results support the latter relationship. No correspondence between slow negative potentials preceding the voluntary response and SSR amplitudes was found. These results are consistent with the assumption that the positive potentials indicate widespread disfacilitation while nagtive shifts are generated specifically in task-related brain regions (Rockstroh et al., 1989, Elbert, 1993). The regulation of slow negativities is therefore closely linked to attentional regulation.

Makeig (1993) links SSR perturbations to shifts in attention. If processing of a foreground stimulus as well as focusing on the execution of a cued or voluntary button press binds attentional capacities, as well as their neuronal substrates, similar perturbations might be expected for different tasks. This hypothesis is supported by the similarity of SSR perturbations following an event in the three experiments. We may even attribute the phase retard during the preparation of the voluntary response to such shifts in attention, if we assume that during this interval, the subjects' attention was focused on the motor response and distracted from the high-frequency stimulus train.

The finding of a CERP induced by a voluntary motor response seems remarkable and highly interesting. It suggests an influence of the preparation and execution

of a motor response, known to be generated in the motor cortex and motor-related areas, on the SSR, generated in the auditory cortex. A suppression of auditory input prior to, during or just following a voluntary movement, which certainly represents controlled processing, should have an impact not only on the conceptualization of the SSR, but also on hypotheses about attentional processes.

It remains to be explored in further experiments, as to what extent the SSR perturbations are global, task-specific and/or modality-specific. If the intensity of SSR perturbations vary systematically with slow potential amplitudes, relating the two phenomena in a functional sense. On the other hand, the conclusion reached by Eckhorn (this volume) that stimulus-dominated synchronization inhibits cortex-dominated synchronization might provide a framework for an interpretation of the present findings.

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