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Hemispheric asymmetry in visual discrimination and memory: ERP evidence for the spatial frequency hypothesis

Received: 16 August 2001 / Accepted: 12 February 2002 / Published online: 13 April 2002
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Abstract Event related potentials (ERPs) were recorded during delayed discrimination of simple spatial frequency gratings in the high and low frequency bands. Analyses of the waveforms N170, P220, N310, P400, and slow wave (SW) indicated significant and regionally specific interaction of spatial frequency and hemisphere for N170 amplitude. This interaction was independent of memory conditions, and appeared to be in the opposite direction of what is predicted by the spatial frequency model of hemispheric asymmetry. Additional interactions between spatial frequency and hemisphere were observed for N310 in the encoding process (reference stimulus) and for SW in the retrieval process (test stimulus). The general hypothesis of an interaction of spatial frequency and hemisphere in visual cognition is supported, but the findings indicate caution in interpreting an increase in physiological measures as an indication of more efficient brain processing. Moreover, several stages of information processing may contribute to the asymmetry observed in behavioral studies, and hemispheric balance may change dynamically during the time course of processing.

Keywords Event related potentials · Spatial frequency discrimination · Perceptual memory · Hemispheric asymmetry

This study was supported by the Norwegian Research Council (MH), grant no. 111230/330 and by a fellowship from the Hanse Wissenschaftskolleg to the first author.

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Introduction

The spatial frequency hypothesis of hemispheric specialization in visual perception and cognition links functional asymmetries of the cerebral hemispheres to well-established principles of visual information processing (Christman 1997; Hellige 1995; Sergent 1982). Briefly, the hypothesis states that asymmetries arise in higher-order perceptual processing as a result of a differential ability of the hemispheres to process information carried by different parts of the spatial frequency spectrum, where the left hemisphere is specialized for processing late available, high spatial-frequency information and the right hemisphere is specialized for processing early available, low spatial-frequency information. This relative specialization for particular combinations of the spatial and temporal characteristics of visual stimuli suggests a link between perceptual asymmetries and information initially carried by the magno- and parvocellular pathways (Lennie et al. 1990; Van Essen and De Yoe 1995).

Visual half-field experiments aimed at direct tests of the spatial frequency hypothesis, looking at the perception of briefly flashed simple and compound gratings, and frequency-filtered stimuli, provide a pattern of results biased in favor of the hypothesis (see reviews by Christman 1997; Grabowska and Nowicka 1996). Consistent with the requirement of higher-order information processing for hemispheric differences to emerge, no visual field differences have been observed in simple (threshold) detection tasks (Fiorentini and Berardi 1984; Greenlee et al. 1993; Kitterle and Kaye 1985; Kitterle et al. 1990; Rose 1983), but in experiments measuring the discrimination and identification of low versus high spatial frequencies of simple gratings, the predicted interactions between spatial frequency and visual field have been reported for both choice reaction times and discrimination thresholds (Kitterle and Selig 1991; Kitterle et al. 1990; Kitterle et al. 1992; Niebauer and Christman 1999; Proverbio et al. 1997; Watten et al. 1998).

A more direct way of studying hemispheric differences in visual perception and cognition is to monitor

brain activity during the performance of relevant perceptual tasks. Several studies, recording visually evoked potentials (VEPs) to flickering gratings and phase reversing checkerboards, have reported asymmetries, somewhat surprisingly in the opposite direction of that predicted by the spatial frequency hypothesis (Mecacci and Spinelli 1987; Spinelli and Mecacci 1990). Rebaï et al. (1993, 1998) recorded VEPs to spatial frequency gratings and observed higher amplitudes with shorter latencies in the right hemisphere as compared with the left hemisphere in an early positive VEP component (P90), and this difference increased as the spatial frequency was increased from 0.5 to 10 cycles/degree (c/deg). They suggest that the right hemisphere is more sensitive to the spatial frequency of the stimulus whereas the left hemisphere is more sensitive to temporal characteristics. However, the relevance of these and other VEP experiments with gratings and checkerboards (reviewed by Grabowska and Nowicka 1996; Mecacci 1997) to the spatial frequency hypothesis of hemispheric processing is uncertain. First, the experiments do not meet the fundamental requirement of the hypothesis, namely the presence of a perceptual-cognitive processing load; in all cases the subjects were merely looking at the stimulus. Hemispheric differences in spatial frequency processing observed in the absence of a cognitive task are hard to interpret; they might reflect differences in early sensory analysis prior to the levels of processing at which the hypothesis aims (Christman 1997; Hellige 1995; Sergent 1982), or they might result from collateral higher-order information processing activated by the stimulus but not under experimental control. Second, even if higher-order cognitive mechanisms were activated by just looking at stimuli, the VEP experiments recording from a few electrodes in the occipital region would tap into a minor part of the process. Recent positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) studies have shown that perceptual discrimination of spatial frequency (Greenlee et al. 2000), orientation (Dupont et al. 1998; Orban et al. 1997) and motion (Cornette et al. 1998; Orban et al. 1998) recruit regions in prefrontal and parietal cortex in addition to striate and extrastriate cortex (reviewed by Cabeza and Nyberg 2000).

There are few studies of spatial frequency processing during active task conditions, but Zani and Proverbio (1995) studied selective attention for the size of chequered patterns and found an effect of attention as early as 90–115 ms poststimulus onset. Most importantly they found a significant interaction of attention condition with spatial frequency and hemisphere for determining the N170 amplitude measured occipitally. They observed a generally higher left- than right hemisphere amplitude in relation to attended stimuli, and this hemispheric difference increased towards higher spatial frequencies. Other electrophysiological experiments that record event related potentials (ERPs) in short-term memory tasks have used complex visual patterns containing many spatial frequencies. In a study of perceptual memory for abstract geometric designs, Begleiter et al. (1993) reported both

memory-related changes and hemispheric asymmetry in ERP activity over the temporal lobes. Their results suggest that hemispheric asymmetries are associated with the ventral processing stream which is believed to be implicated in perceptual identification and memory representation (Van Essen and DeYoe 1995). Most ERP studies of memory for visuospatial stimuli have been concerned mainly with old/new memory effects without relating them to cerebral asymmetry (Johnson 1995). Beisteiner et al. (1996) described lateralization of ERP effects in memory for computer generated figures which were significant in an early time window of 150–200 ms poststimulus onset and with a regionally specific right hemisphere advantage observed at the P7/P8 electrode pair. The local/global hemispheric processing difference has been studied with ERPs and PET by Heinze et al. (1998) with letters as stimuli, and they report evidence for lateralization in cognitive ERP components that may reflect differential spatial frequency processing. They conclude that spatial frequency analysis is asymmetric at higher stages of perceptual processing but not at the earlier stages of visual cortical analysis. There are thus indications in ERP research of hemispheric asymmetries in spatial frequency processing in experiments that relate task relevant spatial frequency composition of the stimuli to task demands, but an explicit test of the hypothesis has not been reported.

In the present experiment we focus on ERP correlates of hemispheric asymmetry in processing of spatial frequency in a delayed visual discrimination task. Previous studies have focused on memory aspects of this paradigm with ERP (Reinvang et al. 1998) and with fMRI (Greenlee et al. 2000) and found that occipitotemporal, parietal and frontal areas are activated, the strength and hemispheric distribution of activation depending on the cognitive demands of the task.

Materials and methods

Cognitive task

The memory task was a modified version of the delayed discrimination experiment (Magnussen and Greenlee 1999; Magnussen et al. 1996). Stimuli were vertical sinusoidal luminance grating strips with a 30% contrast which were generated on a high-resolution color monitor by a Cambridge Research Systems graphic card. The gratings were presented for 100 ms in a circular window subtending a 5 deg visual angle and viewed in central vision, the stimulus onset/offset forming a rectangular wave.

Spatial frequency discrimination was measured by a two-interval forced choice procedure where the subject decided which of two successively presented gratings, termed reference and test gratings, respectively, had the higher spatial frequency. The experimental task is diagrammed in Fig. 1. The difference in spatial frequency between test and reference gratings was individually adjusted to produce around 80% correct responses, and varied between 5% and 15%. The reference spatial frequency was varied by $\pm 10\%$ of a base value to prevent build-up of long-term representations. Thus, each trial introduced two novel gratings with the computer randomly assigning the higher spatial frequency to the first or second interval; between stimulus exposures the subject kept her/his gaze at the blank screen. Reference spatial frequency, 1.25

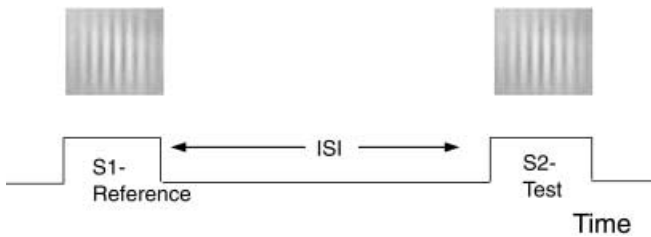


Fig. 1 Diagram of the delayed discrimination experiment. Two sine-wave gratings were presented briefly (100 ms), separated by an interstimulus interval (*ISI*, 1 or 6 s), and the subject decided if the second grating had a higher or lower spatial frequency than the first. In the experiments the spatial frequency difference was 5–15%

or 10 c/deg, and interstimulus interval (*ISI*), 1 or 6 s, were fixed within a single run of 40 trials; the subjects completed three runs for each combination of reference spatial frequency and *ISI* in an approximate counterbalanced order, giving a total of 120 trials in each condition. Accuracy and choice reaction times (*RTs*) were recorded together with ERP measurements. The subject was asked to respond as fast and accurately as possible to the test stimulus by pushing either of two buttons. Pushing the left button signaled that the grating with the higher spatial frequency was presented in the first interval (reference), and pushing the right button signaled that the higher frequency was presented in the second interval (test). The response triggered a new trial, which began after a 3-s delay. The experimental session, including preparation for ERP recording, lasted about 2–2.5 h.

Participants were 15 students, aged 25–35 years, with normal or corrected to normal vision. Three participants were rejected from the analysis because of poor quality of the EEG data or due to instrument failures. All participants were self-reported right handers. The participants were fully informed of their rights to withdraw from the study, and they signed statements of informed consent according to the standards of the Declaration of Helsinki. The anonymity of the participants was protected by assigning arbitrary codes in data recording and processing.

ERP recording

ERPs were recorded from an array of 29 electrodes including ground, mounted in a cap (Electrocap Inc.), and referred to the nosetip. They were placed at frontal (FP1, FP2, F3, F4, F7, F8, FC5, FC6, Fz), central-parietal (C3, C4, CZ, CP1, CP2, CP5, CP6, P3, P4), and occipitotemporal (T3, T4, P7, P8, Pz, PO1, PO2, O1, O2, Oz) locations. An additional set of bipolar electrodes placed above and below the left eye was used to record eye movement related artifacts. Impedance was kept below 5 k Ω , and recordings were made with a 32-channel Synamp AC/DC amplifier (Neuroscan Inc.).

The data were recorded as a continuous EEG sampled with 500 points/s, and the EEG was segmented into epochs from –100 to 800 ms relative to stimulus onset, filtered (high pass >0.1 Hz, low pass <35 Hz, 24 dB/decade attenuation) and baseline corrected in the pre-stimulus epoch. Epochs with >75 μ V amplitude on the eye movement channel were rejected. For purposes of illustration and as a guide for selecting ERP components for further analysis, we generated grand average waveforms showing effects of spatial frequency at symmetrical left- and right-sided electrode pairs, but aggregated across all memory conditions in order to illustrate the spatial frequency related variations in waveforms. The relevant 12 electrode pairs covering occipitotemporal (Fig. 2), central-parietal (Fig. 3) and frontal (Fig. 4) brain areas are shown below.

An early complex of waveforms with a prominent N110 component mainly to high frequency stimuli is seen in the occipital region (Fig. 2), but it is clearly not sensitive to hemispheric differ-

ence. An early positivity (P90) can be seen in grand averages for some conditions, but was too small to be measured reliably in individual subjects. The time window in which hemispheric asymmetry and effects of experimental manipulations are observable starts about 150 ms poststimulus onset, and measurement and analysis focus on these effects.

N170 and P220

N170 is a prominent negative deflection observed under all conditions and with a latency of 160–200 ms. It has a posterior distribution with highest amplitudes for low spatial frequency stimuli and most clearly observed on occipital (O1/O2) and on lateral temporoparietal (P7/P8) electrodes. Additional electrode pairs showing grand average amplitudes of at least –3 μ V in one condition were P3/P4, C3/C4, CP5/CP6, and T3/T4. In general the highest amplitudes were observed on left-side electrodes (see Fig. 2). We therefore followed guidelines for cognitive ERP measurement (Picton et al. 2000) and let the identification of peak latency be guided by the electrodes at which the peak could be most clearly determined, in this case by the left-side electrodes (O1, P3, C3, CP5, P7, T3). There was no indication of a latency difference between hemispheres in the grand average curves, and the amplitudes were therefore measured at the same time point for the left-sided and the symmetrically opposite right-sided lead (i.e., O2, P4, C4, CP6, P8, T4). Although this procedure might put amplitude measures from right hemisphere leads at a disadvantage, it secures consistency in the scoring of individual data.

P220 is a positive potential following the N170 and with a latency of 210–240 ms. When the negative N170 is large, the P220 may also be negative although it can be clearly distinguished in most subjects. An ensuing P400 may also influence and inflate the P220 amplitude, but at least for the reference stimulus, to which there is no response, the P220 is distinguished from the P400 by an intervening negative deflection (N310, see below). We measured P220 on the same electrodes as N170 and with the same general procedure for defining latencies and amplitudes. The characteristic form of N170 and P220 can be seen in Figs. 2 and 3.

N310

This negative component is seen on central (CP5/CP6, C3/C4) and frontal electrodes (F3/F4, FC5/FC6) in the grand averages (Figs. 3, 4) and on midline electrodes. It was obscured by a prominent P400 for the test stimulus, and thus it was only measured with respect to the reference stimulus and has a typical latency range of 290–330 ms. In the response to the reference stimulus the N310 could also be identified on temporal electrodes and for analysis in the posterior region we selected P7/P8 and T3/T4 as the electrodes of interest. For analyzing the frontocentral effects we measured N310 latency on Cz and Fz, and measured amplitudes on the flanking electrodes (C3/C4, and F3/F4) at the latency time point.

P400

The P400 has a typical distribution with a posterior maximum at Pz and a latency in the 390- to 440-ms range. We defined the P400 latency in relation to Pz and measured amplitudes at the latency time point on the central and posterior electrodes previously selected for analysis of N170 and P220 and on a frontal group of electrodes (F3/4, F7/8).

SW

The P400 maximum is followed by a slowly descending tail and we measured the amplitude as average voltage level in a time window 500–700 ms poststimulus onset and measured on occipital

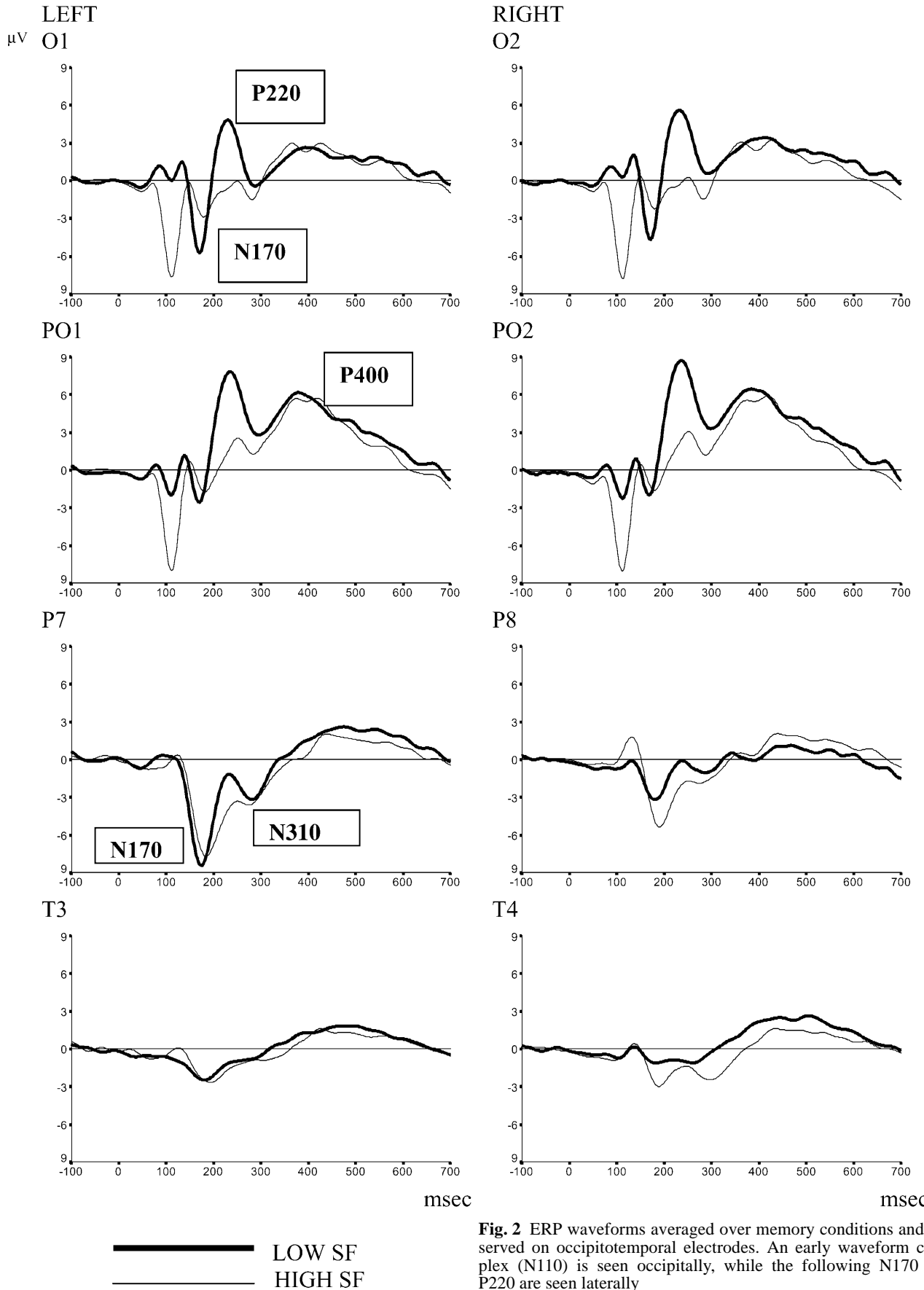


Fig. 2 ERP waveforms averaged over memory conditions and observed on occipitotemporal electrodes. An early waveform complex (N110) is seen occipitally, while the following N170 and P220 are seen laterally

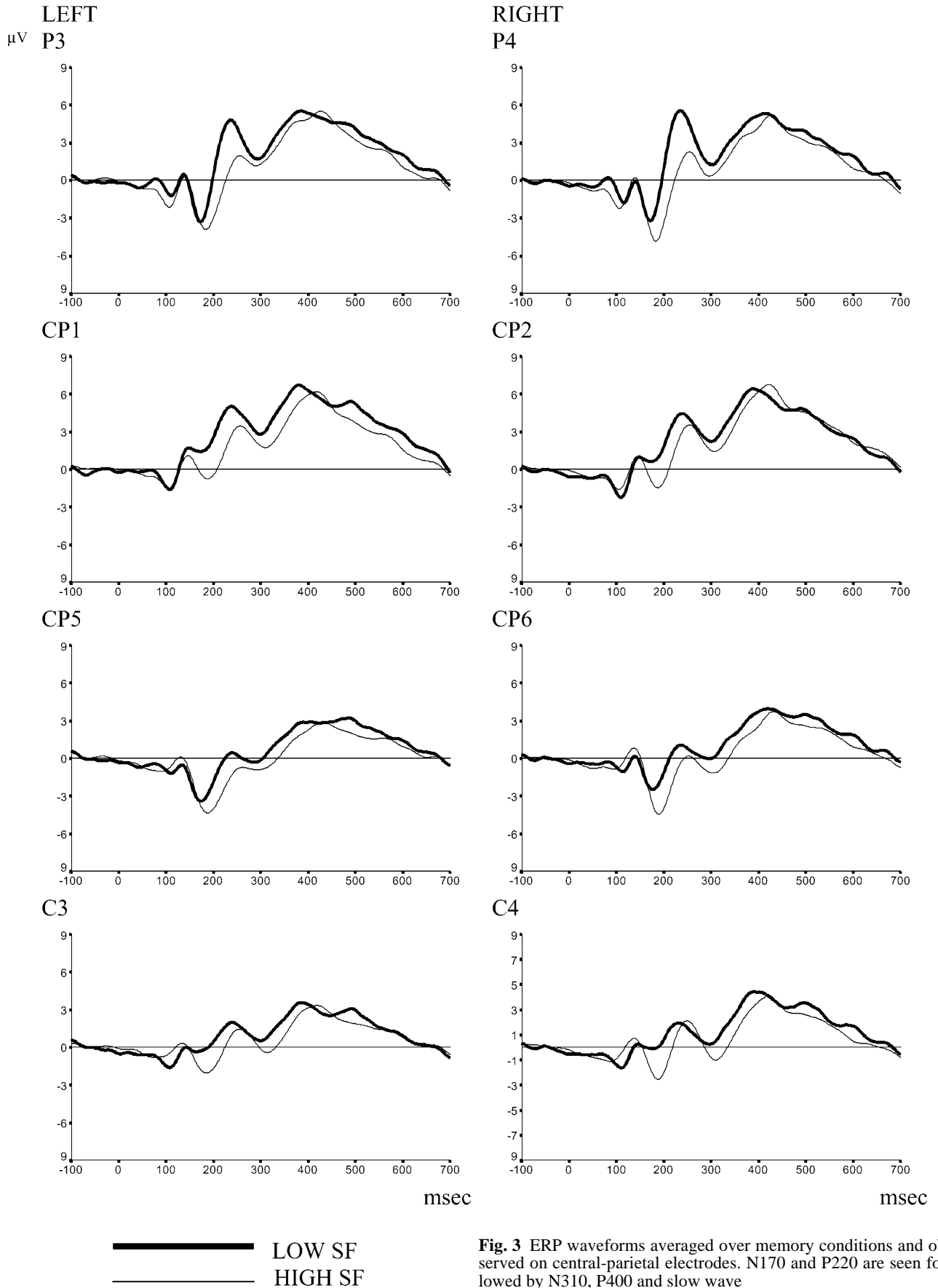


Fig. 3 ERP waveforms averaged over memory conditions and observed on central-parietal electrodes. N170 and P220 are seen followed by N310, P400 and slow wave

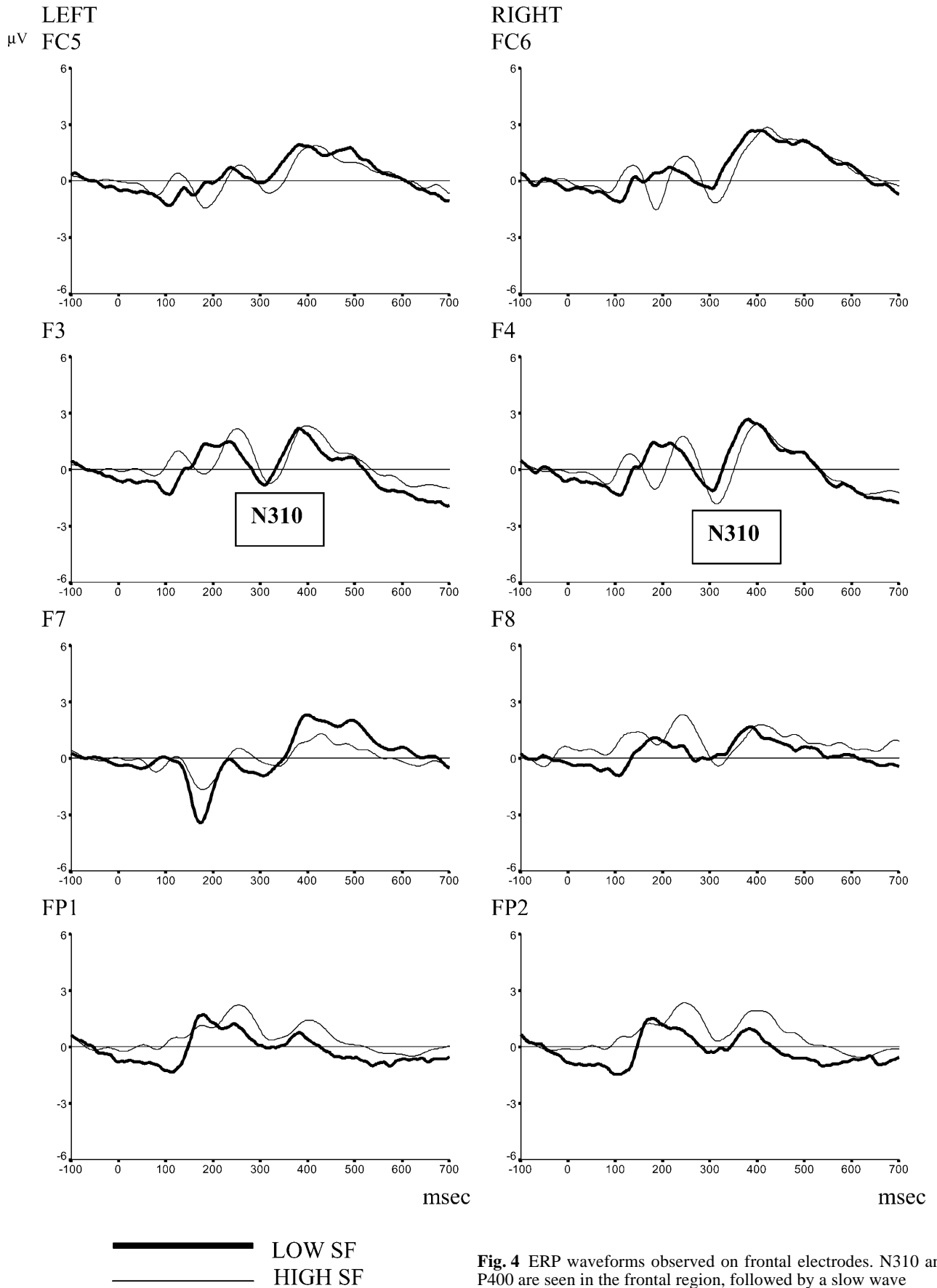


Fig. 4 ERP waveforms observed on frontal electrodes. N310 and P400 are seen in the frontal region, followed by a slow wave

(O1/O2), posterior temporal (P7/P8, T3/T4), posterior central-parietal (P3/P4, C3/C4), and frontal (F3/F4, F7/F8, FP1/FP2) electrode pairs. Experimental effects on SW are most clearly seen in the response to the test stimulus, where the P400 is also most pronounced.

Analytic rationale and statistical analysis

The logic of the two-interval forced choice experiment allows us to make some inferences about the processes that are recruited in the various conditions. First, each trial requires that the subject compares two stimuli, reference and test, that are presented in succession. Both stimuli will activate processes of sensory analysis and perceptual identification, and possibly automatic encoding in memory, but the presentation of the test stimulus must additionally initiate perceptual comparison/discrimination processes and a decision process. Previous psychophysical experiments and ERP experiments (Magnussen 2000; Magnussen and Greenlee 1999) indicate that with short ISIs (<3–4 s) the information on which the discrimination is based is still in a predominantly perceptual mode of representation, but with longer ISIs the discrimination requires retrieval of information from short-term memory representation. This assumption is based on the finding that whereas the accuracy of performance remains stable across 10-s ISIs, choice RT is stable across the first 3–4 s, then starts to increase. For simplicity we term the reference and test events in the latter condition as encoding and retrieval, respectively, acknowledging that encoding is probably common to both events. We performed ANOVAs with repeated measures and including both memory factors, i.e., Stimulus (reference vs test), Interstimulus interval (ISI: 1 s vs 6 s), and the factors of Spatial Frequency (high vs low), Hemisphere (left vs right), and Electrode (the individual electrodes studied in the relevant region). The Greenhouse-Geisser epsilon correction for degrees of freedom was used when appropriate. When the pattern of interactions showed significant associations of spatial frequency or hemisphere with memory variables, we carried out subsequent ANOVAs within the relevant memory factors.

Results

The psychophysical discrimination data are consistent with several previous experiments (reviewed by Magnussen and Greenlee 1999) showing that there is no impairment in delayed spatial frequency discrimination in terms of accuracy as ISI is increased. The choice RTs are prolonged about 50 ms in the longer ISI condition (743 vs 791 ms), and choice RTs to high spatial frequencies are somewhat faster than to low spatial frequencies (749 vs 784 ms). In the present data set none of these RT effects is significant in ANOVAs with spatial frequency

and ISI as independent factors. Subsequent psychophysical experiments (Magnussen 2000) indicate that choice RTs in this task are stable for ISIs in the range of 0–4 s, then increase linearly by, on average, 120 ms as ISI is increased to 10 s; the present results for 6-s ISIs fall on the slope of this curve.

The analysis of the ERP results will be presented in the order of component latency, i.e., starting with N170, and commenting first on the findings in the occipital region. This is of special interest for comparison with previous studies using a small number of electrodes that have focused exclusively on this region and the O1/O2 electrode pair.

N170 and P220

Analyses with ANOVA on the occipital N170 complex show a significant main effect of spatial frequency on N170 amplitude independent of memory variables ($F_{(1,11)}=15.6$, $P<0.01$). Amplitudes are generally higher for low than for high spatial frequencies, as can be easily seen in Fig. 2. There is a further significant interaction of stimulus type (test/reference) with spatial frequency and hemisphere ($F_{(1,11)}=9.66$, $P=0.01$). Further analyses show that the spatial frequency \times hemisphere interaction is only significant for the test stimulus, stimulus 2 ($F_{(1,11)}=9.27$, $P<0.01$). We note here a marked hemispheric amplitude difference (Left >Right) for low spatial frequency stimuli, but not for high spatial frequency stimuli (Fig. 5).

The main effect of ISI is highly significant for N170 amplitude ($F_{(1,11)}=13.99$, $P<0.01$) with higher negative amplitudes for the long ISI, but ISI does not interact with spatial frequency or hemisphere. Analogous memory related effects are found on all occipito-parieto-temporal electrodes, and they are described below.

The N170 complex has been further analyzed in the posterior temporoparietal region with the electrodes defined above (i.e., P3/P4, P7/P8, C3/C4, CP5/CP6, T3/T4). The results show no significant main effects of hemisphere or spatial frequency, but a significant interaction independently of memory load (SF \times H, $F_{(1,11)}=5.53$, $P<0.05$). The interaction is shown in Fig. 6, and entails no difference in the left hemisphere, whereas

Fig. 5 Interaction of spatial frequency and hemisphere for the occipital N170 amplitude. Mean amplitudes for electrodes O1 and O2 are averaged over stimulus types (reference/test) and ISIs. There is a marked hemispheric amplitude difference (Left >Right) for low SF stimuli, but not for high SF

N170 in the occipital region

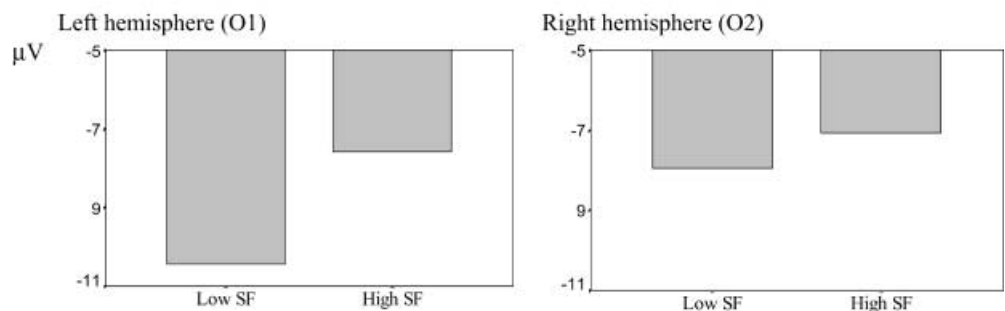


Fig. 6 Interaction of spatial frequency and hemisphere for the parietotemporal N170 amplitude. Bars show mean amplitudes averaged over electrodes, stimulus type (reference/test) and ISI. The interaction entails no difference between spatial frequencies in left hemisphere amplitudes, but a relatively higher right hemisphere amplitude for high spatial frequency

N170 in parieto-temporal region.

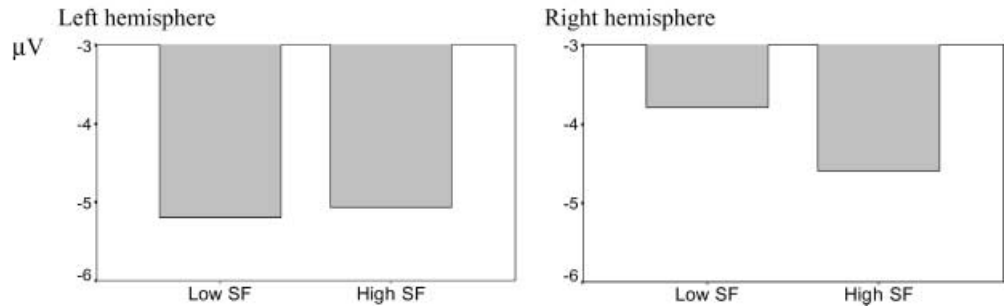
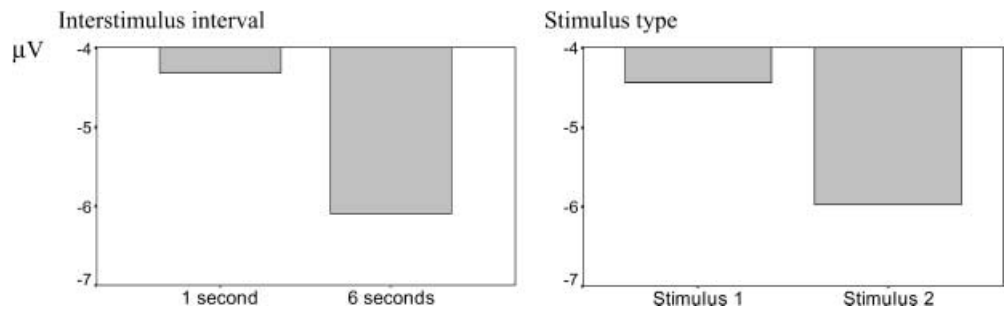


Fig. 7 Memory effects on the N170 amplitude posteriorly. Bars show mean amplitudes averaged over electrodes (occipital, parietal, temporal), spatial frequencies (high/low) and hemispheres (left/right). The effect of ISI is a higher N170 amplitude for the long ISI condition, and higher amplitudes are observed for the test stimulus compared with the reference stimulus

N170 – Memory related effects.



amplitude is higher for high spatial frequency in the right hemisphere.

Adding electrode to the analysis yields a three-way interaction ($SF \times H \times \text{electrode}$) that is statistically non-significant, but the effect is seen quite clearly on electrode pairs in the lower temporal region (P7/P8 and T3/T4, see Fig. 2). The $SF \times H$ interaction is significant for the T3 vs T4 contrast ($F_{(1,11)}=6.08$, $P<0.05$), but not for any other individual electrode pair. Although the results suggest a crossover pattern of interaction, the most striking difference observed is that N170 amplitude for low spatial frequency is higher in the left than in the right hemisphere.

The memory related effects are strong for both interstimulus interval (ISI, $F_{(1,11)}=28.0$, $P<0.001$) and stimulus type (reference/test, $F_{(1,11)}=10.1$, $P<0.01$), but there are no interactions of these variables with spatial frequency or hemisphere. The effect of ISI is a higher N170 amplitude for the long ISI condition, and there are higher amplitudes for the test than for the reference stimulus. The memory variables do not interact between themselves and the effects are therefore in principle additive. The effect of memory conditions is shown in Fig. 7.

P220 amplitude shows a generalized and strong effect of spatial frequency in the whole posterior region with higher amplitudes for low than for high spatial frequency in both hemispheres. Main effects of memory (ISI) are significant ($F_{(1,11)}=8.17$, $P<0.05$), but ISI does not interact with spatial frequency or hemisphere. The memory (ISI) effect shows up as a lower P220 amplitude for con-

ditions with longer ISIs. It is reasonable to view this effect as a continuation of the increased negativity observed for N170 into the time window for the P220.

N310

The N310 has a mean latency of 280 ms in the temporal region, and of 310–320 ms in the frontocentral region. In the temporal region there are no significant statistical effects involving spatial frequency or hemisphere, but in the frontocentral (C3/C4, F3/F4) region there is a significant interaction of spatial frequency and hemisphere ($F_{(1,11)}=8.35$, $P<0.02$). The observed interaction effect in the frontocentral region is that hemispheric asymmetry is greater for high than for low spatial frequency stimuli (Fig. 8).

P400

The mean P400 latency varies between 380 and 420 ms for different stimuli and conditions. The maximum P400 amplitude is measured in the occipitoparietal region and varies between 5 and 8 μV . The P400 probably reflects the much studied P3 component which is found for attended stimuli in all sense modalities, and which is influenced by task difficulty. Analysis with ANOVA of P400 amplitude shows no significant effects of spatial frequency or hemisphere or any interactions involving these

Fig. 8 Interaction of spatial frequency and hemisphere for N310 in the frontocentral region. The hemispheric asymmetry is greater for high than for low spatial frequencies. Mean amplitudes averaged over left and right electrodes (F3/C3 and F4/C4) are shown for the reference stimulus, averaged over interstimulus intervals

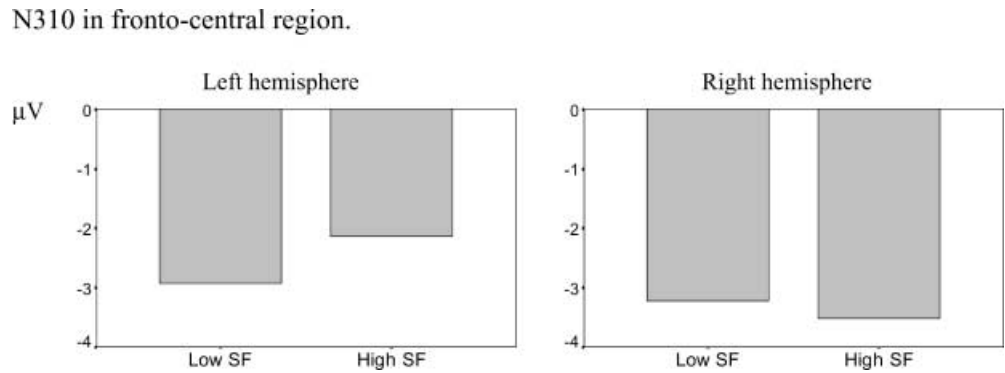
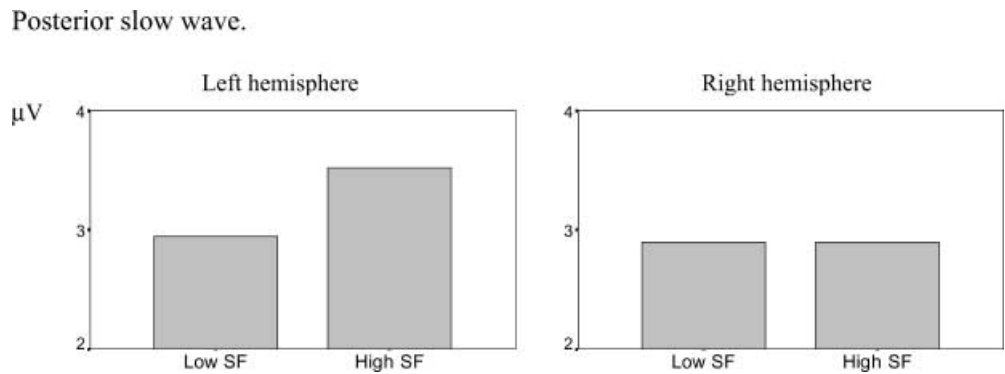


Fig. 9 Interaction of spatial frequency and hemisphere for the late slow wave recorded for the test stimulus. Bars show mean amplitudes averaged over electrodes (occipital, temporal, parietal) and interstimulus intervals for the test stimulus. The pattern of results indicates that the left hemisphere responds discriminately to spatial frequency, but the right hemisphere does not



factors for any condition. P400 amplitude is markedly higher for the test stimulus compared with the reference stimulus, corresponding to the well-known fact that a stimulus associated with task decision and response evokes a marked P400.

SW

It was measured as mean amplitude in the 500- to 700-ms time window poststimulus onset at occipital, posterior ventral, posterior dorsal and frontal electrodes, as previously defined. In an overall ANOVA analysis in which electrodes from the posterior and frontocentral electrodes were analyzed separately, the results indicated that in general no significant interactions involving hemisphere or spatial frequency were observed for electrodes in the frontocentral region. Significant effects of memory interval (ISI) are found for the frontal slow wave, and a more negative going amplitude is found with increasing ISI ($F_{(1,11)}=8.27$, $P<0.05$). In contrast the findings for the posterior region indicated a highly significant three-way interaction of spatial frequency, hemisphere and stimulus ($F_{(1,11)}=14.6$, $P<0.01$). Further analyses carried out to reveal the source of the three-way interaction showed no significant effects for the reference stimulus, but an interaction of spatial frequency and hemisphere for the test stimulus ($F_{(1,11)}=8.75$, $P<0.05$). There were no higher order interactions with electrode, and the pattern of results with mean amplitudes for posterior electrodes is shown in Fig. 9.

Discussion

The present study was designed to allow inferences about hemispheric differences in the processing of high and low spatial frequency information in discrimination and memory by presenting stimuli centrally in the visual field and comparing the ERP activations in the left and right hemisphere. The experiment aimed at testing the hypothesis of preferential hemispheric processing of spatial frequency proposed by Sergent (1982) and the possible influence of memory load on hemispheric asymmetry. ERPs measure several temporally overlapping processing components, which complicates simple conclusions on hemispheric asymmetry, but which may provide a realistic reflection of cerebral processing. The results suggest that several principles of information processing are used by the brain in coding spatial frequency information in the context of a perceptual memory task. These principles include preferential processing of high and low spatial frequencies, preferential hemispheric processing regardless of spatial frequency, as well as complex interactions of hemisphere and spatial frequency. The latter findings are essential for evaluating the initial hypothesis. Evidence for interaction between spatial frequency and hemisphere lateralization was found for N170 amplitude measured on electrodes in the occipito-temporal region, but with a pattern contrary to the hypothesis in that higher left hemisphere amplitudes were found for stimuli with low spatial frequency. A later negative component, N310, showed a pattern of findings on

frontocentral electrodes, which again indicated higher left hemisphere amplitudes for low spatial frequencies. Finally, the late slow wave component showed a pattern of findings for posterior electrodes which did correspond to our hypothesis in that left hemisphere amplitudes were generally higher for high spatial frequency stimuli. Further discussion of the findings must take into account that early ERP components (N170, N310) to a greater extent reflect perceptual processing, whereas later components (slow wave) reflect predominantly cognitive processing.

Spatial frequency and hemisphere

The results confirm previous reports that the early visual potentials observed at the occipital pole are distinctly different for high and low spatial frequency stimuli (Plant et al. 1983; Rebaï et al. 1998; Zani and Proverbio 1995). These differences concern early negativities in which a marked negative peak (N110) is only observed for high spatial frequency stimuli, whereas a later N170 peak is observed for both high and low spatial frequency stimuli. Main effects of spatial frequency were found for N170 and even more strongly for the ensuing P220 component, with higher amplitudes for low than for high spatial frequencies. These findings are partly in agreement with those of Kenemans et al. (1993), who reported higher amplitudes in N170 for low spatial frequencies measured occipitally. Their stimuli were in the low range of spatial frequency (3 c/deg and below) and were presented in an attention task. These findings underline the point that the spatial frequency composition of the stimulus material has a marked influence on visual ERP components including N170/P220, which are strongly focused on in studies of face and object perception (Bentin et al. 1996; Rossion et al. 1999; Doniger et al. 2000). In contrast to previous findings (Zani and Proverbio 1995), we saw no hemispheric asymmetries in the N110, and only later components indicated hemispheric advantages. The N170/P220 waveforms can be studied in the posterior part of the hemispheres, and the trend for N170 is to follow a hemispheric principle in which amplitudes are somewhat higher in the left compared with the right hemisphere, a pattern which is most clearly seen in the occipitotemporal region. This is consistent with the results of Zani and Proverbio (1995), who found this left hemisphere advantage only under active task conditions.

The spatial frequency/hemisphere interaction found for N170 is mainly caused by the fact that low spatial frequency stimuli are processed differently by the two hemispheres with higher amplitudes observed over the left hemisphere. These results are not consistent with our previous study (Reinvang et al. 1998), where we interpreted the results for low frequency stimuli as consistent with the spatial frequency hypothesis of hemispheric asymmetry. A number of differences between the experiments make a direct comparison difficult. The previous report was based on a small number of subjects and a modeling of brain sources in which the results depend on

the choice of model, whereas the present analysis is more empirical and based on a direct analysis of observed waveforms in a higher number of subjects. We therefore think the present results should carry more weight.

The only previous study to look for spatial frequency and hemisphere interactions in a cognitive paradigm (Zani and Proverbio 1995) also reported statistically significant interaction, although the asymmetry was most pronounced for high spatial frequencies. They tested a range of spatial frequencies, in which the highest spatial frequency corresponded to 6 c/deg, whereas we tested two extremes of spatial frequency in which high spatial frequency was defined as 10 c/deg. To facilitate comparison we carried out an analysis only on the occipital electrodes, where Zani and Proverbio (1995) found the significant effects, and confirmed a significant spatial frequency by hemisphere interaction (Fig. 5), but the pattern is the same as described above, with larger hemispheric differences for low compared with high spatial frequencies. Both task factors and the range of spatial frequencies tested may therefore influence hemispheric balance.

The N310 observed in the present study is seen in the frontocentral and in the occipitotemporal region and it shows a consistent spatial frequency \times hemisphere interaction for stimulus encoding. The significant effect is seen in the frontocentral, but not in the posterior temporal, region and shows a greater hemispheric differentiation for high than for low spatial frequency stimuli. The pattern of hemispheric amplitude balance is otherwise similar to the N170 in showing a pattern of higher amplitude for low spatial frequency over the left hemisphere and higher amplitude for high spatial frequency over the right. The N310 corresponds in latency to the N2 described by Heinze et al. (1998) in a task with attention demands on local/global visual feature processing. Their N2 is seen in the 270- to 370-ms time window, and it shows hemispheric asymmetry in the most demanding (divided attention) condition with higher left hemisphere amplitude for local targets. They conclude that differential hemispheric processing of spatial frequency may be reflected in this component.

The pattern of results for SW indicates that the retrieval and decision processes in relation to the test stimulus elicit a complex pattern of differentiated hemispheric processing of spatial frequency in posterior brain regions. The evidence suggests a greater sensitivity to high spatial frequency in the left than in the right hemisphere. Thus the results are in this respect consistent with the initial hypothesis, and they show a pattern which is clearly different from the earlier components of N170 and N310.

Memory

The results show strong effects of the memory variables interstimulus interval and stimulus category (defined as reference or test, and corresponding to encoding or retrieval).

eval). The memory variables mostly exert their influence independently of spatial frequency or hemisphere; in addition, the memory variables do not interact and would seem to act independently and additively. The N170/P220 ERP components correspond in latency and distribution to the visual memory potentials found by Begleiter et al. (1993) and confirmed by Beisteiner et al. (1996) and Reinvang et al. (1998). Our previous observation that ISI is associated with increasing N170 amplitude on electrodes in the posterior temporal region is confirmed in the present data. In the previous ERP experiment (Reinvang et al. 1998), we noted (but did not test) an overall stronger right-hemisphere involvement when visual memory was challenged by increasing the ISI to 10 s. No such effect was observed in the present study, in which the maximum ISI was 6 s. In addition to memory, the N170 has also been shown to relate to face perception (Barrett et al. 1988; Bentin et al. 1996; Rossion et al. 1999) and to selective attention (Heinze et al. 1990; Zani and Proverbio 1995). Thus, N170 is probably related to central aspects of visual cognitive processing, but there may be several temporally overlapping components underlying the observed variations in N170 amplitude. It is possible that the mechanism underlying differential spatial frequency processing, although giving rise to potentials overlapping the memory related N170/P220 waveforms, is dissociable from the visual memory mechanism.

The slow wave (SW) seen in the 500- to 700-ms time window is in the time specter of memory effects observed in various memory paradigms and referred to as the old/new effect or Dm (Johnson 1995). Our paradigm is not identical to the paradigms in which Dm or working memory effects are observed, so the SW in our study cannot be unequivocally identified with either of these effects. It is, however, clearly sensitive to memory aspects of the task.

General discussion

The results do not support the hypothesis originally proposed by Sergent (1982) in any simple straightforward manner. The results indicate that there is a process for spatial frequency analysis associated with N170 measured posteriorly in which the left hemisphere is generally more active than the right, whereas the right is more sensitive to spatial frequency differences in the stimulus information. This is supplemented by later components (frontocentral N310 and posterior SW), and the net result may be an integrated process to which both hemispheres and several brain regions contribute.

In a previous fMRI study (Greenlee et al. 2000), we found massive evidence of posterior activation (superior parietal lobule and extrastriate areas) in the delayed spatial frequency discrimination task with additional evidence of prefrontal activation. No explicit tests of hemispheric asymmetry were made in that study, but it is notable (Greenlee et al. 2000; Fig. 3a, b) that for visual areas BA 18 and 19 the regional activation values are

about 20% higher on the left than on the right side. Although we have no evidence linking specific ERP components to anatomical loci, it is possible that this finding reflects the higher left hemisphere amplitudes for N170 found in the present study. It is further consistent with current conceptions of memory that there is an intimate cooperation between frontal and posterior areas in memory formation and maintenance (Cabeza and Nyberg 2000). Analysis of results from the forced choice spatial discrimination task reviewed by Magnussen (2000) argues that although the task is cognitive, the underlying memory system can most reasonably be interpreted in terms of the perceptual representation system (PRS, Tulving and Schacter 1990), and the present data might indicate visual area activation in the context of encoding and retrieval in the PRS. The novel aspect of the findings is that the activation pattern shows evidence of spatial frequency and hemisphere interaction.

Should the findings on N170 and N310 be regarded then as going against the Sergent hypothesis, since the findings are opposite to those expected from the hypothesis and from cognitive experiments? Other studies have reported similar "paradoxical" results (Mecacci and Spinelli 1987; Spinelli and Mecacci 1990) for temporal VEPs in a passive viewing task carrying no perceptual/cognitive processing load. However, the paradox rests on the assumption that activity observed in ERP or other physiological data (blood flow) is related to processing facility in a simple positively correlated manner. Such a positive relationship might not be valid for all sensory and higher-order cognitive operations. If it is correct that the present task strongly involves a low level memory system (PRS), it is likely that mechanisms involving priming participate in forming memory representations in the PRS. Studies with fMRI (Buckner et al. 1998) have shown that presentation of a primed visual object leads to reduced cerebral blood flow in extrastriate and inferior temporal regions, suggesting in fact a negative correlation between activation increase and processing facility. A recent review (Schacter and Badgaiyan 2001) finds conflicting evidence on the issue. If one speculates that greater ease of processing might be reflected in lower activity of the PRS, the pattern of hemispheric asymmetry observed in the ERP analysis of delayed spatial frequency discrimination for early components (N170, N310) is more consistent with original formulations of the spatial frequency hypothesis (Hellige 1995; Sergent 1982). The reason that the SW does not follow the same principle may be that it reflects a different cognitive process which does not involve the PRS, but rather response related decision mechanisms. The strength of behavioral data reviewed by Christman (1997) and Watten et al. (1998) argues for this interpretation. In a long series of behavioral studies none of the experiments that have failed to support the spatial frequency hypothesis has reported a reversed pattern of results, and all the non-confirmatory findings report no significant differences.

The basic idea of the spatial frequency hypothesis, that spatial frequency information is processed differen-

tially in the left and right cerebral hemisphere, is supported by the present results. The further characterization of this processing difference on the basis of ERP must take into account the stage of information processing reflected in successive ERP components as well as the nature of the cognitive task. The simple hypothesis of hemispheric specialization for spatial frequency is based on a pattern of findings observed at a behavioral level, and our results indicate that the complex stream of processing reflected in ERPs contains several discrete components interacting in determining the effects observed behaviorally. Such a pattern of temporally overlapping components is suitable for study with ERP, but would pose major problems of temporal resolution for other imaging methods.

Acknowledgement We thank Marianne Løvstad, Espen Skorstad and Olof Gøtestam for assistance in running the experiments and data analysis.

References

- Barrett SE, Rugg MD, Perrett DI (1988) Event-related potentials and the matching of familiar and unfamiliar faces. *Neuropsychologia* 26:105–117
- Begleiter H, Porjesz B, Wang W (1993) A neurophysiologic correlate of visual short-term memory in humans. *Electroencephalogr Clin Neurophysiol* 87:46–53
- Beisteiner R, Huter D, Edward V, Koch P, Franzen P, Egkher A, Lindinger G, Baumgartner C, Lang W (1996) Brain potentials with old/new distinction of non-words and geometric figures. *Electroencephalogr Clin Neurophysiol* 99:517–526
- Bentin S, Allison T, Puce A, Perez E, McCarthy G (1996) Electrophysiological studies of face perception in humans. *J Cogn Neurosci* 8:551–565
- Buckner RL, Goodman J, Burock M, Rotte M, Koutstaal W, Schacter D, Rosen B, Dale AM (1998) Functional-anatomical correlates of object priming in humans revealed by rapid presentation event-related fMRI. *Neuron* 20:285–296
- Cabeza R, Nyberg L (2000) Imaging cognition II: an empirical review of 275 PET and fMRI studies. *J Cogn Neurosci* 12:1–47
- Christman S (1997) Hemispheric asymmetry in the processing of spatial frequency: experiments using gratings and band pass filtering. In: Christman S (ed) *Cerebral asymmetries in sensory and perceptual processing*. Elsevier, New York, pp 3–30
- Cornette L, Dupont P, Rosier A, Sunart S, Van Hecke P, Michiels J, Mortelmans L, Orban GA (1998) Human brain regions involved in direction discrimination. *J Neurophysiol* 79:2749–2765
- Doniger GM, Foxe JJ, Murray MM, Higgins BA, Snodgrass JG, Schroeder CE, Javitt DC (2000) Activation time course of ventral visual stream object-recognition areas: high density electric mapping of perceptual closure processes. *J Cogn Neurosci* 12:615–621
- Dupont P, Vogels R, Vandenberghe R, Rosier A, Cornette L, Bormans G, Mortelmans L, Orban GA (1998) Regions in the human brain activated by simultaneous orientation discrimination. A study with positron emission tomography. *Eur J Neurosci* 10:3689–3699
- Fiorentini A, Berardi N (1984) Right-hemisphere superiority in the discrimination of spatial phase. *Perception* 13:695–708
- Grabowska A, Nowicka N (1996) Visual-spatial-frequency model of cerebral asymmetry: a critical survey of behavioral and electrophysiological studies. *Psychol Bull* 120:434–449
- Greenlee MW, Rischewski J, Mergner T, Seeger W (1993) Delayed pattern discrimination in patients with unilateral temporal lobe damage. *J Neurosci* 13:2565–2574
- Greenlee MW, Magnussen S, Reinvang I (2000) Neocortical areas underlying visual short-term memory: evidence from fMRI. *Exp Brain Res* 132:399–403
- Heinze HJ, Luck SJ, Mangun GR, Hillyard SA (1990) Lateralized ERPs index focused attention to bilateral stimulus arrays: I. Evidence for early selection. *Electroencephalogr Clin Neurophysiol* 75:511–527
- Heinze HJ, Hinrichs H, Scholz M, Burchert W, Mangun G (1998) Neural mechanisms of global and local processing: a combined PET and ERP study. *J Cogn Neurosci* 10:485–498
- Hellige J (1995) Hemispheric asymmetry for components of the visual stimulus. In: Hugdahl K, Davidson RJ (eds) *Brain asymmetry*. MIT Press, Cambridge, MA, pp 99–121
- Johnson R Jr (1995) Event-related potential insights into the neurobiology of memory systems. In: Boller F, Grafman J (eds) *Handbook of neuropsychology*, vol 10, sect 14. Elsevier, New York, pp 135–164
- Kenemans JL, Kok A, Smulders FTY (1993) Event-related potentials to conjunctions of spatial frequency and orientation as a function of stimulus parameters and response requirements. *Electroencephalogr Clin Neurophysiol* 88:51–63
- Kitterle FL, Kaye RS (1985) Hemispheric symmetry in contrast and orientation sensitivity. *Percept Psychophys* 37:391–396
- Kitterle FL, Selig LM (1991) Visual field effects in the discrimination of sine-wave gratings. *Percept Psychophys* 50:15–18
- Kitterle FL, Christman S, Hellige J (1990) Hemispheric differences are found in the identification, but not the detection, of low versus high spatial frequencies. *Percept Psychophys* 48:297–306
- Kitterle FL, Hellige J, Christman S (1992) Visual hemispheric asymmetries depend on which spatial frequencies are task relevant. *Brain Cogn* 20:308–314
- Lennie P, Trevarthen C, Van Essen D, Wässle H (1990) Parallel processing of visual information. In: Spillmann L, Werner JS (eds) *Visual perception: the neurophysiological foundations*. Academic, New York, pp 103–128
- Magnussen S (2000) Low-level memory processes in vision. *Trends Neurosci* 23:247–251
- Magnussen S, Greenlee MW (1999) The psychophysics of perceptual memory. *Psychol Res* 62:81–92
- Magnussen S, Greenlee MW, Thomas JP (1996) Parallel processing in visual short-term memory. *J Exp Psychol Hum Percept Perform* 22:202–212
- Mecacci L (1997) Temporal frequency processing. In: Christman S (ed) *Cerebral asymmetries in sensory and perceptual processing*. Elsevier, New York, pp 31–54
- Mecacci L, Spinelli D (1987) Hemispheric asymmetry of pattern reversal visual evoked potentials in healthy subjects. *Int J Psychophysiol* 4:325–328
- Niebauer CL, Christman SD (1999) Visual field differences in spatial frequency discrimination. *Brain Cogn* 41:381–389
- Orban GA, Dupont P, Vogels R, Bormans G, Mortelmans L (1997) Human brain activity related to orientation discrimination. *Eur J Neurosci* 9:246–259
- Orban GA, Dupont P, Bruyn B, Vandenberghe R, Rosier A, Mortelmans L (1998) Human brain activity related to speed discrimination tasks. *Exp Brain Res* 122:9–22
- Picton TW, Bentin S, Berg P, Donchin E, Hillyard SE, Johnson R Jr, Miller GA, Ritter W, Ruchkin DS, Rugg MD, Taylor MJ (2000) Guidelines for using human event-related potentials to study cognition: recording standards and publication criteria. *Psychophysiology* 37:127–152
- Plant GT, Zimmer RL, Durden K (1983) Transient visually evoked potentials to the pattern reversal and onset of sinusoidal gratings. *Electroencephalogr Clin Neurophysiol* 56:137–158
- Proverbio AM, Zani A, Avella C (1997) Hemispheric asymmetries for spatial frequency discrimination in a selective discrimination task. *Brain Cogn* 34:311–320
- Rebaï M, Bagot J-D, Viggiano M-P (1993) Hemispheric asymmetry in transient visual evoked potentials induced by the spatial factor of stimulation. *Brain Cogn* 23:263–278

- Rebaï M, Bernard C, Lannou J, Jouen F (1998) Spatial frequency and right hemisphere: an electrophysiological investigation. *Brain Cogn* 36:21–29
- Reinvang I, Magnussen S, Greenlee MW, Larsson PG (1998) Source analysis of ERPs in visual memory for spatial frequency. *Exp Brain Res* 128:481–484
- Rose D (1983) An investigation into hemispheric differences in adaptation to contrast. *Percept Psychophys* 34:89–95
- Rossion B, Delvenne J-F, Debatisse D, Goffaux V, Bruyer R, Crommelinck M, Guérit J-M (1999) Spatio-temporal localization of the face inversion effect: an event-related potentials study. *Biol Psychol* 50:173–189
- Schacter DL, Badgaiyan RD (2001) Neuroimaging of priming: new perspectives on implicit and explicit memory. *Curr Direct Psychol Sci* 10:1–4
- Sergent J (1982) The cerebral balance of power: confrontation or cooperation? *J Exp Psychol Hum Percept Perform* 8:253–272
- Spinelli D, Mecacci L (1990) Contrast and hemispheric asymmetry: an electrophysiological investigation. *Int J Neurosci* 50:113–119
- Tulving E, Schacter DL (1990) Priming and human memory systems. *Science* 247:301–306
- Van Essen DC, DeYoe EA (1995) Concurrent processing in the primate visual cortex. In: Gazzaniga MS (ed) *The cognitive neurosciences*. MIT Press, Cambridge, MA, pp 383–400
- Watten R, Magnussen S, Greenlee MW (1998) Spatial frequency discrimination, brain lateralization and acute intake of alcohol. *Perception* 27:729–736
- Zani A, Proverbio AM (1995) ERP signs of early selective attention effects to check size. *Electroencephalogr Clin Neurophysiol* 95:277–292