Cerebral Cortex January 2005;15:109–116
doi:10.1093/cercor/bhh113
Advance Access publication July 6, 2004

Oscillatory Brain Activity Dissociates between Associative Stimulus Content in a Repetition Priming Task in the Human EEG

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The retrieval and formation of cortical object representations seem to require the activation of neuronal cell assemblies, correlated by synchronized neuronal activity in the gamma band range (> 20 Hz). In the present electroencephalogram (EEG) study we have analysed induced gamma band activity during the repetition of familiar (meaningful) and unfamiliar (meaningless) line drawings. Results showed a broad posterior distribution of induced gamma band responses (GBRs) after the initial presentation of a familiar stimulus. Repeated presentations of the same picture resulted in a decrease of GBRs, accompanied by a decrease in the number of electrode pairs exhibiting significant phase-locking values. These effects might be linked to a 'sharpening' mechanism within a cell assembly representing a familiar object. In contrast, the representation of primed unfamiliar stimuli was associated with an augmentation of gamma power and an increase in significantly phase-locked pairs of electrodes. These findings might be a signature of the formation of a new cortical network representing an object. Event related potentials (ERPs) showed a decrease in amplitude independent of the stimuli's associative content, and, thus, seem to play a complementary role in repetition priming as compared to high-frequency brain dynamics.

Keywords: induced gamma band response, repetition enhancement, repetition priming, repetition suppression, synchrony

Introduction

The improvement in identifying a stimulus by experience is commonly referred to as repetition priming (Tulving and Schacter, 1990). A neuronal correlate associated with repeated stimulus processing is a reduced firing rate of neurons (Brown and Aggleton, 2001), an effect termed 'repetition suppression' (Schacter and Buckner, 1998). Wiggs and Martin (1998), elaborating on ideas of Desimone (1996), suggested that repetition suppression is a by-product of a 'sharpening' process of cortical object representations. In this view, neurons coding features, which are not essential for processing a repeated stimulus are dropping out of a cell assembly coding this object, and thus, yielding a more efficient cortical representation of a stimulus. Recently, Henson *et al.* (2000) extended this concept by the assumption that a necessary condition for repetition suppression is a pre-existing cell assembly. For primed unfamiliar stimuli they reported 'repetition enhancement' of neuronal activity, speculatively related to the formation of a new cortical object representation.

In general, cortical object representations are considered to be activated by synchronization of neuronal activity within cell assemblies, which represent various stimulus features and can be distributed across different functional areas in the brain (Malsburg and Schneider, 1986; Singer and Gray, 1995). In the human electroencephalogram (EEG) induced gamma band responses (GBRs) are discussed as a signature of such a cell assembly (for reviews, see Tallon-Baudry and Bertrand, 1999; Keil *et al.*, 2001a). Furthermore, spectral power alone might be insufficient to measure synchronized activity within widespread neuronal networks. Therefore, others proposed phase synchrony analysis between recording sites to draw a more conclusive picture of network formation and re-activation (Miltner *et al.*, 1999; Rodriguez *et al.*, 1999).

By integrating the 'sharpening' idea (Desimone, 1996; Wiggs and Martin, 1998) and the hypothesis that gamma activity is a signature of a cortical object representation, we were able to show a reduction of GBRs and a decrease in phase-locking after the repetition of familiar objects (Gruber and Müller, 2002), which can not be explained by habituation (Gruber *et al.*, 2004). However, these two studies did not aim to examine repetition-by-stimulus type (familiar/unfamiliar) interactions. Consequently, present experiment was designed to replicate and extend our previous findings. In particular, based on the above-mentioned idea by Henson *et al.* (2000), we expected dissociable neuronal correlates of repetition priming after the repetition of unfamiliar as compared to familiar stimuli. The repetition of familiar stimuli should result in the sharpening of a pre-existing object representation. Due to spatial summation in macroscopical EEG recordings, we hypothesized that the activation of a sparser network should result in a reduction of induced gamma power and phase synchrony. In contrast, the repetition of unfamiliar stimuli should result in the formation of a new cortical object representation and, thus, to an increase of induced gamma power and phase synchrony. Furthermore, it was hypothesized that ERPs play a functionally different role in perception opposed to induced GBRs (Tallon-Baudry and Bertrand, 1999). Thus, we expected to find different morphologies of repetition effects in the ERP as compared to the high-frequency domain. To control for effects in other frequency bands, we have analysed oscillatory phenomena below 20 Hz as well.

Materials and Methods

Participants

Fourteen healthy, right-handed university students (eight female; aged 19–31 years, mean = 21.2 ± 0.8) received class credit for participation. All had normal or corrected-to-normal visual acuity. Informed consent was obtained from each participant. The study conformed with the Code of Ethics of the World Medical Association.

Stimuli and Procedure

Stimuli were 260 line drawings taken from the Snodgrass and Vandervart inventory (Snodgrass and Vanderwart, 1980) in their unfragmented version (familiar, meaningful line drawings). Unfamiliar, meaningless drawings were created by randomly distorting the original pictures until

they were not recognizable as concrete objects. The number of pixels in the distorted pictures matched the original drawings (see Fig. 1*I* for examples of the stimulus material).

Two experimental lists were created from the stimulus pool: 100 stimuli were randomly chosen from the 'meaningful' and 'meaningless' lists of drawings, respectively. If a stimulus was used for the meaningful list, its distorted version was not used for the meaningless list. Stimuli were presented in the centre of a 19″ computer screen placed 1.5 m in front of the subjects with a frame rate of 70 Hz. The line drawings covering a visual angle of ~4.5 × 5.2° were shown in white on a black background. Picture onset was synchronized to the vertical retrace of the monitor. Each trial consisted of a randomized 500–800 ms baseline period during which a fixation cross (0.3 × 0.3°) was presented, followed by a picture depicted for 700 ms. The stimulus was then replaced by the fixation cross which remained on screen for another 500 ms and was followed by a blank screen (1000 ms). Subjects were instructed to avoid eye movements and blinking during the display of the fixation cross or a stimulus.

Both meaningful and meaningless pictures were presented for three times, with one or two intervening items (see Fig. 1*I*). Participants were instructed to press a key for a meaningful stimulus, and another key for a meaningless stimulus. Key-to-task allocation was counterbalanced across participants. The number of intervening items (one or two) was randomized. The design resulted in six experimental conditions: familiar, meaningful picture presentations (FP) and unfamiliar, meaningless picture presentations (UP). These stimulus types were presented in randomized order and can be subdivided according to their position within the stream of pictures: initial presentation (FP1st and UP1st), second presentation (FP2nd and UP2nd) and a third presentation (FP3rd and UP3rd) as depicted in Figure 1. The experiment consisted of 600 trials, divided into three blocks of 200 trials each, in order to allow for resting intervals between blocks.

Data Analysis: Behavioural Data

Only reaction times between 200 and 1000 ms after stimulus onset were considered to be correct responses. Reaction times shorter or longer than that period were seen as false alarms or missed responses. Behavioural data was analysed by means of a repeated measurement ANOVA with the factors STIMULUS TYPE (FP versus UP) × POSITION (1st, 2nd, 3rd). A schematic graph ANOVA model is given in Figure 1*II*.

Electrophysiological Recordings

EEG was recorded continuously with an EGI (Electrical Geodesics) 128-electrode array, referenced to Cz (impedances <50 kΩ, sampling rate 500 Hz, 0.01–200 Hz bandpass). EEG was segmented to obtain epochs starting 500 ms prior to and 1500 ms following picture onset. Artifact correction was performed by means of 'statistical correction of artifacts in dense array studies' (SCADS; Junghöfer *et al.*, 2000). This procedure is widely accepted in the field and was applied and described in several publications (e.g. Gruber *et al.*, 1999; Keil *et al.*, 2001b; Müller and Keil, 2004). Using this approach, three subjects were excluded due to excessive artifacts. For the remaining 11 subjects the average rejection rate was ~20% resulting in ~80 remaining trials per condition. For further analysis the average reference was used, which, given our high spatial sampling, provides a good approximation of an inactive reference (Junghöfer *et al.*, 1999), preferable for phase-locking analysis described below.

Data Analysis: Induced and Evoked Spectral Changes

A given EEG-epoch can be modelled by the sum of the evoked response plus the trial-by-trial fluctuation around the mean (Priestley, 1988). Since the present analysis focused on non phase-locked oscillatory activity, the evoked reponse (i.e. the ERP) was subtracted from each trial (for a similar procedure, see also Müller *et al.*, 1996). Spectral changes in oscillatory activity were analysed by means of Morlet wavelet analysis, which has been proposed by Bertrand and Pantev (1994) and which provides a good compromise between time and frequency resolution (Tallon-Baudry and Bertrand, 1999). The method provides a time-varying magnitude of the signal in each frequency band, leading to a time by frequency (TF) representation of the signal. TF energy is averaged across single trials, allowing one to analyse non phase-locked components. To that end, complex Morlet wavelets g can be generated in the time domain for different analysis frequencies f_0 according to

$$g(t, f_0) = Ae^{-\frac{t^2}{2\sigma_t^2}} e^{2i\pi f_0 t} \quad (1)$$

with A' depending on the parameter σ_f, specifying the width of the wavelet in the frequency domain, the analysis frequency f_0 and the user-selected ratio m:

$$A = \sigma_f \sqrt{2\pi^3} \sqrt{\frac{m}{f_0\sqrt{\pi}}} \quad (2)$$

with

$$m = \frac{f_0}{\sigma_f} \quad (3)$$

and

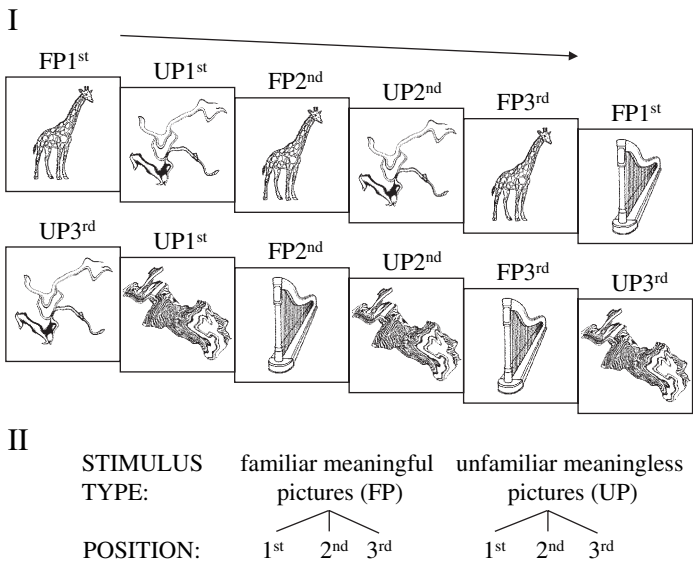

Figure 1. (*I*) Excerpt of stimulus sequence. Meaningful (familiar) and meaningless (unfamiliar) objects are presented for a first (FP1st and UP1st), a second (FP2nd and UP2nd) and a third time (FP3rd and UP3rd). (*II*) Repeated measurement ANOVA model used for statistical analysis.

$$\sigma_t = \frac{m}{2\pi f_0} \quad (4)$$

Thus, given a constant ratio m, the width of the wavelets in the frequency domain, σ_f, and in the time domain, σ_t, changes as a function of the analysis frequency f_0.

In order to achieve good time and frequency resolution in the gamma frequency range the wavelet family used is defined by a constant $m = f_0/\sigma_f = 7$, with f_0 ranging from 2.44 to 97.65 Hz in 0.49 Hz steps. Wavelets were normalized in order to have equal amounts of energy. For each epoch, time-varying energy in a given frequency band was calculated, this being the absolute value of the convolution of the signal with the wavelet for each epoch and each complex spectrum.

In order to identify the latency and frequency range of the induced gamma power peak, mean baseline-corrected spectral power (baseline 400–100 ms prior to stimulus onset) across posterior electrode sites (corresponding 10–20 positions: Cp1, CPz, Cp2, P1, P2, P3, Pz, P4, PO3, PO4, P7, P8, PO7, POz, PO8, O1, O2) was represented in separate TF-plots for each condition in the 30–90 Hz range. Electrode sites used for TF-plots were selected on the basis of previous findings regarding repetition picture priming (Gruber and Müller, 2002; Gruber *et al.*, 2004). For further statistical analysis a time window of maximal gamma power (220–350 ms after stimulus onset) and 36 electrode sites corresponding to the extended 10–20 system were analysed by means of a repeated measurement ANOVA with the factors STIMULUS TYPE (FP versus UP) × POSITION (1^{st}, 2^{nd}, 3^{rd}) × RECORDING SITE (36 electrodes). [The following 10–20 sites were used (approximated to the closest position on the electrode net): Fz, FC1, F3, F7, FC5, C3, T7, CP5, CP1, CPz, P7, P3, P1, PO7, PO3, Pz, P9, O1, POz, PO4, P2, CP2, Iz, O2, P4, PO8, P10, P8, CP6, C4, T8, FC2, FC6, F8, F4, and Cz).] Due to inter-individual differences in the gamma peak frequency, for each subject the wavelet designed for the frequency of his/her maximal power in the gamma range was chosen. To depict the topographical distributions of induced GBRs, in a subsequent step wavelet analysis was calculated for all 129 electrodes. Furthermore, the area showing maximal power was tested against baseline by means of one-group *t*-tests for each condition.

To control for effects in other frequency bands the above ANOVA model was applied to the induced theta (5–7 Hz, 100–700 ms), alpha (9–12 Hz, 200–800 ms) and beta ranges (15–20 Hz, 220–350 ms). TF-windows were chosen on the basis of TF-plots for bands below 20 Hz.

To verify that our findings were based on induced and not evoked gamma activity, the above ANOVA model was applied to the spectra of the averaged and unfiltered evoked response as well. Because visual inspection of TF-plots for the evoked gamma response revealed no clear peak in the frequency domain, the identical frequencies as identified for the induced response were used for statistical analysis. Furthermore, an evoked TF window at ~40 Hz and 70–180 ms after stimulus onset was analysed (for a similar procedure, see also Herrmann *et al.*, 1999). Evoked theta, alpha and beta activity was analysed in a time window from 100–300 ms after stimulus onset.

To exclude baseline differences between conditions as an alternative explanation for our results, we have tested all bands in the evoked and the induced frequency range by means of above ANOVA in a time window from 400 to 100 ms prior to stimulus onset.

Data Analysis: Phase-locking

Phase synchrony analysis was performed, elaborating on procedures suggested by Rodriguez *et al.* (1999) and Tallon-Baudry *et al.* (2001), which provides a method of measuring synchronous oscillatory activity independent of the signal's amplitude. For each subject, phase synchrony was computed for a narrow-band-filtered signal ($f_0 \pm 3$ Hz; see also Rodriguez *et al.*, 1999) for a distinct frequency f_0 of his/her maximal gamma activity. Phase was measured by convoluting the signal with a complex Morlet wavelet designed for f_0. A complex phase value ρ was then computed at frequency f_0, for each electrode, each time bin and each trial by dividing the result of the convolution by the magnitude of this result.

According to Tallon-Baudry *et al.* (2001), subsequently a phase-locking value was computed for each time-point t and trial j as:

$$\rho_{k,l} = \left| \frac{1}{N} \Sigma e^{i(\rho_{j,k}(t,f_0) - \rho_{j,l}(t,f_0))} \right| \quad (5)$$

where N is the number of trials and k and l are the index for the pair of electrodes to be compared. For the sake of data reduction, phase-locking values were computed only for a subset of the 128-channel set, corresponding to 36 electrode sites of the extended 10–20 system (see above); $\rho_{k,l}$ results in a real value between one (constant phase differences) and zero (random phase differences). These values were normalized by subtracting the mean value of the baseline period (black screen; 400–100 ms before stimulus onset) and dividing by the standard deviation of this time window (for a similar procedure, see Rodriguez *et al.*, 1999). To provide a topographical representation of phase locking values over individual pairs of electrodes in a distinct time window a statistical randomization technique was used. Time windows were chosen according to the peak of the induced GBRs. Furthermore, a non-overlapping time window before (70–200 ms) and after (370–500 ms) the gamma peak was analysed. Averaged phase synchrony for these time windows ($W_{k,l}$) between electrodes k and l were calculated. For each of these averages 200 values were analogously computed on shuffled data. Shuffling was done by randomizing the order of trials and calculating synchronies between events that were not recorded at the same time. The average $W_{k,l}$ was retained as statistically significant if it was greater than the maximum (synchrony) or less than the minimum (desynchrony) of the 200 shuffled values, therefore indicating a two-tailed probability value of $P = 0.01$. On a topographical template of the electrode layout any significant value $W_{k,l}$ was indicated by a line from electrode k to electrode l. Data of all subjects were pooled in the randomization test.

Data Analysis: Event Related Potential (ERP)

A 25 Hz low-pass filter was applied to the data before all ERP analysis. Based on previous findings regarding repetition priming (e.g. Rugg *et al.*, 1995) and the grand mean evoked potential (see Fig. 5), four ERP components were defined: two early components P1 (110–140 ms) and N1 (160–190 ms) and two late components L1 (230–370 ms) and L2 (380–490 ms). Mean amplitudes averaged across the respective time windows at 10–20 electrode sites were analysed using STIMULUS TYPE (FP versus UP) × POSITION (1^{st}, 2^{nd}, 3^{rd}) × RECORDING SITE (36 electrodes) repeated measurement ANOVAs. *Post hoc* comparisons were calculated for the three electrodes showing maximal amplitude differences between initial and repeated presentations.

Where appropriate, *P*-values were adjusted by Huynh–Feldt correction in all ANOVA models. *Post hoc* comparisons were calculated by means of paired *t*-tests. Means and standard errors (SE) are presented.

Results

Behavioural Data

Participant's correct responses were 96.2 ± 0.8%. The following reaction times were found: $FP1^{st}$, 515 ± 8 ms; $UP1^{st}$, 521 ± 9 ms; $FP2^{nd}$, 477 ± 5 ms; $UP2^{nd}$, 508 ± 8 ms; $FP3^{rd}$, 465 ± 7 ms; $UP3^{rd}$, 495 ± 7 ms. *Post hoc* tests, based on a significant STIMULUS TYPE × POSITION interaction [$F(2,20) = 20.3$, $P < 0.0001$], revealed that participants reacted significantly faster after the first picture repetition [$FP1^{st}$ versus $FP2^{nd}$, $t(10) = 9.0$, $P < 0.0001$; $UP1^{st}$ versus $UP2^{nd}$, $t(10) = 3.3$, $P < 0.01$] and the second picture repetition [$FP2^{nd}$ versus $FP3^{rd}$, $t(10) = 3.6$, $P < 0.01$; $UP2^{nd}$ versus $UP3^{rd}$, $t(10) = 7.7$, $P < 0.0001$]. No significant reaction time difference was found between initial familiar and unfamiliar stimulus presentations. Familiar drawings repeated for the first time resulted in faster reaction times as opposed to the first repetition of unfamiliar stimuli [$t(10) = -7.0$, $P < 0.0001$]. The same was true for second picture repetitions [$t(10) = -5.3$, $P < 0.001$].

Induced and Evoked Spectral Changes

Figure 2 depicts the baseline-corrected TF-plots for all experimental condition averaged across posterior electrode sites and 11 subjects.

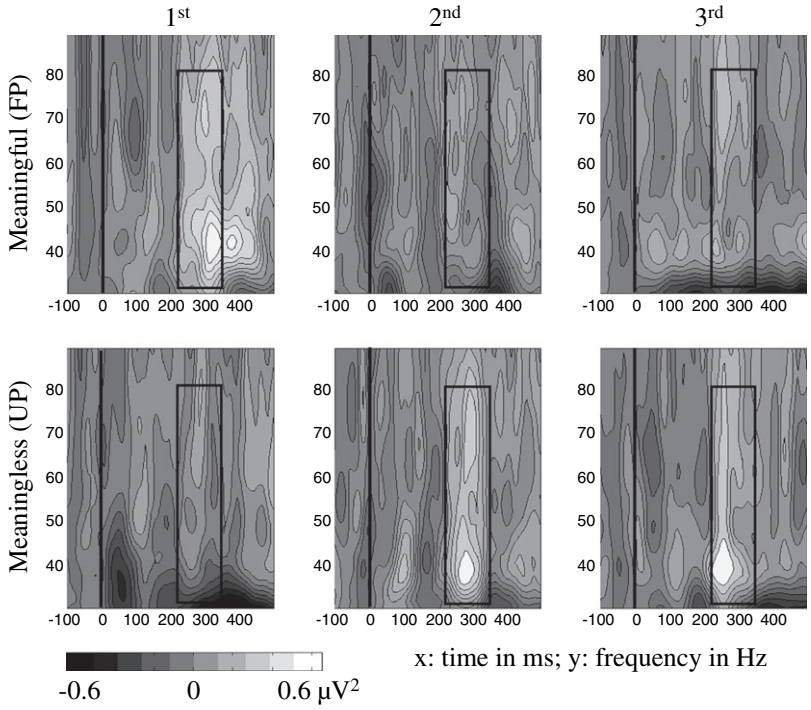

Figure 2. Grand mean baseline-corrected TF-plots averaged across posterior electrode sites (see text) for all experimental conditions.

Spectral power induced by initial familiar meaningful picture presentations showed a clear peak in a time window from ~220 to 350 ms after stimulus onset in a frequency range between 30 and 80 Hz. The same was true for repeated unfamiliar and meaningless items. Statistical analysis for each subject's maximal gamma activity resulted in a significant STIMULUS TYPE × POSITION interaction [$F(2,20) = 6.2$, $P < 0.01$]. No significant interaction with the factor RECORDING SITE was found. *Post hoc t*-test of averages across 36 electrode sites revealed a significant power decrease from first to second familiar, meaningful picture presentations [$t(10) = 2.6$, $P < 0.05$]. Furthermore, we found a significant increase in spectral power from first to second unfamiliar, meaningless picture presentations [$t(10) = -2.8$, $P < 0.05$]. No significant difference was found between second and third meaningful and meaningless drawings, respectively. Importantly, initial meaningful objects revealed higher gamma activity as compared to initial meaningless line drawings [$t(10) = 2.4$, $P < 0.05$].

Topographical distribution of induced gamma power for individual peak wavelets in a time window from 220 to 350 ms for the conditions FP1st and UP1st and averages across FP2nd; FP3rd and UP2nd; UP3rd are depicted in Figure 3.

Induced GBR showed a broad posterior scalp distribution. *Post hoc* tests of a regional mean covering this posterior area (around Cp1, CPz, Cp2, P1, P2, P3, Pz, P4, PO3, PO4, PO7, POz, PO8, O1, O2) revealed significant differences of spectral power from baseline for all three meaningful picture presentations [FP1st, $t(10) = 4.2$, $P < 0.01$; FP2nd, $t(10) = 2.4$, $P < 0.05$; FP3rd, $t(10) = 2.2$, $P = 0.05$]. Furthermore, gamma power induced by repeated unfamiliar stimuli differed significantly from baseline [UP2nd, $t(10) = 2.3$, $P = 0.01$; UP3rd, $t(10) = 2.6$, $P < 0.05$]. Initial unfamiliar items showed no significant increase from baseline.

With respect to evoked GBRs, the analysis revealed no significant effects. No significant effects in the induced and evoked theta, alpha and beta range were found. Furthermore, the tests for baseline differences between conditions revealed no significant effects.

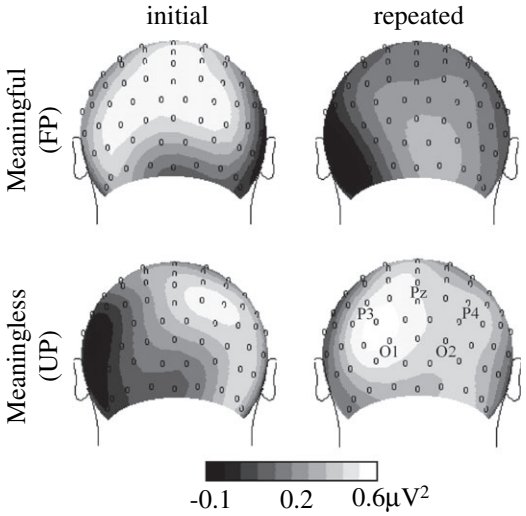

Figure 3. Grand mean spherical-spline isocontour power-maps based on the individual maximal power in the gamma range in the time window between 220 and 350 ms after stimulus onset. Topographies for repeated stimuli were obtained by averaging across second and third presentations.

Phase Locking

Figure 4 depicts the results of phase-locking analysis for initial presentations (FP1st and UP1st) and averages across repetitions of meaningful and meaningless stimuli, respectively. A line between two electrode sites is only drawn if the phase-locking value is beyond the distribution of randomized data ($P < 0.01$).

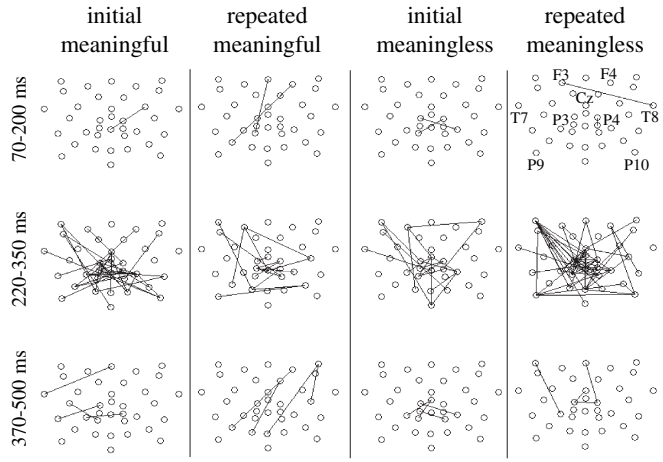

Figure 4. Phase-locking in the gamma band between 10 and 20 electrode pairs for initial and repeated picture presentations. Lines are drawn only if the phase-locking value is beyond the distribution of randomized data ($P < 0.01$).

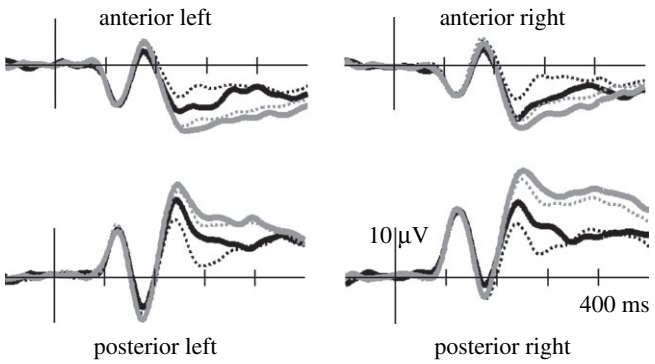

Figure 5. Grand mean baseline corrected ERPs for initial meaningful object presentation (bold black line), repeated meaningful object presentations (dotted black line), initial meaningless object presentation (bold gray line) and repeated meaningless object presentations (dotted gray line) at four regional means (corresponding 10–20 sites: anterior left = F7, F3, FC5, FC1, C3; anterior right = F8, F4, FC6, FC2, C4; posterior left = P7, P3, PO3, PO7, O1; posterior right = P8, P4, PO4, PO8, O2).

For initial familiar pictures the most dense formation of significant phase-locking values was found in the time window of 220–350 ms after stimulus onset predominantly among posterior but also temporal and frontal electrode sites. This indicates synchronous neuronal activity in a broadly distributed network. Less phase synchrony was observed for repeated meaningful items in the same time window. For meaningless line drawings this pattern of results was reversed. In the time window from 220 to 350 ms after stimulus onset more significant phase-locking values were found for repeated meaningless items as compared to initial meaningless stimuli. For both conditions the time windows 70–200 ms and 370–500 ms revealed only a minor number of significant phase-locking values. Thus, the time window of maximal increase of phase-locking was coincident with the spectral power peak.

Visual Event Related Potential (ERP)

Figure 5 depicts the ERPs of left/right posterior and anterior regional means (see figure legend for 10–20 sites) for initial familiar and unfamiliar items ($FP1^{st}$ and $UP1^{st}$) and averages across repeated familiar and unfamiliar stimuli, respectively.

We found no significant effects for the P1 and N1 components. The late component L1 (230–370 ms) revealed a significant STIMULUS TYPE × POSITION × ELECTRODE interaction [$F(70,700) = 2.1$, $P < 0.05$], reflecting a general reduction in amplitude for repeated familiar and unfamiliar stimuli (decreased positivity at posterior sites and decreased negativity at anterior sites). *Post hoc* tests for the three electrodes showing maximal amplitude differences between initial and repeated presentations (P3, PO7 and P8) revealed that the effect was maximal at parieto-occipital electrode sites [P3: $FP1^{st}$ versus $FP2^{nd}$, $t(10) = 2.2$, $P < 0.05$; $UP1^{st}$ versus $UP2^{nd}$, $t(10) = 2.2$, $P < 0.05$; PO7: $FP1^{st}$ versus $FP2^{nd}$, $t(10) = 4.9$, $P < 0.001$; $UP1^{st}$ versus $UP2^{nd}$, $t(10) = 3.8$, $P < 0.01$; P8: $FP1^{st}$ versus $FP2^{nd}$, $t(10) = 2.4$, $P < 0.05$; $UP1^{st}$ versus $UP2^{nd}$, $t(10) = 2.6$, $P < 0.05$]. No significant differences were found between second and third familiar and unfamiliar items, respectively. Furthermore, initial presentations of meaningless stimuli evoked significantly higher amplitudes as compared to initial meaningful pictures [P3: $t(10) = -2.4$, $P < 0.05$; PO7: $t(10) = -3.4$, $P < 0.01$; P8: $t(10) = -5.2$, $P < 0.001$].

The late component L2 (380–490 ms) resulted in a significant STIMULUS TYPE × POSITION interaction, reflecting mainly an increase in amplitude for repeated familiar drawings. However, *post hoc* tests revealed only a trend towards higher amplitudes for second as opposed to first familiar stimuli [$t(10) = -2.1$, $P = 0.07$]. No significant differences were found for the conditions $FP2^{nd}$ versus $FP3^{rd}$ nor between $UP2^{nd}$ versus $UP3^{rd}$.

Discussion

The present study was guided by three major hypotheses, as follows. (1) Induced GBRs are a physiological correlate of activity within a network related to cortical object representation (Tallon-Baudry and Bertrand, 1999). (2) Stimulus repetition leads to the 'sharpening' of such a network (Wiggs and Martin, 1998). (3) A prerequisite for the sharpening of a cortical network is a pre-existing object representation. Thus, repetition of unfamiliar stimuli leads to dissociable neuronal correlates of repetition priming as compared to familiar stimuli (Henson *et al.*, 2000).

After the first presentation of a familiar meaningful drawing, induced GBRs showed a topographically widespread increase above baseline level. Importantly, the augmentation of spectral power was accompanied by a dense pattern of significant phase-locking values between distant electrode sites. In line with hypothesis (1) and previous gamma studies (e.g. Rodriguez *et al.*, 1999; Gruber *et al.*, 2002) this increase in synchronous gamma power was significantly higher for (initial) meaningful as compared to meaningless stimulus presentations. Although, other studies reported interhemispheric alpha synchrony for meaningful opposed to meaningless picture presentations (e.g. Mima *et al.*, 2001), we found no effect in the alpha range, but rather parallel the findings of Rodriguez *et al.* (1999) and Gruber *et al.* (2002).

Replicating previous findings (Gruber and Müller, 2002; Gruber *et al.*, 2004), we found a decrease in induced gamma power and a marked reduction in electrode pairs exhibiting significant phase-locking values after the repeated presentation of the same meaningful line drawing. Based on the assumption that a neuronal assembly, which codes features of a stimulus, becomes sparser and more selective with repeated experience (Desimone, 1996; Wiggs and Martin, 1998), we interpret our findings as a physiological correlate of such a 'sharpening'

mechanism. Due to spatial summation in macroscopic EEG recordings, activity within a sparser network must result in a decrease of induced gamma band amplitude and a reduced number of electrode pairs exhibiting significant phase-locking. Importantly, no difference between second and third familiar picture presentation was found, and synchronized gamma activity after repeated stimulus presentation was still above baseline level. Evidently, the activity within a network related to a cortical object representation, although 'sharpened', cannot be suppressed completely.

In contrast to the repetition of familiar pictures, the repetition of unfamiliar and meaningless stimuli was accompanied by an increase in induced gamma power, and in the number of electrode pairs exhibiting significant phase-locking values. Theoretical considerations (Henson *et al.*, 2000) and previous gamma band findings during memory formation (Miltner *et al.*, 1999; Keil *et al.*, 2001b), suggest that the reported increase in synchronous gamma activity might be a correlate of encoding-related processes, i.e. the formation of a new cell assembly. The fact that we found no difference between the second and third repetition of a meaningless line drawings, indicates that suppression of the newly established network does not occur immediately. The question of how many repetitions are needed until an unfamiliar, meaningless stimulus becomes familiar and, thus, will underlie suppression phenomena is subject of future studies.

Regarding behavioral data we found speeded reaction times for repeated as compared to initial picture presentations. The same was true for the repetition of meaningless items. This suggests that not only repetition suppression in the gamma band is a neuronal correlate of the behavioral phenomenon 'repetition priming'. Under distinct stimulus conditions repetition enhancement in the gamma band might be linked to repetition priming.

Although our results in the induced high-frequency domain mirror previously reported repetition-by-stimulus type interactions as found for hemodynamic markers of brain activity (Henson *et al.*, 2000), it has to be mentioned, that other studies were not able to replicate these findings (e.g. van Turennout *et al.*, 2000; Vuilleumier *et al.*, 2002). A possible explanation for these discrepancies might be the fact that repetition effects are highly sensible to the subjects' task (Henson *et al.*, 2002). In particular, Turennout *et al.* used an object-naming task as opposed to the classification task in our study. Furthermore, in the study by Vuilleumier *et al.* relatively long-lag repetitions were used, which might explain the discrepancies. Although, we have analysed the influence of lag on gamma responses induced by primed familiar stimuli and found no significant effect (Gruber *et al.*, 2004), the influence of repetition lag on gamma responses induced by unfamiliar stimuli needs to be addressed in a follow-up study.

With respect to our stimulus material, it may be argued that even the distorted line drawings can be perceived without being recognized as concrete objects and, thus, require the integration of early visual areas. If our results would be due to mere perceptual integration, we would have expected similar suppression effects as found during the repetition of familiar pictures for 'meaningless' stimulus types. Most interestingly, such a pattern of results was found in the ERP: Repetition of familiar and unfamiliar stimuli leads to amplitude suppression in a time window from 230–370 ms after stimulus onset. Although other studies failed to find any significant repetition effects on ERP patterns with repetition of meaningless pictures (e.g. Zhang *et al.*, 1997), it was clearly present in our study. Analogous to previous picture priming studies (Rugg *et al.*, 1995; Gruber and Müller, 2002; Gruber *et al.*, 2004) the results in the ERP showed a topographically more distinct distribution around parieto-occipital electrode sites as compared to the topographically widespread distribution of our findings in the gamma band. We take present results as further evidence for the fact that ERPs play a functionally complementary role in stimulus processing as opposed to induced GBRs. The visual evoked response during repetition priming may reflect differences in the activity of more distinct repetition-sensitive brain structures (Rugg *et al.*, 1995), which are not affected by the associative stimulus content. Recently, it was suggested that ERPs reflect neuronal activity within discrete cortical areas, which are defined by characteristic functional properties, whereas induced cortical activity is seen as the neuronal activity, which integrates these areas (Müller and Keil, 2004). The fact, that we have found no significant effects in the induced and evoked lower frequency bands, nor in the evoked gamma range, points towards a functionally specific role of the induced gamma band range in the processing of associative stimulus content and the integration of various functional areas.

As mentioned above, several research groups have reported an increase in gamma power induced by a meaningful as compared to meaningless stimulus (e.g. Rodriguez *et al.*, 1999). Obviously, in these studies stimuli were repeated a large number of times. Reconciling present findings with data from the literature, one might ask why earlier studies did not result in gamma suppression for meaningful, and gamma enhancement for meaningless material? First, in most of the experiments comparing meaningful with meaningless objects, repetition priming was not part of the experimental design [different stimuli were used throughout the experiment in Rodriguez *et al.* (1999) and in Gruber *et al.* (2002)]. Secondly, studies in which the same stimulus was repeated during the study the large number of repetitions might have led to a familiarization of an unfamiliar stimulus and, thus, annulment of enhancement and suppression effects. Furthermore, in a number of gamma band studies stimuli yielded no substantial associative content (e.g. simple Kanizsa triangles as in Tallon-Baudry *et al.*, 1996) and, thus, might have engendered different mechanisms in the brain as opposed to our study.

A possible alternative explanation for the present findings might be, that initial compared to repeated picture presentations were attracting more attention. Indeed, induced GBRs are known to be modulated by attention (Gruber *et al.*, 1999; Müller *et al.*, 2000; Müller and Gruber, 2001). In order to control for these effects, we introduced a task, in which the occurrence of meaningful and meaningless stimuli was unpredictable. Thus, subjects had to pay the same amount of attention to every picture presentation. Given an average correct response rate of ~96% it is very unlikely that the attentional effort is reduced after the first presentation of a meaningful picture, or increased after the repetition of a meaningless items. In addition, we found no differences in the number of correct responses between the 'familiar' and 'unfamiliar' stimulus types.

In contrast to two previous repetition priming studies (Gruber and Müller, 2002; Gruber *et al.*, 2004), in the present experiment a motor response was necessary in each trial. Thus one might argue that our findings in the high-frequency domain are due to motor activation. However, the pattern of gamma

results does not markedly differ from our previous studies, in which no response was required. Furthermore, motor-related gamma activity was previously reported in a time window from 450 ms after stimulus onset onwards (Rodriguez *et al.*, 1999). Thus, we exclude an influence of motor related gamma activity on our results. Furthermore, we rule out the possible influence of muscle activity, because muscle activity would result in a maximum at electrode sites close to the neck, which was not the case. With regard to the influence of volume conduction on measurements of phase synchrony it was stated that volume conduction would lead to a diffusion in the measurement of synchrony (Lachaux *et al.*, 1999). We did not find such diffusion, i.e. synchrony between two distant electrode sites was not automatically accompanied by significant phase-locking of recording sites located between those two. Yet, it has to be mentioned that this rule of thumb is not a reliable test to identify conduction synchronies and cannot provide a complete solution to the problem.

In sum, the present experiment has several implications for the understanding of neuronal mechanisms underlying repetition priming. Induced GBRs showed a dissociable morphology depending on the associative content of stimulation material. We are aware that the 'sharpening' and 'formation' metaphors, which we have proposed to explain our results, might be too simplistic to describe complex processes in a highly interconnected neuronal network as the human brain. However, we believe that they offer a heuristic approach for future perceptual priming studies. This notion is underpinned by the fact that our findings in the high-frequency domain, but not in the ERP, show analogous properties to results from the imaging literature (Henson *et al.*, 2000). Furthermore, given that synchronized local field potentials are significantly correlated with the BOLD response (Logothetis *et al.*, 2001), the analysis of induced GBRs will be of benefit for the integration of electrophysiological and hemodynamic indices of brain activity.

Notes

Research was supported by grants from the Deutsche Forschungsgemeinschaft.

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