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Memory-matches evoke human gamma-responses

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Abstract

Background: Human brain activity in the gamma frequency range has been shown to be a correlate of numerous cognitive functions like attention, perception and memory access. More specifically, gamma activity has been found to be enhanced when stimuli are stored in or match with short-term memory (STM). We tested the hypothesis that gamma activity is also evoked when stimuli match representations in long-term-memory (LTM). EEG was recorded from 13 subjects performing a choice reaction task. Visual stimuli were either known real-world objects with a memory representation or novel configurations never seen before.

Results: All stimuli evoked an early gamma response which was maximal over occipital electrodes. This evoked gamma activity was significantly larger for items that matched memory templates.

Conclusions: Therefore, we argue that gamma activity results from the feedback from memory into perception systems. This assumption seems to be true for STM as well as LTM.

Background

Human and animal brain activity frequently shows oscillations in the gamma frequency range (approx. 30–80 Hz) [1,2]. This activity is either phase-locked to the stimulation (evoked activity) or not (induced activity) [3]. Irrespective of this phase-locking these oscillations have been shown to be correlates of numerous cognitive functions. Among the first functions to be associated with gamma activity was visual feature binding, coherent visual objects inducing more gamma oscillations than others [4,5]. Also tones evoke such gamma responses [6] and attention was associated with auditory gamma activity, attended tones evoking larger auditory gamma peaks than unattended ones [7]. In addition, it has been shown that object perception seems to be a crucial factor for the presence of gamma activity [8]. For example, faces induced more

gamma activity than rotated faces which were not recognizable [9] leading to more synchronization among brain areas within the gamma band [10]. In addition, gamma activity can be found when subjects suddenly see a meaningful picture in random-dot patterns (autostereoscopic pictures) [11]. Also the human ability of language has been associated with gamma activity: words evoke more gamma oscillations in human cortex than do pseudo-words [12] and language-related gamma activity is most prominent over the language-specific left hemisphere [13]. One mechanism which underlies many of these cognitive functions is access to memory. It has been demonstrated that access to working memory induces gamma activity: when subjects have to actively maintain visual stimuli in working memory the stimuli induced more gamma oscillations as compared to not memorizing them

[14]). Also other studies have positively correlated gamma activity with learning and memory [15-18].

In addition, personal variables like the inter-individual arousal levels of subjects are also reflected in evoked gamma activity [19]. It has even been argued that human gamma activity may be a correlate of consciousness, since it was found to be higher during waking and REM sleep than during deep sleep [20] and anaesthesia [21]. Recently, it has been demonstrated that also the IQ scores of subjects correlate with the amount of gamma activity which is evoked by auditory stimuli [22].

In a series of previous experiments we tried to reveal which of the mentioned cognitive functions are more important for human gamma activity and which others might be less important. We used four different stimuli to directly contrast visual feature binding and attention. Two of the stimuli were Kanizsa figures for which the constituting parts can be bound together while for the remaining two stimuli this was not possible. One out of the four stimuli was defined as a target and had to be detected. The experiment revealed that the attended target evoked significantly more gamma oscillations as compared to three the standards [23]. Even when stimuli were used as targets which consisted of features that could not be bound together to coherent objects those targets evoked larger gamma responses than non-target stimuli which could be bound together [24]. This indicated that attention towards a target stimulus is more important for the modulation of gamma activity than the feature binding required to bind together coherent objects. Of course, target detection also requires access to working memory. Every stimulus has to be compared to a template of the target which was previously stored in short-term memory. Therefore, in a subsequent experiment, we explicitly tested whether comparing stimuli to memory templates increased gamma activity. When subjects had to identify targets by discriminating multiple stimulus features via comparison with a template in short-term memory (STM) all stimuli evoked significantly more gamma activity than stimuli which could be discriminated by a single feature (their color) [25]. We recently obtained similar results for auditory stimuli depending on whether targets match a template in working memory or whether novel stimuli do not match [26]. Targets evoked significantly more gamma oscillations than novel stimuli even though both types of stimuli attract attention and evoke strong P3 components in human EEG. This lead us to the hypothesis that memory access may be crucial for the generation of gamma activity. It might be assumed that not only acces to STM but also to long-term-memory (LTM) shows a similar effect. Thus, we set out to test whether access to LTM modulates human gamma responses. We investigated whether simple visual stimuli evoke more gamma activity when

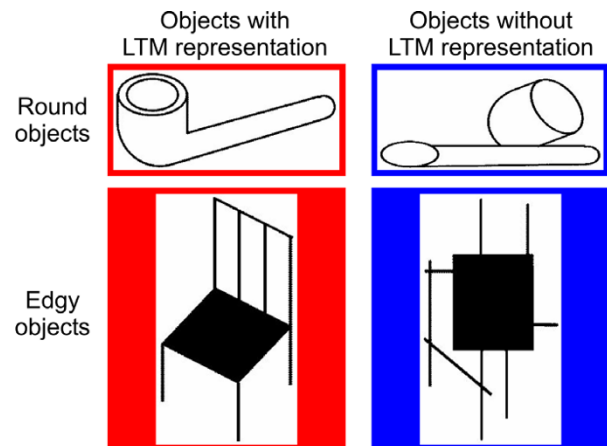


Figure 1
Examples of the stimuli used in the experiment. Two objects with a representation in LTM (red) and the corresponding non-objects which are composed of the same parts but have no such representation in LTM (blue). Subjects were to differentiate round (top row) from edgy figures (bottom row) in order to keep the results free of confounds through their responses.

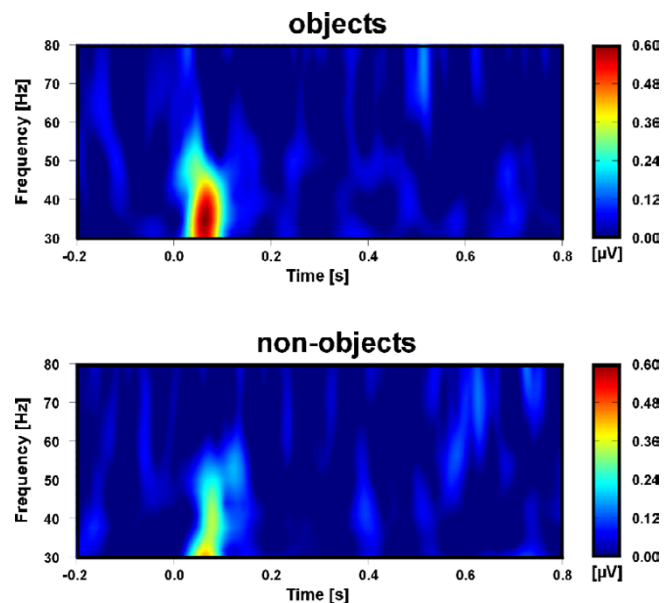


Figure 2
Average time-frequency representation of the EEG activity at electrode O2 (averaged across all 13 subjects). A clear peak of evoked gamma activity is visible shortly before 100 ms in the frequency range of 30 to 40 Hz. This peak is significantly stronger for objects (top) than non-objects (bottom).

subjects already have a memory representation of the presented objects as compared to when they perceive novel visual stimuli which do not match LTM. Indeed, stimuli for which subjects already had a representation in their LTM evoked significantly larger gamma responses.

Results

We recorded EEG from 13 healthy subjects while they perceived figural stimuli on a computer monitor. The stimulus material consisted of two different types of black and white drawings (210 total). The first type of figures were line drawings of objects for which subjects already had a representation in LTM because they were well-known real-world objects. The second type of stimuli were non-objects. In order to keep the two stimulus types comparable, the non-objects were composed of the same components as the objects but were newly arranged. Thus, each non-object stimulus comprised the parts of one object stimulus (cf. Fig 1). Subjects were instructed to judge whether the stimuli appeared to be either edgy or curvy by pressing one of two buttons (right index finger for edgy, left for curvy objects). Thus, subjects were naive about the purpose of the experiment. This was important, since we did not want subjects to be influenced by the stimulus type which we investigated.

An ANOVA comparing the reaction times in response to edgy versus round objects yielded a significant main effect

($F_{(1,12)} = 10.7, p < 0.05$). Responses to edgy objects were faster (557 ms) than to round objects (591 ms) due to the fact that subjects responded with their dominant right hand to edgy objects while they responded to curvy objects with their left hand. No significant differences were found comparing reaction times in response to objects versus non-objects. This indicates that responses to objects versus non-objects were not influenced by the task or the response hand.

The EEG was convolved with Morlet wavelets in order to compute the gamma activity evoked by each stimulation condition. The grand-average of the time-frequency representations of all subjects revealed a clear peak of evoked gamma activity (cf. Fig. 2). As revealed in Fig. 3 frequency and amplitude of this response vary across subjects. Fig. 4 shows the time course of the averaged gamma response. It is maximal around 70 ms after stimulus onset.

An ANOVA comparing the gamma responses evoked by objects versus non-objects yielded a significant main effect ($F_{(1,12)} = 5.171, p < 0.05$). In order to exclude the possibility that the 4 subjects with no clear gamma peak might have biased our results, we repeated the analysis with the remaining 9 subjects. The effect remains almost identical, objects evoking larger gamma responses than non-objects ($F_{(1,8)} = 5.59, p < 0.05$).

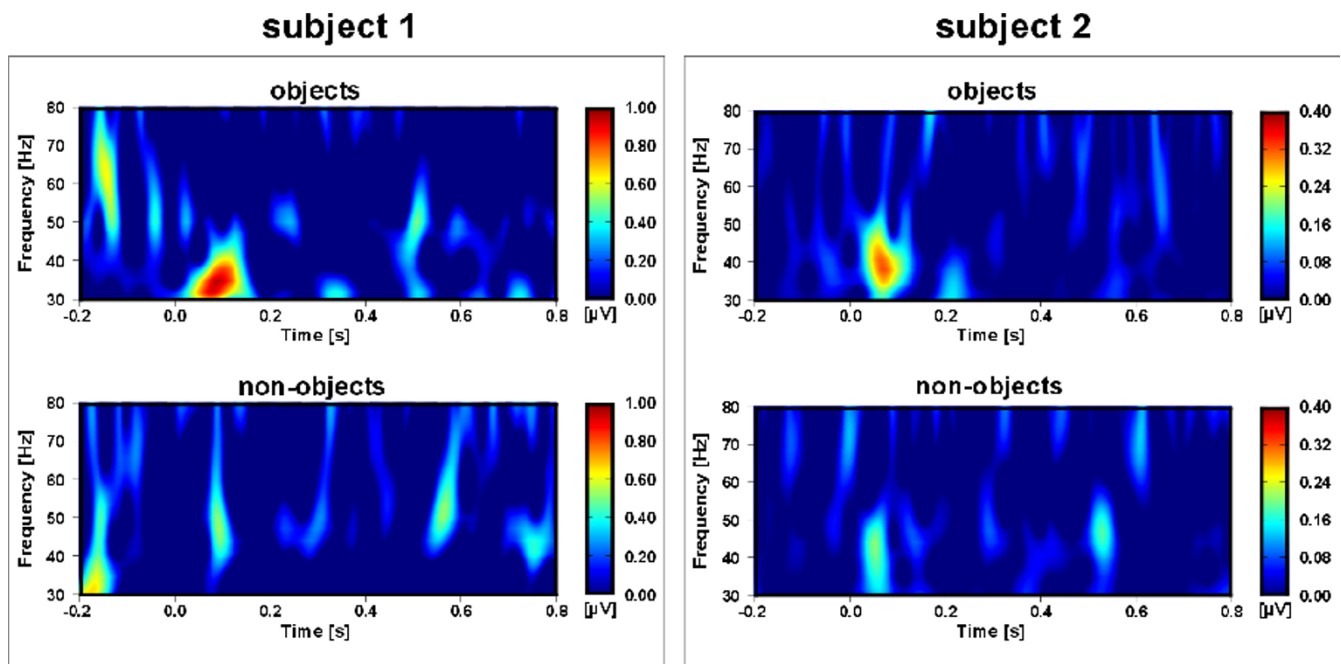


Figure 3 Individual time-frequency representations of the EEG activity at electrode O2 for two subjects. The plots reveal different amplitudes and frequencies of the evoked gamma response (subject 1: 35 Hz, subject 2: 40 Hz). Both subjects show a stronger activation for objects than non-objects.

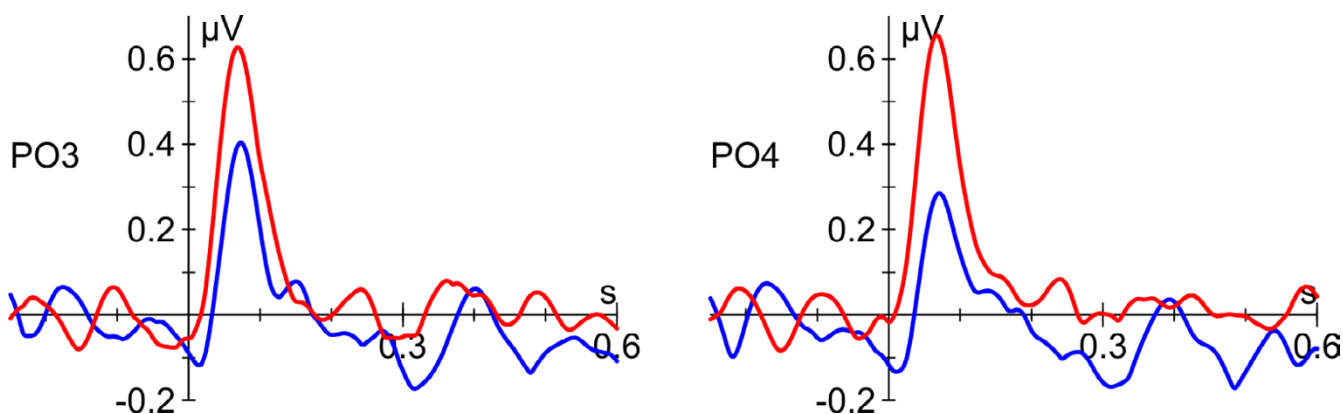


Figure 4

The evoked peak of gamma activity shows a clear difference between known objects (red) and non-objects (blue).

No significant main effect was found comparing edge versus round objects ($F_{(1,12)} = 0.861$, $p = 0.372$). Thus, objects for which subjects already have a representation in LTM evoke significantly more gamma activity than do non-objects which are perceived for the first time and have no such representation.

The topographic maps of the evoked gamma peak demonstrate that the amplitude is largest over occipital cortex indicating that the activity stems from visual brain areas (cf. Fig. 5).

Discussion

Our data show that visual stimuli evoke enhanced gamma responses if they match with contents of LTM. We assume that feedback loops from the memory system to perception mechanisms are responsible for this phenomenon. It has been demonstrated that neurons in medial temporal cortex fire in synchrony and at approx. 40 Hz when stimuli are subsequently remembered [18]. In our experiment the topography of the gamma oscillations was over occipital areas indicating that they were generated by neurons of visual cortex. However, since stimuli for which subjects had a memory representation evoked larger oscillatory responses, we argue that the feedback from memory systems enhances gamma activity in visual areas. The memory processes which modulate the visual gamma response seem to not elicit gamma activity themselves, since only occipital responses were found. Such memory processes would, however, be expected to reside in frontal or temporal cortex where no gamma activity was found. A similar phenomenon has been observed for event-related potentials (ERPs). Patients with frontal lobe damage show altered early auditory and visual ERPs which indicates that frontal cortex modulates temporal and occipital cortex in

the generation of electrophysiological responses [27,28]. However, no frontal ERP component has been identified which represents this modulatory process.

The notion that memory access modulates human gamma responses is supported by a great number of experimental findings on evoked gamma activity in the human EEG. For instance, words probably evoke more gamma activity as compared to pseudo-words [12] because we have memory representations of words but not of pseudo-words. Language-specific gamma activity could be lateralized to the left hemisphere [13] since the mental lexicon where words are stored resides in the left hemisphere. Attended objects reach STM more easily than unattended ones and thus lead to more gamma oscillations [7]. A target is defined by matching a template stored in STM for all criteria while a standard stimulus will represent a mismatch for at least one criterion. Thus, auditory as well as visual target stimuli receive more positive feedback from STM than standards [23,24,29].

Due to the similar topographical distributions of our evoked response and induced gamma responses [14,17], it seems plausible to assume that evoked and induced gamma activity are generated by the same neural systems only varying in their degree of phase-locking. Under this assumption our memory-explanation might even hold for the induced gamma band responses. We would argue that objects induce more gamma activity than non-objects [30] because we have only objects stored in LTM but no non-objects. This is not to claim that gamma activity is not related to binding processes. Our main argumentation is that a memory comparison must occur in order to initiate a binding process in case of a match. The same would be true for faces versus rotated faces [9] and meaningful pic-

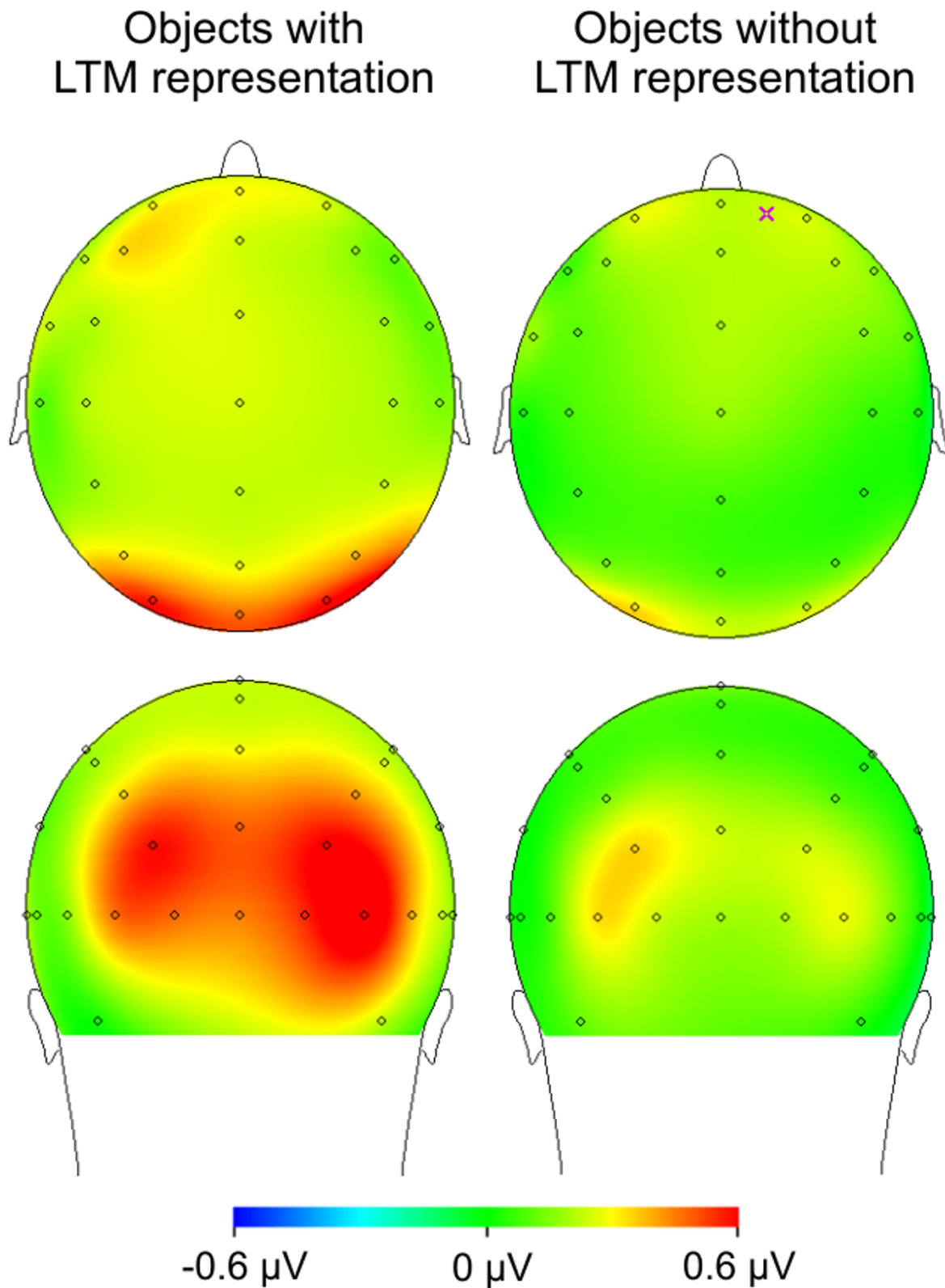


Figure 5
The difference between objects and non-objects is also clearly visible in the topographic maps. The bilateral occipital distribution indicates that the gamma activity results from extrastriate visual cortices.

tures versus random-dot patterns [11]. However, it is probably not the aspect of meaningfulness per se that enhances early gamma band activity. In the experiment by Debener et al target tones evoked more gamma activity than novel stimuli. In this experiment targets were simple sine waves while novels were real world (meaningful) sounds. Thus, the effect should have been reversed if meaningful stimuli should evoke more gamma activity. Also, behavioral relevance is probably not a crucial factor involved in the modulation of gamma activity. In the present study the factor of interest (memory vs. non-memory) was totally irrelevant for the subjects' task.

Even the notion that gamma activity might reflect aspects of consciousness [20,21] is supported by our data: During conscious states we always compare every perception to the contents of LTM [31] which yields the observed gamma activity. During unconscious states of sleep or anaesthesia this comparison is no longer carried out.

Conclusions

Taken together, we propose that gamma activity is modulated by access to STM and LTM. When perceived stimuli match with existing representations in STM or LTM they evoke larger gamma responses as if there were no existing representations. Of course also other cognitive processes without explicit memory access may modulate human gamma activity. It is known, for example, that task difficulty [32] and the speed of manual reaction [33] covary with gamma activity. Multiple modulatory mechanisms of gamma responses are very probable, since multiple oscillatory responses can be found in the human EEG at different frequencies in the gamma range with different topographies and time-courses.

Methods

Subjects

13 subjects (7 female) with a mean age of 25.4 (± 4.6) years participated in our experiment. All subjects had normal or corrected-to-normal vision and showed no signs of any neurologic or psychiatric disorder. They gave their written informed consent and were paid for their attendance. The experiment was conducted in line with local ethics guidelines.

Apparatus and stimuli

In order to avoid electrical interferences during our measurement, the experiment was performed in a specially shielded cabin, where no electric devices requiring AC power supply were operated. Therefore, the visual stimulation was provided by a Sony VPL X600E VGA projector which projects the stimuli into the cabin via a system of mirrors. The projection plane was placed 60 centimeters in front of the subjects.

Before the actual experiment, we performed a pre-experiment with another 10 subjects to select the stimuli and to ensure that each stimulus is consistently perceived as a known object or an unknown non-object. Only those stimulus-pairs were used, for which both figures were judged correctly as objects and non-objects, respectively, by more than 7 subjects. On average this yielded classification rates of 95% and 94% for objects and non-objects, respectively. Objects and non-objects were matched for size and subtended visual angles of 5° to 10°. Sample stimuli are presented in Fig. 1.

The experiment was divided into one short practice block and 2 experimental blocks, each separated by a brief pause. The practice block contained 18 figures with 9 figures of each stimulus type. The experimental blocks included the remaining 192 figures (96 objects and 96 non-objects). The temporal sequence of stimuli was pseudo-randomized and equal for each subject. Each figure was shown for 1000 ms, followed by a randomized interstimulus interval of 1300 to 1700 ms in which a black fixation cross was shown.

Procedure

Before the experiment, all subjects received a written instruction on the projection screen explaining their task. Subjects were instructed to judge whether the stimuli appeared to be either edgy or curvy by pressing one of two buttons (right index finger for edgy, left for curvy objects). Thus, subjects were naive about the purpose of the experiment. At the end of the experiment all subjects received a questionnaire to inquire some demographic data and information about possible strategies used.

EEG recording

EEG was recorded with 52 Ag-AgCl electrodes mounted in an elastic cap according to the international 10-10 system. All electrodes were referenced to the left mastoid and the ground electrode was placed at the right mastoid. The vertical electrooculogram (VEOG) was recorded by electrodes placed above and below the right eye, while the horizontal EOG (HEOG) was recorded from positions at the outer canthus of each eye. Electrode impedances were kept below 5 kOhm. Both EEG and EOG data were analog-filtered to accept signals in the range of DC to 100 Hz. EEG was sampled at 508.63 Hz.

Data analysis

An automatic artefact rejection was computed which excluded trials from averaging if the standard deviation within a moving 200 ms time interval exceeded 50 μV . Event-related potentials were averaged from -250 to +1000 ms relative to stimulus onset. Before averaging, baseline-activity from -250 to -100 ms was subtracted for each electrode. In order to analyze gamma activity a wave-

let transform was applied [23]. The frequency used for this wavelet analysis was individually adapted via the time-frequency plane of the O2 electrode: The individual gamma frequency was defined as the highest peak in response to objects in a frequency range of 30 to 80 Hz and in a time range of 50 to 150 ms as has been done in previous studies [32]. Resulting individual frequencies ranged from 31 Hz to 40 Hz. If no clear peak was visible in the gamma-range, 40 Hz was chosen for analysis. This had to be done for four subjects. After computation of the wavelet transform the baseline activity in the time interval from -250 to -100 ms was subtracted for each frequency. In order to avoid a loss of statistical power that is inherent when repeated measures ANOVAs are used to quantify multi-channel EEG data electrodes had to be pooled to regions of interest [23]. Since visual stimulation usually evokes gamma responses over parieto-occipital electrodes, we defined a region of interest comprising the following eight electrodes where strong gamma responses occurred: PO7, PO3, O1, POZ, OZ, PO4, O2, and PO8. For statistical analysis we performed a repeated measures ANOVA to compare the evoked gamma band activity between objects and non-objects in the time-interval between 50 and 80 ms. To verify whether subject's reactions had an influence, we performed another ANOVA comparing curvy and edgy stimuli.

Authors' contributions

CSH has designed the experiment and drafted the manuscript. DL and SJ have programmed the experimental stimulation and ran the analyses. NAB helped with the analyses and drafting of the manuscript. BM carried out the recording of the data and helped during analyses. All authors have read and approved the final manuscript.

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