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Does visual flicker-phase at gamma frequency modulate neural signal propagation and stimulus selection?

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Abstract

Oscillatory synchronization of neuronal populations has been proposed to play a role in perceptual integration and attentional processing. However, some conflicting evidence has been found with respect to its causal relevance for sensory processing, particularly when using flickering visual stimuli with the aim of driving oscillations. We tested psychophysically whether the relative phase of gamma frequency flicker (60 Hz) between stimuli modulates well-known facilitatory lateral interactions between collinear Gabor patches (Experiment 1), or crowding of a peripheral target by irrelevant distractors (Experiment 2). Experiment 1 assessed the impact of suprathreshold Gabor flankers on detection of a near-threshold central Gabor target ('Lateral interactions paradigm'). The flanking stimuli could flicker either in phase or in antiphase with each other. The typical facilitation of target detection was found with collinear flankers, but this was unaffected by flicker phase. Experiment 2 employed a 'crowding' paradigm, where orientation discrimination of a peripheral target Gabor patch is disrupted when surrounded by irrelevant distractors. We found the usual crowding effect, which declined with spatial separation, but this was unaffected by relative flicker-phase between target and distractors at all separations. These results imply that externally driven manipulations of gamma-frequency-phase cannot modulate perceptual integration in vision.

Introduction

Oscillatory synchrony in the brain has been shown to undergo significant changes during visual processing (e.g. Eckhorn et al., 1988; Gray, Konig, Engel & Singer, 1989) and during various tasks (Jensen, Kaiser & Lachaux, 2007). Neuronal synchrony has been proposed to play a role in mediating contextual interactions among local stimulus attributes (Eckhorn 1994, Singer 1999, Tallon-Baudry & Bertrand, 1999), and in selective attentional processing (Gruber, Muller, Keil & Elbert, 1999; Bauer, Oostenveld, Peeters, Fries, 2006; Womelsdorf & Fries 2007). Mechanistically, local synchrony among neuronal populations may enhance the impact of signals on downstream targets through more effective summation at postsynaptic neurons (Salinas & Sejnowski, 2001). The role of selective *phase* synchronization between neuronal populations involved in stimulus processing has initially been emphasized in the original 'binding-by-synchrony' hypothesis (Singer, 1999) but also more recently by Fries (2005) to selectively strengthen the effective connectivity between different neuronal populations. Computational studies have demonstrated that oscillatory dynamics can modulate network responses to inputs (Borgers, Epstein & Kopell, 2008; Zeitler, Fries & Gielen, 2008), and can in principle accurately and selectively control the gain of signal flow between networks (Akam & Kullmann 2010).

However, much evidence for the functional importance of gamma oscillations (40-100 Hz) in visual processing is correlational (e.g., Tallon-Baudry & Bertrand, 1999), and the topic remains controversial (Lamme & Spekreijse, 1998; Shadlen & Movshon, 1999; Thiele & Stoner, 2003). One approach to directly testing the causal significance of oscillatory synchronisation in visual processing is to measure the effect on perception of perturbing patterns of oscillatory activity. Visual flicker offers a potential means to do this in humans as it profoundly affects EEG and MEG response (Cosmelli et al., 2004; Srinivasan, Russell, Edelman & Tononi, 1999; Kamphuisen, Bauer & van Ee, 2008; Müller, Malinowski, Gruber & Hillyard, 2003). Neurophysiological studies have shown that displays flickering with frequencies up to approximately 100 Hz reliably entrain activity in early visual cortex (Rager & Singer 1998; Herrmann 2001; Williams, Mechler, Gordon, Shapley & Hawken, 2004).

Several studies have addressed the effects of putative gamma-frequency entrainment by flicker on perception (Fahle & Koch, 1995; Kiper, Gegenfurtner & Movshon, 1996; Leonards, Singer, & Fahle, 1996; Usher & Donnelly, 1998; Elliott & Muller, 2000; Dakin & Bex, 2002). A recent report by Frank Bauer and colleagues (Bauer, Cheadle, Parton, Muller & Usher, 2009) argued that gamma-frequency flicker in particular can enhance stimulus saliency, in accord with some of the theoretical emphasis placed on this frequency band for vision (Salinas & Sejnowski, 2001; Womelsdorf & Fries, 2007). However, for studies that compare flickering to non-flickering stimuli, or to flicker at other frequencies, potential stimulus confounds might arise to explain the results (e.g.van Diepen, Born, Souto, Gauch, & Kerzel, 2010).

Here we set out to manipulate specifically the *phase* between stimuli that flickered at 60 Hz (the typical frequency for human visual gamma oscillations, Hoogenboom, Schoffelen, Oostenveld, Parkes & Fries, 2006) to test theimpact of phase synchrony on the effective summation of oscillatory signals at postsynaptic sites on the one hand and on the functional segregation of different processing streams on the other hand. We studied these questions using two well-established visual psychophysical paradigms, which measure of the perceptual interaction between task-irrelevant stimuli and a separate target stimulus.

Several previous reports have also tested the impact of phase-manipulation on contextual integration (e.g. Fahle & Koch, 1995; Kiper, Gegenfurtner & Movshon, 1996; Leonards, Singer, & Fahle, 1996; Kiper, Gegenfurtner & Movshon, 1996; Usher & Donnelly, 1998) but with a different theoretical emphasis. These studies manipulated phase between different figure parts to test the binding by synchrony hypothesis by having the subjects making judgements on stimuli that were explicitly defined by their relation to other context stimuli. Our study differs from these approaches theoretically in that we set out to test two different theoretical accounts on the role of neuronal synchronization: namely the hypothesis that local synchrony affects effective summation of postsynaptic potentials (experiment 1), and the hypothesis that selective synchronization facilitates attentional selection of different processing streams (experiment 2). On a more operational level, in our experiments the context stimuli (distractors or flankers) were completely task irrelevant and the subject only needed to make a judgement on the target stimulus itself, independent of the status of the contextual flanker stimuli. Experiment 1 employed the ‘lateral interactions’ paradigm, whereby collinear flanking Gabor patches usually enhance detection of a nearby central target (Polat & Sagi,1993; Polat & Sagi, 1994; Freeman, Sagi, & Driver, 2001). This experiment tested the idea that manipulations of the phase synchrony of local inputs at gamma-frequencies could modulate their impact on postsynaptic neurons (Salinas & Sejnowski, 2001). The collinear facilitation effect is thought to be mediated predominantly by lateral connections in early visual cortex from neuronal populations representing the flankers to those representing the target (De Weerd, 2006). We hypothesized that facilitation of a *static* target by collinear flankers was greater in the context of flankers which were flickering at 60 Hz in phase with each other due to the imposed synchronous oscillations compared to when these flankers were flickered in antiphase to each other. The central target itself did not flicker because we wanted to test the impact of synchronous versus asynchronous entrained flanker oscillations on the target, under identical stimulation conditions for the latter. Flickering only the flanker stimuli at 60 Hz (presented equidistant to target position) implies that in-phase (versus antiphase) flicker of the flankers would result in synchronous (versus asynchronous) oscillatory inputs to the target population from both flankers via lateral interactions. If entrained synchronous rhythmic activity can enhance the efficacy of driving postsynaptic neurons, then the flanker effect on target detection should be more pronounced (benefiting central target detection more) for flankers that flicker in phase-synchrony, than for the case where they are flickered out-of-phase.

In Experiment 2 we utilized a ‘crowding’ paradigm, where judgements of a peripheral target are typically impeded by the presence of nearby distractors (Pelli, 2008). Here we tested whether the desynchronization of activity related to target and distractor populations could result in improved selective processing of the target and distractors (Fries 2005, Womelsdorf & Fries 2007). Therefore, in this experiment target and distractor stimuli were flickered and their relative phase was manipulated (in-phase or in anti-phase). We hypothesised that anti-phase flicker between flankers and target would improve selective processing of the target, thus counteracting crowding, while in-phase flickering would enhance crowding. Hence, in this experiment the rationale was not to test for differential propagation effects from the distractor (representing) population to the target (representing) population, but to test for the effect of desynchronizing activity in target and distractor-populations particularly on downstream processing stages (Womelsdorf & Fries 2007).

Methods

Experiment 1: Flicker phase and target detection

Subjects had to judge which of two presentation intervals contained a near-threshold central grating that could be surrounded by either collinear or orthogonal gratings. Previous research (Polat & Sagi, 1993; Polat & Sagi, 1994; Freeman, Sagi & Driver, 2001) had shown that target detection benefitted from the presence of collinear gratings. Here we added the further manipulation of flicker-phase.

<u>Participants</u>

Fourteen adult participants had normal or corrected to normal visual acuity. Eleven were paid for participation and were naïve to the purpose of the experiment. The others were some of the present authors but their results did not differ qualitatively. All subjects had undergone four practice blocks (of 45 trials each) involving the central target detection task (see below) prior to the experimental sessions, to estimate contrast thresholds. A total of twelve subjects participated in three separate sessions each; two individuals were excluded earlier due to chance performance in initial sessions, leaving N = 12.

<u>Stimuli</u>

The stimuli comprised localized gray-level Gabor patches, i.e. small sinusoidal gratings within a Gaussian contrast window. The standard deviation of the Gaussian envelope (σ) was equal to the wavelength (λ) of the carrier. Here $\lambda = \sigma = 0.439$ degrees of visual angle, with a spatial frequency of 2.28 cycles per degree. Stimuli were presented on a linearised 19-inch CRT monitor, using ‘colour bit-stealing’ to achieve up to 12 bit gray-level resolution (Tyler, 1997). The effective size of the monitor was 40.5 x 32.4 cm. The video mode was 1280 x 1024 pixels with a vertical refresh rate of 120 Hz, and the background luminance was 53 cdm^{-2} (mid-gray). The viewing distance was 65cm, in a darkened room.

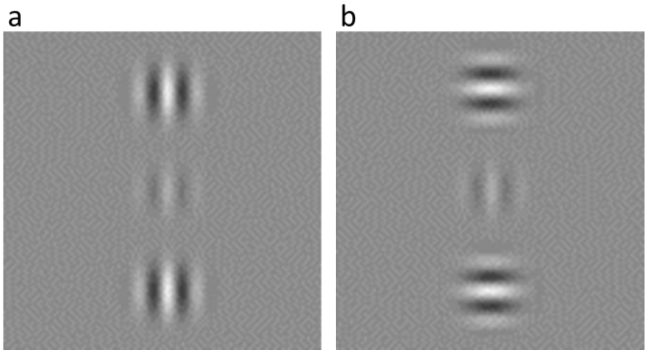

Figure1: Stimulus displays for experiment 1

Static snapshots of stimulus displays consisting of a central low-contrast Gabor target and two high-contrast peripheral flankers. **(a)** collinear flanker-to-target configuration. **(b)** orthogonal flanker-to-target configuration. The two flankers could flicker at 60Hz, either in- or out-of-phase with each other.

Stimulus displays comprised a low-contrast Gabor target centred at fixation, plus two high-contrast (60% Michelson contrast) Gabor flankers (Figure 1). The contrast of the target varied over a range of levels. We ran the first six participants on seven contrast levels, logarithmically spaced between 0.05% - 2%. We then dropped the lowest two contrast levels (due to poor performance on them) for subsequent participants, to give 5 levels logarithmically spaced between 0.17% and 2%. The target stimulus was a vertical Gabor located at screen centre, surrounded by two flankers arranged along the vertical axis (see Fig 1). The flanker-to-target distance was set to 3λ. While the orientation of the central target was held constant, the flanker orientations varied over experimental conditions. The flankers were both either oriented vertically (thus collinear with the central target, Fig. 1a) or horizontally (orthogonal configuration, Fig 1b). The collinear condition was expected to facilitate detection of the lower-contrast central target, to produce the usual facilitation effect (Polat & Sagi, 1994). The novel flanker manipulations here concerned changes in flicker-phase between the two *flankers* on each trial. Both flanker patches flickered either in phase, or in antiphase (with a 180-degree phase shift) to each other, at a modulation frequency of 60Hz. Hence, this experiment manipulated phase between the two flankers, rather than between flankers and target, while the central target itself remained static (redrawn on every screen refresh cycle, as usual for non-flickered stimuli). Static flankers were also used in Experiment 1 as a further baseline, to provide the standard conditions for the lateral interactions paradigm.

Experimental Design

The 2 x 3 repeated-measures factorial design had two flanker-to-target configurations (collinear, orthogonal) crossed with three flanker-flicker possibilities (both flankers flicker in-phase with each other; or out-of-phase with each other; or both flankers are static with no flicker), resulting in four flickering experimental conditions (in-phase-flicker orthogonal flankers; out-of-phase-flicker orthogonal flankers; in-phase-flicker collinear flankers; out-of-phase-flicker collinear flankers) plus two baseline conditions (static orthogonal flankers, static collinear flankers). All six conditions were equiprobable, with each blocked in random order. If in-phase flicker at 60 Hz does modulate perceptual integration, then the central target detection should benefit more from in-phase flankers than from antiphase flankers.

Procedure

Each 90 minute experimental session contained 35 blocks of 45 trials. Target contrast was varied pseudorandomly and unpredictably between trials. Observers were trained to detect a low-contrast Gabor target flanked by two high-contrast Gabor masks in a two-interval forced-choice (2AFC) task. Each trial comprised two successive displays, with identical flankers, but with a central target present in only one of these displays, equiprobably the first or second; see Figure 2 for an example of a trial sequence.

Each trial was preceded by a fixation display comprising a high-contrast central cross, with peripheral markers forming the corners of a square centred on the fixation point with side length of 2λ. This fixation display demarcated the area of the screen at which a central target stimulus could appear. The fixation display was followed by a stimulus sequence. After the fixation display was presented, the stimulus sequence contained a display of flankers (650 msec) with or without a central target (150 msec, centred within the 650 msec timewindow of the flankers, see figure 2). This was followed by a second stimulus display, containing flankers (650 msec) plus a central target (150 msec) if there had been no central target in the first display on that trial, or just flankers with no central target if the target had appeared in the first display. Thus a target stimulus appeared only in one of two successive presentation intervals, whereas identical flankers appeared in both intervals (see Fig. 2). Each interval was paired with a beep sound to reduce temporal uncertainty (this was identical in all conditions). The observer's task was to determine which of the two stimulus intervals on each trial contained the central visual target. Observers responded by button press (left arrow for the first interval and right arrow for the second on a standard computer keyboard). When an incorrect response was made, auditory error feedback (beep) was given at trial end. The stimulus contrast was temporally enveloped so that stimulus intensity slowly ramped up and down. These envelopes were Hanning tapers of 650 msec length for the flankers and 150 msec for the target, the latter being presented halfway in the middle of flanker presentation (if there was a target) so that their amplitude peaks precisely overlapped. This was done to minimise any potential effect of different timings in the stimulus-onset of target and distractor stimuli from the manipulation of relative phase.

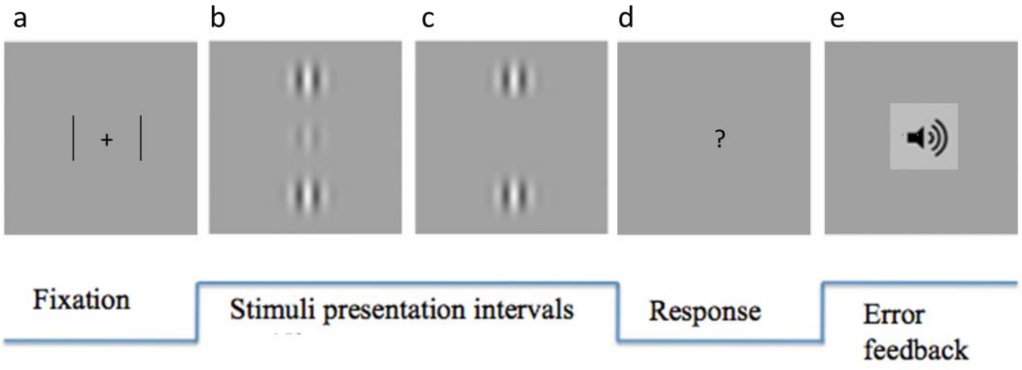

Figure 2: Example trial sequence from experiment 1

(a) Fixation display comprising a high-contrast central cross, with peripheral bar markers. The figure is schematic rather than displaying exact spatial relations. **(b)** Interval 1, here shown with a collinear target present. The target was presented for 150 msec in either Interval 1 or Interval 2. **(c)** Interval 2, shown here with no target. **(d)** Observers pushed a button to indicate which interval contained the stimulus**. (e)** In case of an error, an auditory feedback signal was given.

Fitting of the Psychometric Function

The data from the 2AFC visual detection task were used to determine the detection threshold, corresponding to the contrast necessary for achieving 75% of correct target detection. This was estimated from the psychometric function (accuracy against target contrast), by first fitting a Weibull function to each participant's data, and then reading off from this the target contrast at which detection was midway between ceiling and floor (Wichmann & Hill, 2001a). Psychometric functions were fitted to the raw data for each of the six configuration x flicker conditions in each subject, using the PSIGNIFIT toolbox version 2.5.6 for Matlab (http://bootstrap-software.org/psignifit). We derived from these functions the contrast level (and bootstrapped estimates of its variance) associated with 75% performance levels, similar to procedures used in previous studies of lateral interactions (Polat & Sagi 1994; Freeman, Sagi & Driver, 2001).

Group analysis

A factorial repeated-measures 2 x 3 Analysis of Variance (ANOVA) was conducted on the 75% performance thresholds estimates. (For completeness we also ran an analogous ANOVA on the slope parameter of the fitted psychometric functions instead; see below). The first experimental factor was

‘Collinearity’, with two levels: collinear vs. orthogonal flanker configurations. The second experimental factor was ‘Flicker’, with three levels: static flankers, in-phase flankers, out-of-phase flankers. To specifically assess the impact of flicker-phase, a further 2x2 ANOVA was conducted with the same factors but now excluding the static flanker conditions.

Experiment 2: Flicker phase and crowding

We specifically adopted a task and display parameters used by Mareschal, Morgan, & Solomon (2010). Participants had to judge whether a target Gabor patch, presented unpredictably in the left or right hemifield, was tilted slightly clockwise or anticlockwise from vertical (see Fig 3a for an example of a clockwise tilt). This target could be surrounded by nearby crowding distractors, comprising vertical Gabors, which could be located at different distances from the target location. Previous research (Pelli, 2008, Mareschal, Morgan, & Solomon, 2010) had shown that target orientation discriminations decline when the crowding distractors are closer to the target. Here we added the further manipulation of flicker-phase.

Participants

Thirteen adult participants had normal or corrected to normal visual acuity. All were paid for participation and naïve to the purpose of the experiment. Each participated in five experimental sessions.

Stimuli

We specifically adopted the display parameters and target orientation discrimination task used by Mareschal et al (2010). All stimuli comprised Gabor patches. Each sinusoidal luminance Gabor patch was presented at 90% contrast level and had a spread of $\sigma = 0.175$. Target Gabors were almost vertical (see figure 3) with a spatial frequency of 2.85 c/deg. Distractor Gabor stimuli were perfectly vertical and had 2.85 c/deg. The size of each target or flanker stimulus was 1degree of visual angle. On each trial, the target (and distracters) was presented at 5 degrees of visual angle (from vertical meridian) to the left or right of the fixation cross with equal probability in a randomized order; thus hemifield of target (and distractor) stimulation was unpredictable. All stimuli were presented for 400 msec in all conditions. Stimuli flickered at 60 Hz (refresh rate 120 Hz) at three spatial separations (1°, 1.17° or 1.33° of visual angle) between the target and the distractors above and below. The display characteristics and viewing distance were the same as in Expt. 1.

Experimental Design

The two factors were flicker-phase (target in- or out-of-phase with the distractors, at 60 Hz) and spatial separation between target and distractor (1°, 1.17° or 1.33°). All six conditions were equiprobable, presented in a randomly interleaved stimulus sequence. The crowding effect (suppression of target detection from distractors) was expected to be most pronounced for the closest spatial distances (see Mareschal Morgan, & Solomon, 2010).

Procedure

In all sessions observers were instructed to fixate a small white fixation cross ('+' sign at 4pt font-size) at the centre of the screen during each trial and this was carefully monitored via online eyetracking with an Eyelink 1000 table mounted system. Observers performed an orientation discrimination task for the peripheral target appearing unpredictably on left or right (always at 5 degrees eccentricity), reporting the orientation of that target (tilted clockwise or anti-clockwise from vertical). They responded by button press (right arrow for clockwise and left arrow for anti-clockwise). Feedback on error rate was now given at the end of each block consisting of 24 trials each. No feedback was given on individual trials here in order to speed up the task.

The first two experimental sessions contained only target stimuli (no flankers), as practice, lasting for 10 minutes each. The first session was used as a staircase procedure to find approximate tilt angles from vertical to yield ~ 90% correct performance. Subsequently, in order to identify more precisely the appropriate value for target deviation from vertical, a method of constant stimuli (MOCS) was employed in the second session to get a more reliable estimate of performance as a function of target orientation offset. These two sessions also allowed for some learning and stabilization of performance. The third 20 minutes session contained target and distractor stimuli. The orientation offset was chosen from the ~90% correct MOCS performance level in session 2 (mean 5.65 degrees offset, SD +- 2.23 degree). Participants underwent two further 25 minutes sessions with such flicker. The target unpredictably flickered either in-phase or in anti-phase, on each trial, with the two distractors that could be presented at three spatial separations. The two distractors on any one trial were always in phase with each other, only their relative phase to the target now varied. The spatial separations were randomly intermingled within blocks.

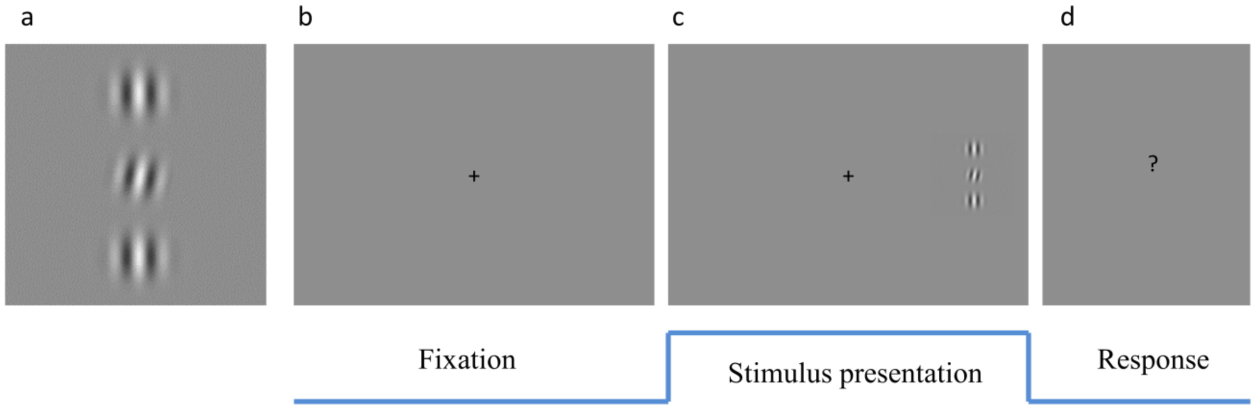

Figure 3: Stimulus display for experiment 2

(a) Example display (close-up) of target and distractor stimuli. **(b-d)** Timeline of experiment: **(b)** Fixation period, prior to grating stimulus onset either in left or right hemifield, unpredcitable and uncued. **(c)** Target (middle) and Distractors were presented at 5 degrees of lateral eccentricity for 500 ms and subjects had to indicate the direction of the tilt-offset in the target (see a). Figure is schematic and does not represent actual spatial relations. Target and distractors flicked either in-phase or out-of-phase at 60 Hz. In either case, the distractors were always in phase with each other, only their phase relative to the target varied. **(d)** The response could be given at any time after stimulus onset, there was no cue.

<u>Data Analysis</u>

Two repeated measures ANOVAs were conducted on the accuracy data, each including the factor of flicker-phase (in- or out-of-phase) crossed factorially with spatial distance. A 2 x 3 ANOVA included all three target-distractor separations; a further 2 x 2 ANOVA focused on just the closest two separations, the difference between which can also provide a standard measure of crowding (see Mareschal et al., 2010).

Results

<u>Experiment 1</u>

In this experiment we addressed the question whether synchronized gamma-band oscillations entrained by flickering flanker gratings (at 60 Hz) could enhance the impact of the flanker stimuli on detection of a low contrast collinear central target (Polat and Sagi, 1993; Polat and Sagi, 1994; Freeman, Sagi & Driver, 2001) when compared to asynchronous (or non-flickering) flanker gratings. Subjects had to detect a centrally and statically presented low-contrast target grating, presented at individually adjusted contrast levels. In Figure 4 We show that contrast thresholds for the central target were systematically lower when the target was collinear with the flankers, replicating previous research (Freeman, Sagi & Driver, 2001; Polat & Sagi, 1994). This pattern was observed alike in all three flanker flicker conditions (static, in-phase, and out-of-phase flankers). The 2x3 factorial repeated-measure ANOVA confirmed a significant main effect of collinearity [$F(1, 11) = 14.60$, $p < 0.01$], revealing the classic Lateral interaction effect, with central target detection thresholds lower (less contrast needed to achieve 75% detection) when the flankers were collinear with the target. There was no main effect of the flicker factor [$F(2, 11) = 1.18$, $p > 0.25$, ns]. Critically, there was also no interaction between collinearity and flicker [$F(2, 11) = 0.14$, $p > 0.8$, ns]. The collinearity effect was significant on pairwise t-tests for the static, in-phase or out-of-phase conditions alike (all $t (11) >2.2$, all $p<0.05$)

A further 2x2 ANOVA excluding the static flanker conditions showed a similar pattern: a significant main effect for collinearity [$F (1, 11) = 13.364$, $p < 0.01$]; there was no main effect of the flicker factor [$F (1, 11) = 0.45$, $p > 0.4$], and critically no interaction between the two factors [$F (1, 11) = 0.25$, $p > 0.6$]. The slight tendency for lower thresholds in the anti-phase condition versus the in-phase, regardless of collinearity, was far from significant [$F (1,11) = 0.50$, $p > 0.4$].

For completeness, an analogous ANOVA was computed on the slope values for the fitted psychometric functions at the 75% performance level, but this found no significant terms (all $Fs < 1.5$, n.s.).

To summarize, we could reproduce the classical lateral interactions effect (Polat & Sagi, 1994) whereby two high contrast Gabors enhance detection (less contrast needed for 75% detection performance) of a centrally presented target Gabor when all stimuli were collinear, compared to when the flankers were orthogonal to the target. We observed this collinearity effect robustly under all presentation levels, ‘static’, ‘in phase’ flicker and ‘out of phase’ flicker. But contrary to the hypothesis that (externally driven) synchrony may enhance perceptual integration, there was no difference in the collinearity effect for in- versus out-of-phase flanker flicker.

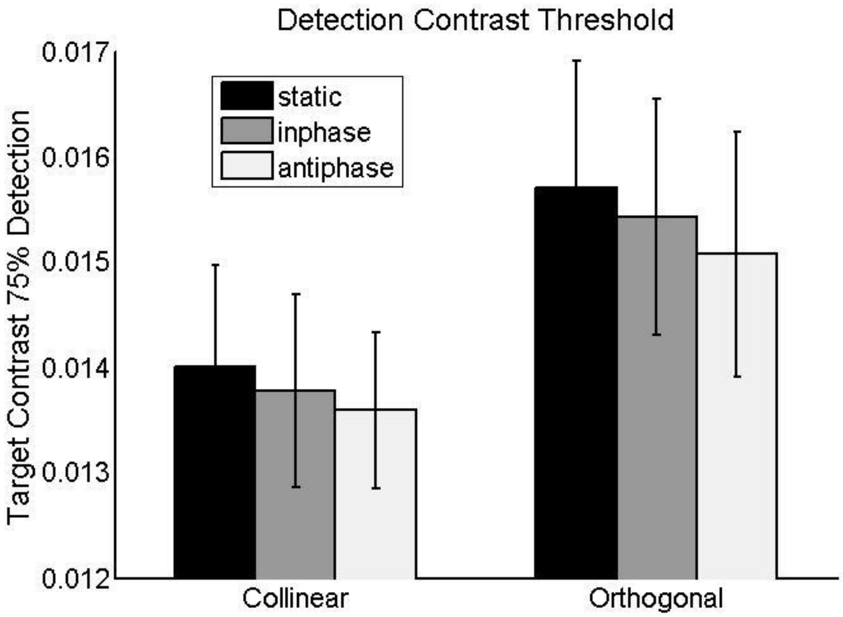

Figure 4: **Results from experiment 1**

Contrast thresholds (in units if Michelson contrast) of central target at detection threshold – corresponding to 75% performance. These were derived from the individually fitted psychometric curve. Group means are plotted with SEMs as errorbars. A main effect of Collinearity was significant, but not of Flicker conditions ('static', 'inphase', 'antiphase'). Neither was the interaction, nor any simple effect between Flicker conditions significant.

Experiment 2

In Experiment 2 we addressed the question whether the selective processing of target amongst nearby distractor stimuli could be modulated by manipulating the phase-synchrony between target and distractor stimuli. Subjects had to discriminate the orientation of a central target surrounded by distractor stimuli at various (small) distances. Both target and distracters were flickered, either in phase synchrony or in antiphase.

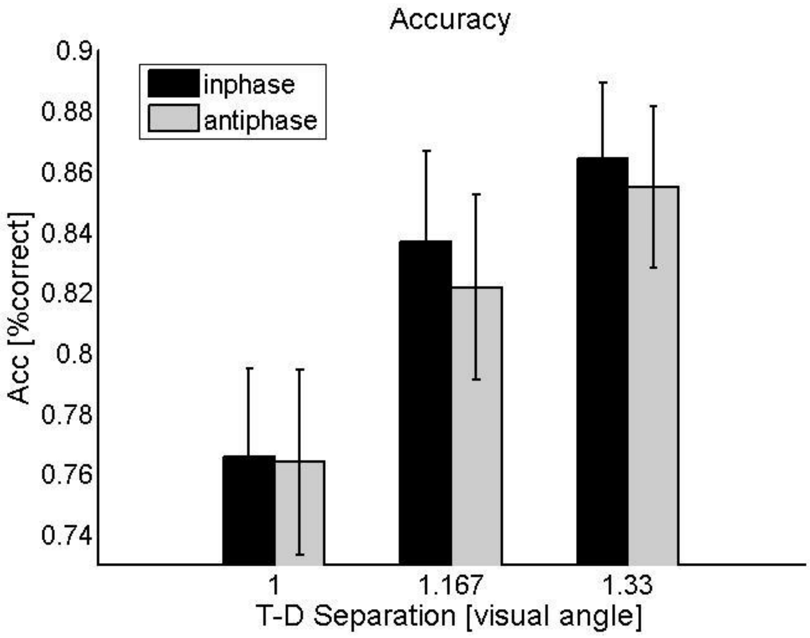

Figure 5: Results from experiment 2

Behavioural data (Accuracy) under 3 spatial target-distractor (T-D) separation conditions and two Flicker conditions. This reveals a highly significant main effect of Space but no effect of Flicker condition. The more separated target and distractors are, the more accurate the behaviour.

Figure 5 plots mean accuracy for each condition in the 2 x 3 design. Performance declines as the distractors appear closer to the peripheral target, reproducing the well-known ‘crowding’ effect. But this pattern is equivalent for the in-phase and out-of-phase cases. The 2 x 3 ANOVA confirmed a highly significant main effect of spatial distance [F (2, 11) = 22.90 , p < 0.001]. There was no main effect of flicker-phase [F (1, 11) = 0.684 , p > .4, ns], but more importantly no interaction between spatial separation and flicker phase [F (2, 11) = .16 , p >0.8. ns]. This indicates that the crowding phenomenon was unaffected by the target-flanker flicker-phase manipulation.

In sum, the manipulation of spatial distance had a highly significant impact on target discrimination, revealing the classic crowding effect for peripheral targets, whereby performance is most impaired by the closest distractors. However, the relative phase between target and distractor, as manipulated by the flicker conditions had no influence on performance. Neither did we observe a significant main effect, nor was the flicker effect more pronounced for crowded stimuli (smallest distances) compared to larger target-distractor separations.

Discussion

In this study we used two well-established psychophysical paradigms (Polat & Sagi, 1993; Polat & Sagi, 1994; Freeman, Sagi & Driver, 2001, Mareschal, Morgan, & Solomon, 2010) to test whether contextual influences on perceptual processing were influenced by the relative phase between visual stimulus components that were flickered in the gamma range (60 Hz). In experiment 1 we set out to test whether local synchrony modulates propagation of neural activity through lateral connections in visual cortex (deWeerd 2006) and in experiment 2 we set out to test whether synchrony between competing stimulus representations modulates selective processing of these in the visual system (Pelli 2008). We neither found that the well established collinear facilitation effect (Experiment 1) was modulated by phase synchrony between the contextual flanker stimuli, nor did we find that crowding effects (Experiment 2) depended on the relative phase between target and distractor stimuli.

In these experiments, flicker manipulations served as an external perturbation for causally testing the influential proposal that phase relations at gamma frequency may modulate propagation of neural signals or selective processing of different input streams (Salinas & Sejnowski, 2001; Fries, 2005; Womelsdorf & Fries 2007). It has been shown by several electrophysiological studies that flickering visual displays can entrain neuronal activity at frequencies of up to 100 Hz (Herrmann, 2001; Williams, Mechler, Gordon, Shapley & Hawken, 2004). While several studies suggest that visual entrainment of oscillatory activity can spread through virtually all levels of the cortical hierarchy (Srinivasan, Russell, Edelman & Tononi, 1999; Cosmelli et al., 2004), others suggest that such entrainment may be most pronounced in early visual cortex (Kamphuisen, Bauer & van Ee, 2008). Accordingly we used two psychophysical paradigms here for which the stimuli (Gabor patches) and tasks (contrast detection in Experiment 1, orientation discrimination in Experiment 2) are thought to tap into relatively ‘early’ visual processes.

In contrast to previous studies (e.g. Bauer, Cheadle, Parton, Muller & Usher, 2009) we avoided the potential stimulus confound of manipulating whether the to-be judged stimulus was either flickered or not, or flickered at different frequencies. Furthermore here the appearance of flicker could also not serve as a potentially informative cue for correctly identifying the target stimulus (see also van Diepen, Born, Souto, Gauch & Kerzel 2010). In our tasks, the crucial comparisons only involved manipulation of relative flicker-phase between stimulus components (or the flickered/static presentation of a task irrelevant stimulus as an additional control in experiment 1) which provided no predictive cues that could aid task performance. Under such more stringent conditions we did not find any impact of gamma-frequency flicker on stimulus detection or selection. While the results of both experiments show that manipulating the phase-synchrony between two neuronal populations does not impact on perceptual integration, the results from each experiment may have different theoretical implications.

In Experiment 1 the hypothesis was that synchronous flickering of the flankers at a frequency typical for human gamma-band oscillations (60 Hz, see Hoogenboom, Schoffelen, Oostenveld, Parkes & Fries, 2006) should enhance detection of a central target compared to flankers flickering in antiphase. This outcome would have been consistent with proposals by Salinas & Sejnowski (2001) and Fries (2005) that synchrony in neuronal populations can enhance the synaptic gain, particularly at higher frequencies (Azouz & Gray 2003). While there is numerous evidence for this from correlational studies (e.g. Gruber, Muller, Keil & Elbert, 1999; Bauer, Oostenveld, Peeters, Fries, 2006;Womelsdorf & Fries, 2007; Jensen, Kaiser, Lachaux, 2007), our results suggest that this does at least not apply for externally driven gamma-band oscillations.

In Experiment 2 the hypothesis was that in-phase flicker would impair selective processing of target-orientation, particularly for very nearby distracters. While several theoretical frameworks trying to explain the crowding effect exist (Dayan & Solomon, 2010; Pelli, 2008), one obvious interpretation of the results in the context discussed here is that separation of oscillating neuronal populations in phase space does not separate processing streams as theoretically predicted (Fries 2005; Womelsdorf & Fries 2007).

The clear null-result of gamma frequency flicker phase manipulations on these two carefully controlled psychophysical measures of perceptual interaction argue against a strong causal influence of relative gamma oscillation phase on processing in early visual cortex. In that respect this study adds to a number of other studies using flickering visual displays that failed to find positive effects of gamma-band flicker (van Diepen, Born, Souto, Gauch, & Kerzel, 2010; Fahle & Koch 1995; Leonards, Singer, & Fahle, 1996), contrasting with others that found such effects (Usher & Donnelly 1998; Bauer, Cheadle, Parton, Muller & Usher, 2009).

However, it is not entirely clear to what degree entrainment of neural activity at a particular frequency can reproduce the complex neuronal interactions thought to underlie the generation of brain-rhythms. Pikovsky, Rosenblum & Kurths (2001) emphasize different regimes of periodic activity, such as coupling between autonomous oscillators versus entrainment by an external force. For intrinsic gamma oscillations, it is thought that a complex interplay between excitatory and inhibitory neurons determines their periodicity (Mann, Suckling, Hajos, Greenfield, & Paulsen, 2005; Tiesinga, Fellous, Jose, & Sejnowski, 2001; Traub et al., 2000). External flickering stimuli may not perfectly mimic this, even if they undoubtedly do entrain oscillations in visual cortex at the flickered frequencies (Herrmann, 2001; Williams, Mechler, Gordon, Shapley & Hawken, 2004). In both our experiments Gabor patches were placed near to each other and it is known that genesis of intrinsic gamma-oscillations is brought about by lateral interactions of neuronal populations with similar feature preferences (Engel, König, Kreiter & Singer 1991; Robinson 2006). In both regimes (externally entrained and intrinsically generated rhythms) only a subset of neurons take part in the oscillatory rhythm (Williams, Mechler, Gordon, Shapley & Hawken, 2004; Maier, Adams, Aura & Leopold, 2010), therefore it is possible that external flicker does not entrain the relevant populations for contextual integration or that the forces underlying these different rhythm generators may have counteracted each other and therefore yield in a null-result on the behavioural level.

In conclusion, our study found that lateral interactions between a central visual target and flankers, or visual crowding of a peripheral visual target by close distractors, were both unaffected by the flicker phase manipulation here. Future variations of the manipulations we have introduced could extend the phase-manipulation to other visual tasks, consider other frequencies, or introduce random phase relations (rather than in versus 180 degrees out of phase), to fully decorrelate rather than segregate flankers from targets. However, the present results argue against a special role for oscillatory phase of zero lag versus higher lag, when driven externally by flickering visual stimuli. More research is needed to understand the relation between externally entrained rhythms as widely used to study the causal role of brain oscillations and the dynamics underlying the intrinsically generated rhythm.

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