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The properties of induced gamma oscillations in human visual cortex show individual variability in their dependence on stimulus size

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ABSTRACT

The role of gamma-band (typically 30–100 Hz) oscillations in visual processing is a topic of increasing interest. One hypothesis is that gamma oscillations reflect the action of GABAergic inhibitory processes in the visual cortex responsible for surround-suppression. Evidence from primate neurophysiology [Gieselmann & Thiele, A., 2008. European Journal of Neuroscience 28, 447–459.] suggests that the amplitude of the gamma-band response increases as a visual grating stimulus expands outside of the classical receptive field into the inhibitory surround; with the amplitude of the response increasing, and the frequency of the response decreasing, monotonically with stimulus size. In this study, we tested the relationship between the gamma-band response and the size of visual grating stimuli in humans using MEG. In two initial experiments we found that, while the absolute magnitude of the gamma-band response varied considerably across participants, in all cases the amplitude of the response had a monotonically increasing relationship with size. In contrast, we did not find any relationship between the frequency of the response and the size of the stimulus. Previously, the frequency of the visual gamma-band response has been found to correlate across individuals with the surface area of cortical area V1 [Schwarzkopf et al., 2012. Journal of Neuroscience 32, 1507–12.] We, however, were unable to find any correlation between the frequency or the magnitude of the gamma-band response and the dimensions of V1 cortical gray matter as measured from participants' MR images. Consistent with a saturation of the gamma-band response found for some individuals in the first two experiments, in a third experiment we found that the magnitude of the response to our largest stimulus (8°) was less than that predicted from the response to the stimulus' parts.

Introduction

Neuronal oscillations in the gamma frequency band (typically 30–100 Hz), have been implicated in a number of brain processes, such as attention (Fries et al., 2001, 2002), memory (Jensen et al., 2007), object recognition (Tallon-Baudry and Bertrand, 1999) and motor control (Muthukumaraswamy, 2010). Invasive animal studies have demonstrated that high-contrast grating stimuli generate induced (i.e., not phase-locked to stimulus onset) gamma oscillations in local field potential (LFP) recordings of activity in primary visual cortex (V1) (e.g. Gail et al., 2000; Logothetis et al., 2001; Rols et al., 2001). An analogous effect has been demonstrated non-invasively in humans using magnetoencephalography (MEG) (see for instance Adjamian et al., 2004; Hall et al., 2005; Hoogenboom et al., 2006; Muthukumaraswamy et al., 2010; Swettenham et al., 2009), and evidence suggests that this too may be primarily generated in V1 (Perry et al., 2011). Both human and animal studies have demonstrated that characteristics of these gamma-band oscillations are sensitive to visual properties of gratings, such as contrast (Hall et al., 2005; Logothetis et al., 2001; Ray and Maunsell, 2010), spatial frequency (Adjamian et al., 2004; Hadjipapas et al., 2007) and orientation (Duncan et al., 2009; Friedman-Hill et al., 2000; Frien et al., 2000; Koelewijn et al., 2011), and in humans it has been shown that, across individuals, the frequency of the visual gamma-band response correlates with orientation discrimination thresholds (Edden et al., 2009). The optimal spatial frequency (3 c.p.d.) of high contrast static gratings which induce gamma oscillations in the visual cortex, is also the spatial frequency most likely to generate visual 'discomfort' in observers, and to generate epileptiform activity in individuals with visual pattern-sensitive epilepsy (Wilkins, 1995). Thus, properties of visually-induced gamma oscillations appear to be related to perceptually important properties of visual stimuli, and may serve as markers of disease states.

It remains an open question, however, as to how these oscillations are generated within the relevant areas of cortex, and which (if any) differences in the underlying physiology and/or anatomy of the cortex across individuals can account for the individual variability present in the parameters and morphology of the gamma-band (see e.g. Muthukumaraswamy et al., 2009). One important development in this direction has been the finding that the frequency of the human visual gamma-band response to grating stimuli is correlated across individuals with gross GABA concentration in the medial visual

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cortex, measured using magnetic resonance spectroscopy (MRS) (Muthukumaraswamy et al., 2009). As GABA is the main inhibitory neurotransmitter in the cortex, this suggests that inhibitory interactions play a crucial role in generating gamma-band activity. Consistent with this, LFP recordings from macaque V1 have demonstrated that the amplitude of gamma oscillations increases monotonically as visual gratings of increasing size expand outside the classical receptive field and into the inhibitory surround (Gieselmann and Thiele, 2008). Thus, one source of gamma-band activity in the visual cortex may be the local inhibitory circuits that underpin surround-suppression effects, suggesting that differences in the gamma-band response across individuals may be due to differences in the strength of GABAergic inhibition.

Adding to this picture is the more recent finding that, in humans, the frequency of the visual gamma-band response is correlated across individuals with the surface area of cortical areas V1 and V2 (but not V3), as determined by fMRI retinotopic mapping (Schwarzkopf et al., 2012). The authors of that study speculated that this may be due to horizontal connections traversing shorter distances in visual space as V1 surface area gets larger, leading to greater local homogeneity of responses and a concomitant increase in the frequency of oscillations. In support of this, they point to previous studies of macaque V1 (Gieselmann and Thiele, 2008; Ray and Maunsell, 2010) in which the frequency of LFP gamma-band oscillations increased with decreasing stimulus size, and predict that a similar effect may be present in humans, with the largest increases being found for those with the smallest V1 surface area.

To our knowledge, the relationship between grating size and the sustained gamma-band response has not yet been tested in humans. The work of Gieselmann and Thiele (2008) would suggest that the gamma-band amplitude should increase and the frequency decrease with increasing stimulus size. It remains an open question, however, as to whether the effects of stimulus size on mass activity measured over a large area of cortex will be the same as that measured locally over much smaller areas (activity present in LFP recordings being thought to originate within just 500 μm of the electrode tip). This is due to the fact that it is unknown to what extent the visual gamma-band response is driven by a single coherent oscillation across the primary visual cortex, or to what extent it is driven by a series of local oscillatory domains with differing frequencies and levels of coherence. For this reason, we used MEG to measure the amplitude of the sustained gamma-band response to high-contrast square-wave gratings of varying size in healthy volunteers, in order to determine the relationship between visual stimulus size and the gamma-band response. To allow comparison of our data with that Schwarzkopf et al. (2012) we also measured the surface area and thickness of V1 from each individual's structural MRI.

Materials and methods

Participants

Twelve healthy volunteers (3 female, 9 male; mean age: 30.67 yrs, range: 20–43 yrs) took part in Experiment 1. A subset of five of these volunteers took part in Experiment 2, and a subset of eight plus one additional volunteer (male, age: 55 years) took part in Experiment 3. All participants gave informed consent each time they participated. All had normal or corrected-to-normal vision. Each participant had a previously acquired structural MRI scan that was used for source localisation. Approval by the local ethics committee was granted for all procedures.

Stimuli and procedure

In each recording session participants viewed a series of visually-presented gratings. All stimuli were stationary, vertically-oriented black/white square-wave gratings with a spatial frequency of 3 c.p.d presented at maximum contrast on a gray background. Stimuli were masked by a square window that varied in size by condition. All displays were generated by Matlab (The Mathworks, Inc.: Natick, MA) using the Psychophysics Toolbox extensions (Brainard, 1997; Kleiner et al., 2007; Pelli, 1997), and presented on a Mitsubishi Diamond Pro 2070 monitor (1024×768 pixel resolution, 100 Hz refresh rate).

During each trial a red square (~0.2° in width) was present continuously and participants were instructed to maintain fixation on the square throughout. Stimuli were positioned so that their top right-hand corner always coincided with fixation so as to ensure that they were presented to the lower-left visual quadrant. Due to the largest stimulus taking up the full height of the screen, the fixation square was presented in the top right-hand corner of the display, rather than the centre. Each trial consisted of a 1500 ms baseline period in which only the fixation square was present, followed by presentation of the stimulus for a random duration between 1000 & 1500 ms, followed by a 1000 ms response period, resulting in a total trial time of 3500–4000 ms.

In experiment 1, gratings were presented at one of three different sizes - 2°, 4° & 8° - while in experiment 2 they were presented at one of five different sizes - 2/3°, 1°, 2°, 4° & 8°. In experiment 3, gratings were presented at two sizes - 4° & 8° - and also in an 'L'-shaped patch, which was formed by subtracting the 4° window from the 8° window.

In experiment 1, participants were instructed to indicate which of the three different sizes had been presented by pressing one of three buttons using their right hand during the response period (i.e. after grating offset). In experiments 2 & 3, they were instructed simply to press a single button with the index finger of their right hand as rapidly as possible after grating offset. In both experiments, if no response had been made within 750 ms of grating offset the fixation square was replaced by text reading 'Response not detected' for 250 ms. In order to prevent button presses during the baseline period, participants were instructed to try to respond rapidly enough in every trial to prevent this text from appearing.

In experiments 1 & 3, participants viewed 100 trials per condition (300 trials in total), and in experiment 2, they viewed 75 trials per condition (375 trials in total). All trials were presented in random order.

MEG data acquisition and analysis

Whole-head MEG recordings were made using a 275-channel CTF radial gradiometer system sampled at 1200 Hz. An additional 29 reference channels were recorded for noise cancellation purposes, and the primary sensors were analysed as synthetic third-order gradiometers (Vrba and Robinson, 2001). Two of the 275 channels were turned off due to excessive sensor noise.

To achieve MRI/MEG co-registration, fiduciary markers were placed at fixed distances from three anatomical landmarks (nasion and pre-auricular) identifiable in the subjects' anatomical MRIs. Fiduciary locations were verified afterwards using high-resolution digital photographs.

Data were recorded in 3 s epochs beginning at 1 s before stimulus onset. Artefact rejection was performed offline by manually inspecting the data and discarding trials with excessive muscle or head-movement-related artefacts. No more than 40 trials were excluded from any individual dataset in this way.

After recording, each data set was bandpass filtered using a fourth-order bi-directional IIR Butterworth filter at 30–70 Hz (this choice was based on the frequency range of visual gamma found across individuals in previous studies; Muthukumaraswamy et al., 2010). The synthetic aperture magnetometry (SAM) beamformer algorithm (Robinson and Vrba, 1999) as implemented in the CTF software was used to create differential images of source power (pseudo-T statistics) for 1 s of visual stimulation (0 to 1 s) contrasted with 1 s of baseline (−1 to 0 s), for all trials collapsed across conditions. Mathematical details of the calculation of SAM pseudo-T source image statistics are described elsewhere (Hillebrand et al., 2005; Robinson and Vrba, 1999; Vrba and Robinson, 2001). For source localisation, a multiple local-spheres forward model (Huang et al., 1999) was derived by fitting spheres to the brain surface