

Attention induces synchronization-based response gain in steady-state visual evoked potentials

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When attention is voluntarily directed to a spatial location, visual sensitivity increases at that location. What causes this improved sensitivity? Studies of single neuron spike rates in monkeys have provided mixed results in regard to whether attending to a stimulus increases its effective contrast (contrast gain) or multiplicatively boosts stimulus-driven neural responses (response or activity gain). We monitored frequency-tagged steady-state visual evoked potentials (SSVEPs) in humans and found that voluntary sustained attention multiplicatively increased stimulus-driven population electrophysiological activity. Analyses of intertrial phase coherence showed that this attentional response gain was at least partially due to the increased synchronization of SSVEPs to stimulus flicker. These results suggest that attention operates in a complementary manner at different levels; attention seems to increase single-neuron spike rates in a variety of ways, including contrast, response and activity gains, while also inducing a multiplicative boost on neural population activity via enhanced response synchronization.

Perceptual abilities vary immensely as a function of where an individual voluntarily allocates attention. How does attention increase sensitivity to visual stimuli that are presented at an attended location? Three competing hypotheses have been proposed to explain how attention modulates the activation of visual cortical networks. According to the contrast gain hypothesis, the effects of attention are equivalent to increasing stimulus contrast. Thus, this hypothesis predicts that attention should cause a leftward shift in the neural contrast-response function. Neural responses grow with increasing stimulus contrast, following a nonlinear sigmoidal contrast-response function. Therefore, attention should boost neural responses when stimulus contrast is within or below the dynamic range of the neural contrast-response function, but not when stimulus contrast is above the point of response saturation (**Fig. 1a**). According to two other hypotheses, the response gain and activity gain models, attention multiplicatively increases the responses of the visual neurons that selectively respond to the attended stimulus. Both of these hypotheses predict that attention should boost neural responses most strongly for stimuli with high contrast (**Fig. 1b**). The response and activity gain hypotheses differ in terms of the effects of attention on spontaneous neural activity. The response gain hypothesis postulates that attention multiplicatively increases only the stimulus-driven component of neural responses, predicting that attention should have no effect on spontaneous neural activity, whereas the activity gain hypothesis postulates that attention multiplicatively boosts the net neural activity, including spontaneous activity (**Fig. 1b**).

To test these hypotheses, stimulus contrast must be varied from a sub-threshold level to a response-saturation level to obtain full contrast-response functions for attended and ignored stimuli. The contrast gain hypothesis predicts that the effects of attention should

be largest for moderate-contrast stimuli (in the middle of the dynamic range), whereas the response and activity gain hypotheses predict that attention effects should be largest for high-contrast stimuli, either with (activity gain) or without (response gain) the boosting of spontaneous activity. Numerous electrophysiological and neuroimaging studies have demonstrated that attention increases neural activity for attended, relative to ignored, stimuli. Fixed stimulus contrasts, however, were typically used in these studies, so that the results are equivocal for evaluating the three hypotheses. Only rarely have the effects of attention on contrast-response functions been examined^{1–9}.

For single neurons in areas V4 and MT, several studies reported that voluntary visual attention affected spiking activity, primarily on the basis of contrast gain^{1,10,11}; attention modulated the later component of responses (~200–450 ms after stimulus onset), even for high-contrast stimuli^{1,12}, but not as strongly as for low- to moderate-contrast stimuli¹. Recent recordings from a large number of V4 neurons, however, found a variety of attention effects on neuronal contrast-response functions. The attention effect on each neuron was partially consistent with contrast, response or activity gain, yielding a statistical tie across the population, but slightly favoring response and activity gain⁷. Behavioral results are also mixed with respect to the three hypotheses. Consistent with contrast gain, a recent study⁴ reported that voluntary attention improved orientation discrimination for low- to moderately high-contrast stimuli, corresponding to the dynamic range of the psychometric function (behavioral performance plotted as a function of contrast). However, attention did not affect performance for high-contrast stimuli, corresponding to the saturated portion of the psychometric function. If attention only operates through mechanisms that induce contrast gain (**Fig. 1a**), then attention should be generally

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Received 5 September; accepted 27 November; published online 17 December 2006; doi:10.1038/nn1821



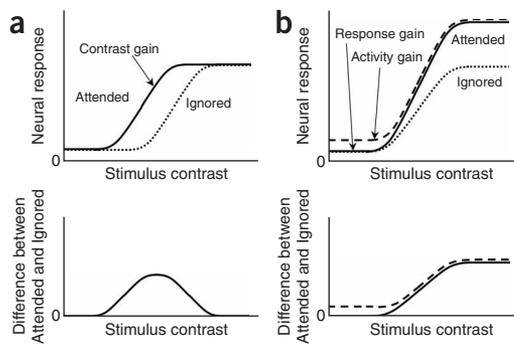


Figure 1 The contrast, response and activity gain hypotheses of the voluntary visual-spatial attention boosts neural responses. **(a)** According to the contrast gain hypothesis, attention increases the effective contrast of attended stimuli, shifting the contrast-response function to the left. **(b)** According to the response and activity gain hypotheses, attention multiplicatively increases neural responses to attended stimuli, either with (activity gain) or without (response gain) attention effects on spontaneous neural activity. Upper, hypothetical contrast-response functions for attended and ignored conditions. Lower, difference between attended and ignored contrast-response functions.

ineffective for high-contrast stimuli. Contrary to this prediction, robust behavioral attention effects are generally found with high-contrast stimuli, as such stimuli are more readily detected and processed when presented at the focus of attention^{8,9,13}. Furthermore, some behavioral results provide evidence for multiplicative attention effects consistent with response gain (for example, attention improved the discrimination of contrast, orientation and spatial frequency more for a higher-contrast than for a lower-contrast stimulus)^{8,9} or evidence for the involvement of both contrast gain and response gain⁵. In sum, for both neuronal spike rates and behavioral performance, the evidence to date has been mixed as to whether voluntary visual attention primarily affects neural activity based on contrast^{1,3-6,10,11}, response^{5,7-9} or activity⁷ gain.

The three hypotheses have not previously been examined at the level of the neural population. This examination is important for two reasons. First, it is intrinsically difficult to compare the contrast-response functions of individual neurons with behavioral results because it is unclear how neural signals from different visual areas (or sub-areas) contribute to performing a specific behavioral task¹⁴. An examination of neural population responses will identify the primary population activity that is induced by a given stimulus and determine how that population activity is affected by allocation of attention to the stimulus. Second, neural population activity takes on emergent characteristics that are not reflected in the spike rates of individual neurons. Response synchronization is one such example, and there is evidence that attention modulates synchronization. For example, visual attention led to increased 35–90-Hz (gamma-frequency) synchronization among V4 neurons that were responding to an attended stimulus¹². For another example, attention to tactile (as opposed to visual) stimuli increased the synchronization among somatosensory neurons¹⁵. Because the synchronization can increase the impact of the involved neurons on postsynaptic targets¹⁶, these results suggest that response synchronization is one of the mechanisms that are important for attentional selection^{17,18}. Recent evidence suggesting that the coding of stimulus contrast in V1 involves synchronization¹⁹ is also consistent with a function for neural response synchronization in modulating the strength of stimulus representation. Because response synchronization is not limited by the saturation of neuronal spike rates at high contrasts¹⁹, we hypothesized that attentional modulations of the

coherence of neural population responses might provide a mechanism that is especially effective for increasing the salience of high-contrast stimuli. This would complement the attentional modulations of neuronal spike rates, which may be potentially limited by response saturation at high contrast.

Our strategy for investigating the effects of attention on the coherence of neural population activity in humans was to monitor SSVEPs that were elicited by flickering stimuli²⁰. These electroencephalographic (EEG) measures can index the increased synchronization of neural responses even if the firing rate of individual neurons is saturated because of high contrast. Hypothetically, if attention induced contrast gain in individual neurons, while also inducing multiplicative response (or activity) gain in terms of increased phase locking of population activity to stimulus flicker, SSVEP amplitudes might be sensitive enough to demonstrate response (or activity) gain. Indeed, some of the data reported in a prior SSVEP study² are suggestive of multiplicative attention effects on SSVEP amplitudes. Here we rigorously tested the attentional response and activity gain hypotheses for neural population activity by recording frequency-tagged SSVEPs from both attended and ignored stimuli simultaneously (thus controlling for influences on SSVEPs that were unrelated to attention), analyzing the scalp topography of attention effects (crucial for evaluating the attentional response and activity gain hypotheses) and examining the effects of attention on response synchronization.

The response and activity gain hypotheses predict that attention directly boosts visual responses that are elicited by the attended stimulus (**Fig. 1b**). Evidence in support of these hypotheses must demonstrate that there is a multiplicative attention effect on population activity that is stimulus selective. Therefore, we recorded frequency-tagged SSVEPs from numerous scalp locations to identify patterns of activity that were specific to each of the competing stimuli. We then sought to demonstrate that attentional boosts in SSVEP amplitudes occur with a topographic pattern that is indicative of the selective enhancement of sensory activation and that this enhancement is multiplicative (**Fig. 1b**). The presence or absence of attention effects on subthreshold activity allowed us to distinguish between response and activity gain.

Care must be taken to ensure that SSVEP modulations can clearly be attributed to selective attention. This requires that attended and ignored conditions be equated in terms of arousal and the type of visual processes engaged. Accordingly, we presented two flickering circular gratings, one to be attended to and the other to be ignored, in the left and right visual hemifields (**Fig. 2a**). When the observer attended to one grating, he or she simultaneously ignored the other grating, such that the level of arousal and general task requirements were comparable while we recorded SSVEPs from both the attended and ignored gratings simultaneously²¹. We made two gratings flicker at different frequencies so that the Fourier band-power value for each frequency could be extracted from the EEG activity to measure coherent neural responses to the respective gratings separately²¹⁻²³. This frequency-tagging method allowed us to simultaneously monitor SSVEPs from attended and ignored stimuli so that we could determine whether attentional modulation of stimulus selective population electrophysiological activity (recorded as EEG) reflected contrast gain (**Fig. 1a**), response gain or activity gain (**Fig. 1b**).

We found that (i) each grating elicited SSVEPs that were localized in the contralateral posterior scalp region, (ii) voluntary visual attention selectively and multiplicatively boosted these stimulus-induced SSVEPs in a manner that was consistent with response gain and (iii) this attentional boosting was at least partially attributable to the enhancement of neural response synchronization by attention.

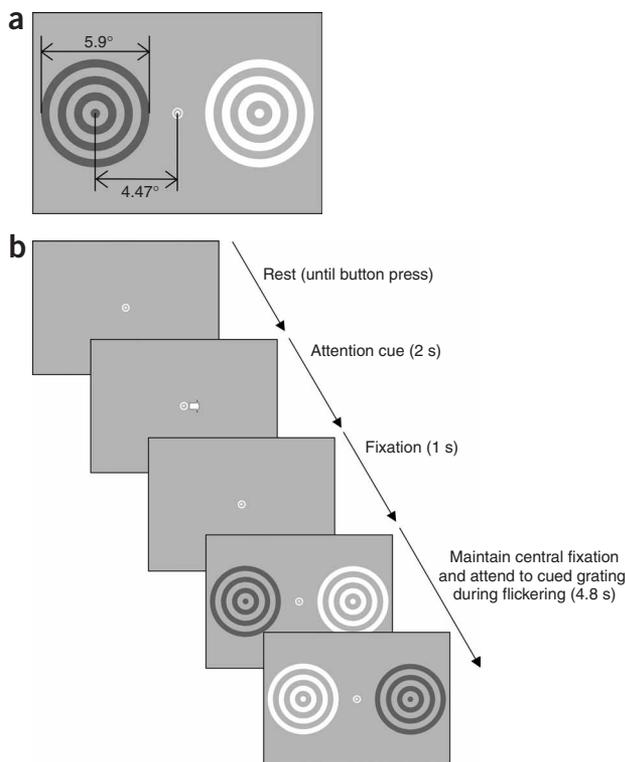


Figure 2 Stimuli and a trial sequence. (a) Two circular gratings were presented in opposite hemifields. Both gratings were flickered (one at 12.50 Hz and the other at 16.67 Hz) between a dark phase and a light phase; for illustration, the dark phase is shown on the left and the light phase is shown on the right. (b) Each trial was initiated by a button press, followed by a central arrow (attention cue) indicating the grating to be attended, a fixation screen and then a 4.8-s presentation of the flickered gratings.

RESULTS

We elicited SSVEPs by using circular gratings flickering at 12.5 Hz and 16.67 Hz. Two gratings appeared simultaneously in the left and right visual hemifields (Fig. 2a), with flicker frequency randomly assigned to each hemifield on each trial. Each trial lasted 4.8 s, during which the observer maintained fixation at a central marker while voluntarily attending to the grating that was indicated by a central arrow that was presented prior to each trial (Fig. 2b). We contrasted SSVEPs that were derived from the second-harmonic EEG responses (see Methods) for attended and ignored conditions.

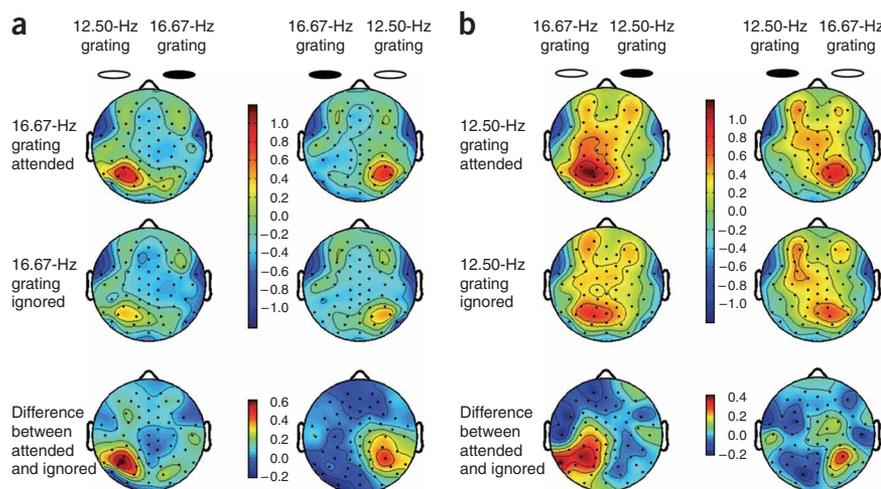
The SSVEP topographies for the responses to the 16.67-Hz grating (Fig. 3a) showed that the maximal SSVEP amplitudes occurred contralateral to the stimulus over posterior cortical regions and that attention boosted these localized responses. The topography of the

SSVEP differences between the attended and ignored conditions showed that the contralateral posterior focus of attentional enhancement closely resembled the SSVEP topographies for the attended and ignored conditions. This topographic similarity between SSVEP responses and SSVEP enhancement suggests that the attentional modulation occurred in the same brain regions that were selectively activated by the grating. A parallel set of results for SSVEPs that were synchronized to the 12.50-Hz grating (Fig. 3b) showed a similar pattern, except that the SSVEP amplitudes were generally larger.

These findings demonstrated that the stimuli elicited focal SSVEPs at contralateral posterior scalp regions and that voluntary spatial attention boosted these localized visual responses. We next evaluated whether this attentional boost of stimulus-evoked population electrophysiological activity was consistent with contrast gain (Fig. 1a), response gain or activity gain (Fig. 1b). To evaluate SSVEP contrast-response functions, we used data from ten scalp locations (five on each side of the scalp; Fig. 4a) that were selected to correspond to the foci of maximal sensory activation and attentional boost. We averaged SSVEPs separately for locations contralateral and ipsilateral to the side of stimulation (combining left and right stimulus presentations).

For SSVEPs that were elicited by the 16.67-Hz grating, the contralateral contrast-response functions for the attended and ignored conditions showed that the effect of attention monotonically increased with increasing stimulus contrast, with attention having no effect at the lowest contrasts (Fig. 4b). This finding is consistent with the response gain hypothesis (Fig. 1b). To quantitatively confirm the multiplicative attention effect, we first fit both the attended and ignored contrast-response functions using the Naka-Rushton equation, which is typically used to fit neural contrast response functions (Fig. 4). If attention multiplicatively boosted visual responses, then the difference between the attended and ignored contrast-response functions should also be well fit by the Naka-Rushton equation¹. This was indeed the case (Fig. 4b; $F_{1,7} = 41.582, P < 0.001$). Attention had negligible effects

Figure 3 Topographic plots of the second-harmonic SSVEPs in response to the two gratings, averaged across observers and stimulus contrasts. (a) 16.67-Hz grating. (b) 12.50-Hz grating. Color-scale data were interpolated based on a fine Cartesian grid. SSVEP amplitudes have been standardized so that the positive and negative values indicate responses above and below the mean level, respectively, in z units. Left, SSVEP topographies when the relevant grating was presented to the right visual field. Right, SSVEP topographies when the relevant grating was presented to the left visual field. Separate rows show conditions in which the relevant grating was attended to (upper), ignored (middle) or the difference between attended and ignored conditions (lower). In all cases, maximal responses and maximal attention effects occurred at contralateral posterior scalp locations.



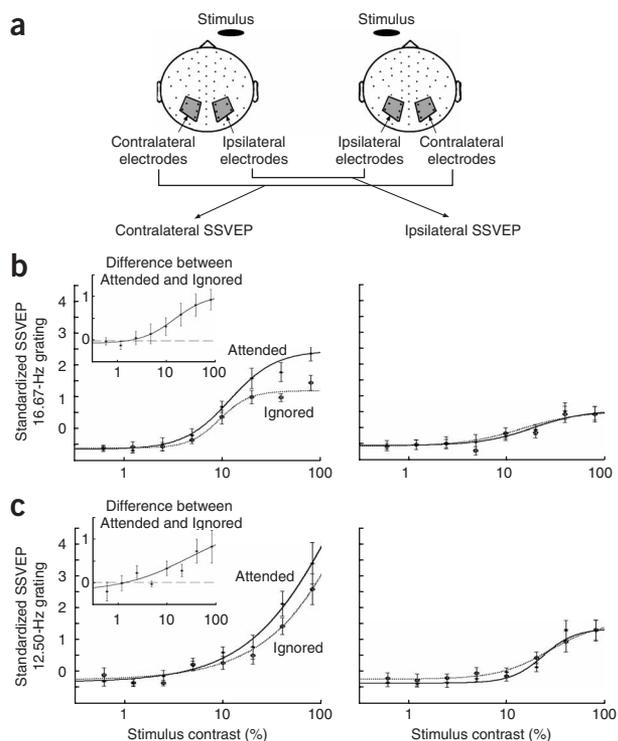


Figure 4 Second-harmonic SSVEP contrast-response functions.

(a) Illustration of the contralateral and ipsilateral electrodes used for this analysis. (b,c) SSVEP contrast-response functions for the 16.67-Hz grating (b) and the 12.50-Hz grating (c), computed from the 10 scalp electrodes illustrated in a, from which strong stimulus responses and attention effects were obtained (Fig. 3). In b and c, the left panels show contralateral responses and the right panels show ipsilateral responses. Solid curves show contrast-response functions obtained when the relevant grating was attended. Dotted curves show contrast-response functions obtained when the relevant grating was ignored. For the contralateral responses, the insets show the contrast dependencies of the attention effects (the difference between the attended and ignored conditions). The continuous curves show fits based on the Naka-Rushton equation; for the 16.67-Hz grating, r^2 for the fits are 0.995 (contralateral attended), 0.991 (contralateral ignored), 0.982 (ipsilateral attended) and 0.956 (ipsilateral ignored); for the 12.50-Hz grating, the corresponding r^2 are 0.994, 0.987, 0.975 and 0.992. SSVEP amplitudes have been standardized and averaged across observers (see Fig. 3), and the error bars indicate ± 1 s.e.m.

on the weak responses recorded from ipsilateral locations, which confirmed the spatial selectivity of the attention effect (Fig. 4b).

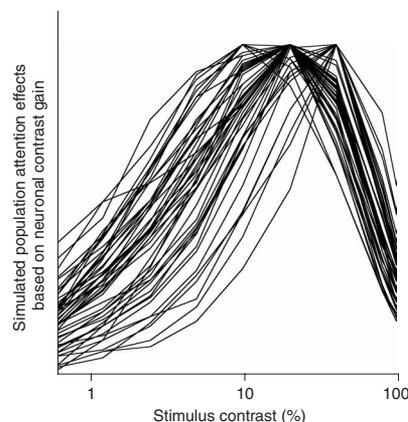
We found essentially the same pattern of results for SSVEPs that were elicited by the 12.50-Hz grating (Fig. 4c). The attentional boosting of SSVEPs was spatially selective (confined to contralateral locations) and the contrast-response functions indicated response gain; the difference between the attended and ignored contrast-response functions grew monotonically with increasing stimulus contrast, conforming to the Naka-Rushton equation (Fig. 4c; $F_{1,7} = 9.107$, $P < 0.02$), with attention having no effect at the lowest contrasts.

In addition to these primary results that consistently supported the idea that the effects of attention on SSVEPs have response gain

characteristics, we also found some frequency dependencies. First, SSVEPs were generally stronger for the 12.50-Hz grating than for the 16.67-Hz grating (compare Figures 3a and b). This could be related to differences in perceived contrast. Although the amplitude of luminance modulation was physically identical for the two flicker frequencies, subjectively the 12.50-Hz grating appeared slightly higher in contrast than the 16.67-Hz grating, probably owing to a higher perceptual sensitivity to the slower flicker. Second, the effects of attention were generally greater for the 16.67-Hz grating than for the 12.50-Hz grating (compare Figures 4b and 4c). Indeed, the magnitude of the attention effects might depend systematically on flicker frequency²⁴. We note that the examined EEG second-harmonic responses (33.33 Hz) were in the gamma range for the 16.67-Hz grating and that some evidence suggests that gamma-range synchronization is closely associated with attention^{12,25}. Third, within the contrast range used, SSVEP contrast-response functions saturated for the 16.67-Hz grating (Fig. 4b), but not for the 12.50-Hz grating (Fig. 4c). Perhaps the higher-frequency grating activated a higher ratio of magno-type to parvo-type neurons than did the lower-frequency grating. Magno-type neurons may disproportionately contribute to the perception of a faster flicker²⁶ (but see ref. 27,28) and they also tend to saturate at a lower contrast²⁹.

These frequency dependencies merit further investigation, and it is unclear how SSVEP results might differ for frequencies that were not tested in this experiment. Nevertheless, our SSVEP results provided strong evidence that is pertinent to the response gain hypothesis. Both the 16.67- and 12.50-Hz gratings elicited electrophysiological responses

Figure 5 Representative simulation results indicate that an attentional response or activity gain effect could not emerge from averaging neuronal contrast gain effects over a population of neurons with a variety of contrast-response functions and contrast gain magnitudes. The average attention effect (the difference between attended and ignored responses) is plotted as a function of contrast for each simulated neural population ($N = 1,000$), characterized by specific distributions of neuronal contrast-response functions and attentional contrast gain magnitudes. The 48 representative attention effect-versus-contrast curves shown are based on an even sampling of population-parameter statistics from the following ranges. Because neurons in higher visual areas tend to saturate at lower contrasts (see ref. 44 for a review), mean C_{50} was sampled between 0.43 (reported for V1)³¹ and 0, and its standard deviation was fixed at 0.31 (reported for V1)³¹. The mean neuronal attentional contrast gain (the mean percentage reduction in C_{50} due to attention) was sampled between 0% (no attention effect) and 100% (maximal attention effect), and its standard deviation was sampled between 0% and 200%. The mean and standard deviation for the parameter n were 2.5 and 1.4 (reported for V1)³¹, and those for b were 0.1 and 0.2; a was set to unity. See text and equation (1) for an explanation of these parameters. To clearly show the shape of each attention-effect curve, each curve has been normalized to its peak value. Though not shown, our simulation also produced peaked attention-effect curves that were consistent with contrast gain when we sampled the population-parameter values from wider ranges of means and standard deviations.



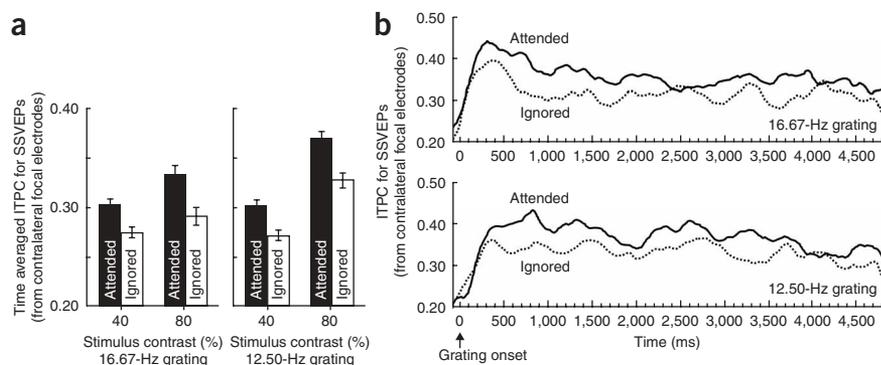


Figure 6 ITPC for second-harmonic SSVEPs averaged across contralateral focal electrodes, which are illustrated in **Figure 4a**. **(a)** Time-averaged ITPCs (averaged over the entire trial period) when gratings were attended versus ignored. ITPCs are shown separately for the two flicker frequencies (16.67-Hz and 12.50-Hz) and for the two highest contrasts (40% and 80%). Attention significantly increased ITPC in all conditions; $t_7 = 2.758$, $P < 0.03$ and $t_7 = 2.409$, $P < 0.05$ for 40% and 80% contrasts, respectively, for the 16.67-Hz flickered grating, and $t_7 = 3.608$, $P < 0.01$ and $t_7 = 2.878$, $P < 0.03$ for 40% and 80% contrasts, respectively, for the 12.50-Hz grating. **(b)** Time course of ITPCs when gratings were attended versus ignored. ITPCs (averaged across 40% and 80% contrasts) are shown separately for the 16.67-Hz grating (upper) and the 12.50-Hz grating (lower). Time zero corresponds to the grating onset. Note that it takes a few hundred milliseconds for the effects of attention on synchronization to emerge after the grating onset. The data have been averaged across observers and the error bars shown in **a** indicate ± 1 s.e.m., with individual variability in baseline ITPC removed.

that were localized to the contralateral posterior scalp regions, and attention boosted these focal responses in a manner that was consistent with the response gain hypothesis.

DISCUSSION

To understand how the voluntary allocation of spatially focused attention modulates neural activity, previous research has considered three hypotheses: contrast gain (the effects of attention being equivalent to increasing stimulus contrast), response gain (attention multiplicatively boosting stimulus-evoked neural activity) and activity gain (attention multiplicatively boosting the net neural activity). As discussed above, to date the evidence at the level of single neurons has been mixed. Here we investigated these hypotheses at the neural population level by using flickered stimuli and monitoring the corresponding SSVEPs. Voluntary visual attention multiplicatively increased the synchronized electrophysiological activity, which likely arose from contralateral neocortical regions in response to these stimuli. As attention did not affect the baseline activity, we have demonstrated attentional response gain at the neural population level.

There are at least two possible ways by which attention could increase SSVEPs in accord with response gain, even if attention increased neuronal spike rates predominantly in accord with contrast gain. First, a response gain pattern might emerge for a neural population when responses are averaged across neurons with a variety of contrast-response functions (showing different half-saturation contrasts and maximum responses) and various magnitudes of attention-based contrast gain. Note that we cannot make any firm predictions about SSVEPs on the basis of single-cell spike rate activity because SSVEPs reflect aggregate local field potentials, which are more closely associated with the synaptic activity of a neural population than with spike rates^{19,30}. Nevertheless, we conducted a simulation analysis to show that attentional response gain at the population level cannot emerge from a linear summation of attentional contrast gain on single-cell spike rate activity. We assumed that each neural contrast-response function was reasonably approximated by the Naka-Rushton equation (a neural response, R , as a

function of contrast, C ; equation (1))³¹ and that the parameters a (maximum response relative to baseline), C_{50} (half-saturation contrast), n (steepness of the contrast-response function) and b (spontaneous baseline response) were normally distributed across the responding population of neurons.

$$R(C) = a \frac{C^n}{C^n + C_{50}^n} + b \quad (1)$$

We considered a wide range of population means and standard deviations for the distributions of these contrast-response parameters, including published values for monkey V1 (ref. 31) and V4 (ref. 7) neurons. In simulating the effects of attention, we assumed that the magnitude of attentional contrast gain (the reduction in the C_{50} parameter with attention) was normally distributed across the responding neurons, and we tested a wide range of population means and standard deviations for the attention effect (the mean percentage reduction in C_{50} was varied from 0% (no attentional contrast gain) to 100% (maximum attentional contrast gain) with the standard deviations ranging from 0% to 1,000%). For

each simulated neural population, we computed the average attention effect (the difference between attended and ignored responses) as a function of contrast. All of our simulated population-averaged attention effects peaked at mid-range contrasts (**Fig. 5**), consistent with contrast gain (**Fig. 1a**). This indicates that the average population responses from neurons with a variety of contrast-response functions and attentional contrast gain magnitudes should still produce an overall contrast gain effect. Thus, it is unlikely that the attentional response gain effects we observed on SSVEPs were due to the simple averaging of contrast gain effects from individual neurons.

An alternative possibility is that attention increases the phase coherence of neural responses at the population level, in addition to producing contrast gain or a mixture of contrast, response and activity gain at the neuronal level. Because SSVEPs are measured as frequency-locked electrophysiological responses to flickered stimuli, increased SSVEPs could arise from increased amplitudes or from an increase in the coherence of underlying neural responses^{32,33}. One way to evaluate whether attention increased neural response synchronization is to examine intertrial phase coherence (ITPC)^{34,35}. ITPC provides an amplitude-independent measure of the degree to which stimulus-evoked EEG responses are phase-locked to the stimulus volleys. For example, when the neuronal responses underlying SSVEPs are not synchronized, there will be substantial random variability in the phase lags among those responses, producing SSVEPs with large variability in phase from one stimulus volley to another. In contrast, when the neuronal responses underlying SSVEPs become more synchronized to stimulus dynamics, there will be less random variability in the phase lags among those responses, producing coherent SSVEPs with less variability in phase from one stimulus volley to another. ITPC provides a measure of this phase consistency in terms of the degree to which EEG responses of a specific frequency are time-locked to stimulus dynamics. ITPC values vary from 0 (a complete absence of synchronization) to 1 (perfect synchronization).

Voluntary attention increased the average ITPC in the contralateral focal electrodes by $\sim 10\%$ for both 16.67-Hz and 12.50-Hz gratings at

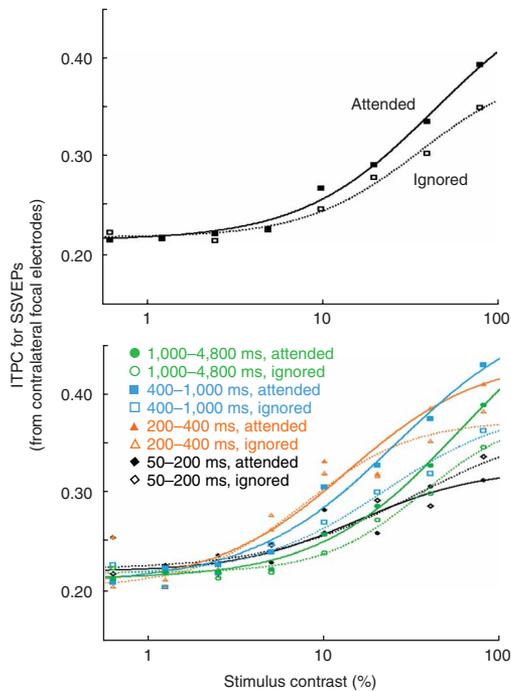


Figure 7 Contrast dependence of ITPC for second-harmonic SSVEPs (averaged across contralateral focal electrodes, see Fig. 4a) when gratings were attended versus ignored. Upper, time-averaged (50–4,800 ms) ITPC contrast-dependence functions. Lower, ITPC contrast-dependence functions shown separately for different time periods during sustained attention. The data have been averaged for the 16.67-Hz and 12.50-Hz gratings and across observers. The continuous curves indicate fits based on the Naka-Rushton equation; in the upper panel, r^2 values for the fits are 0.991 (attended) and 0.987 (ignored) for the 50–4,800-ms period; in the lower panel, r^2 are 0.692 (attended) and 0.933 (ignored) for the 50–200-ms period (black), 0.946 (attended) and 0.951 (ignored) for the 200–400-ms period (orange), 0.985 (attended) and 0.967 (ignored) for the 400–1,000-ms period (blue) and 0.994 (attended) and 0.985 (ignored) for the 1000–4,800-ms period (green). Note that, except for the earliest interval that shows no attention effect, ITPC contrast-dependence functions for all of the other periods show a response gain-type profile.

the higher end of the stimulus contrast range (40% and 80%; Fig. 6a). The time course of the ITPC (averaged across 40% and 80% contrasts) shows that the effect of attention emerged within 300–500 ms (Fig. 6b), which is within the temporal range of voluntary attention effects reported for single-cell spike rates^{1,12,36,37}.

A previous single-cell study¹² reported faster (within 50–150 ms) attentional boosting of gamma-range synchronization (and reduction of low-frequency synchronization) between single-cell spikes and local field potentials in V4. It is possible that it takes longer for synchronization to develop over the large population of neurons that generate SSVEPs. Additionally, the two studies examined different types of neural synchronization; whereas the single-cell study found attentional modulations of local neuronal synchronizations within intrinsic frequencies, we found attentional enhancement of population synchronization to stimulus dynamics. Future research is necessary to clarify the relationship between these two types of synchronization. We also acknowledge the need to be cautious in comparing SSVEP results with single-cell results. Specifically, single-cell studies have examined attention effects when stimuli are presented within the neurons' classical receptive fields, whereas SSVEPs combine responses from a large population of neurons, including those for which the stimulus falls on the border of, or outside, their classical receptive fields. Future single-cell research, in which attention effects are examined using large stimuli spanning multiple receptive fields, would be necessary to understand how our SSVEP results relate to attention effects on single neurons.

An important aspect of our results is that the attentional boosting of ITPC increased with contrast, indicating that attention enhanced population synchronization most strongly for high-contrast stimuli (Fig. 7). This response gain-type attentional enhancement of ITPC occurred throughout the time period of sustained attention (200–400-ms, 400–1,000-ms and 1,000–4,800-ms intervals), except for the initial period (50–200 ms), in which no attentional modulation of ITPC occurred (Fig. 7). Overall, converging evidence from our simulation (Fig. 5) and ITPC analyses suggests that the observed attention-based multiplicative boost in SSVEPs is attributable to attentional modula-

tion of neural response synchronization. Further research will be necessary to understand how voluntary attention increases neural response synchronization, but a recent computational study suggests that one possible mechanism might be for attention to reduce the driving current to inhibitory neurons¹⁸.

Our results might be criticized on the grounds that natural images are not flickered. In fact, rapid luminance modulations frequently occur in both natural and artificial environments—rippling water, motion through a textured environment, rapid saccades, micro saccades that always occur even during voluntary eye fixation³⁸, TV displays and artificial illuminations that generate periodic flicker. Thus, one might argue that flickered stimuli are more ecologically valid²³ than the briefly flashed stimuli that are often used in visual attention research. Furthermore, our ITPC analysis has shown that attention increases phase-locking of SSVEPs to rapid changes in luminance, suggesting that attention increases the synchronization of neural population responses to dynamic signals from an attended stimulus. Because retinal stimulation is nearly always dynamic, it is plausible that the synchronization-based multiplicative attention mechanism demonstrated here is also operational in natural situations.

To conclude, visual sensitivity is enhanced for stimuli presented at the focus of attention. Many previous studies have investigated the neural mechanisms underlying the beneficial effects of attention on performance. The present findings add to this body of research by implicating separate functions for the effects of attention on neural population activity and neuronal spike rate activity.

On a fine spatial scale—that is, when attended and ignored stimuli activate many of the same neurons—attention appears to increase the influence of the attended stimulus relative to the influence of the ignored stimulus in determining neuronal activity. This mechanism has been formalized in the biased-competition model^{36,39}. In this model, attention can affect the relative weighting of signals from attended and ignored stimuli and can mediate attention effects on high-contrast and low-contrast stimuli if both attended and ignored stimuli fall within a single receptive field. For example, when a high-contrast preferred stimulus and a high-contrast null stimulus both fall within a single neural receptive field, attention can boost the neuron's response by preferentially weighting the signal from the preferred stimulus and can reduce the neuron's response by preferentially weighting the signal from the null stimulus; the response would be intermediate if both stimuli were ignored. Some suggest that this biased-competition mechanism is closely associated with contrast gain because both selective attention and the relative contrast of competing stimuli similarly modulate the relative influence from within-receptive-field stimuli^{10,11}. A biased competition–contrast gain mechanism can thus

mediate attentional boosts in visual sensitivity for low- to moderate-contrast stimuli in general (Fig. 1a) and also for high-contrast stimuli when the competing stimuli are near enough to activate a single receptive field. Note that increasing neuronal activity via response or activity gain would be ineffective for selecting among within-receptive-field stimuli; in that case, input modulation would be necessary to accomplish attentional selection, either via contrast gain or via response (or activity) gain occurring in the previous processing stage in which the competing stimuli fall in separate receptive fields.

The biased competition–contrast gain mechanism, however, would be ineffective when attended and ignored stimuli were both high contrast and presented relatively far apart, so as not to fall within a single neuron's receptive field. For example, in our experiment, the two gratings were presented in opposite visual hemifields. The attended and ignored gratings would have activated separate receptive fields in nearly all of the cortical visual areas throughout the ventral pathway (V1, V2, V4, through the inferotemporal cortex) thought to be closely associated with object perception and pattern visibility^{40–42}. Even in the inferotemporal cortex, where visual neurons have very large receptive fields, neurons respond primarily to contralateral stimuli regardless of the direction of attention³⁷. In such circumstances, our results implicate a synchronization-based attention mechanism that multiplicatively enhances population neural activity.

In summary, a biased competition–contrast gain mechanism can modulate neuronal spike rates for both low- to moderate-contrast stimuli and spatially proximate stimuli (regardless of contrast). Subpopulations of neurons showing response and activity gain properties may extend attention effects across a broader range of contrasts⁷. However, an additional synchronization-based response gain mechanism, operating at the neural population level, allows robust attentional selection of the high-contrast stimuli typically encountered in everyday life even when attended and ignored stimuli are too far apart to be detected by the same neuron's receptive field. Both neuronal and synchronization-based mechanisms of attention may operate concurrently to fulfill the demands of attentional regulation in diverse environmental circumstances.

METHODS

Observers. Eight observers with normal or corrected-to-normal vision participated as paid volunteers after giving informed written consent. The group included five men and three women. Their ages ranged from 23 to 45 years.

Stimuli. We displayed stimuli on a 19-inch CRT monitor set to a 100-Hz refresh rate. We presented two identical square-wave modulated circular gratings (1.1 cycles per degree in fundamental spatial frequency) to the left and right visual hemifields (Fig. 2a).

We always flickered the two gratings at different frequencies (12.50 Hz and 16.67 Hz, with assignment to visual hemifield randomized across trials). We induced flicker by modulating the luminance of the concentric rings symmetrically (darker and lighter) against the mid-gray (64.7 cd m⁻²) background, which prevented the creation of negative afterimages. Because visual neurons are primarily driven by luminance changes, we define the contrast, C , of the flickered gratings as, $C = (L_{\text{light}} - L_{\text{dark}}) \times (L_{\text{light}} + L_{\text{dark}})^{-1}$, where L_{light} and L_{dark} indicate the luminance during the light and dark phases, respectively.

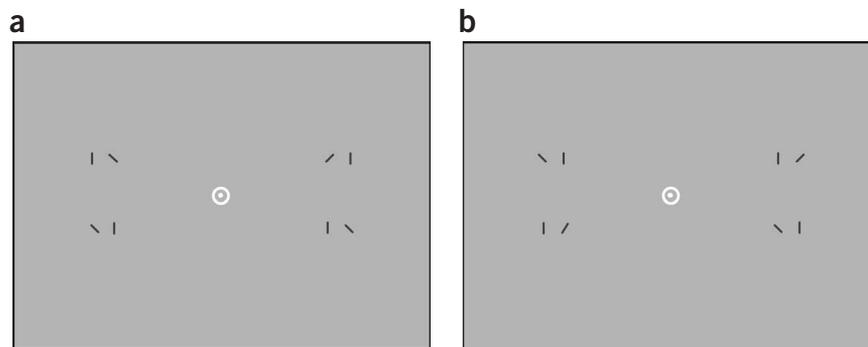


Figure 8 Examples of probe displays for the control experiment. (a) A target-present display (the target is the pair of identically oriented oblique lines at the location of the left grating). (b) A target-absent display (oblique lines are oriented differently within each pair). Vertical distractors were added so that grouping did not create an easily detectable emergent feature.

Experimental procedure. The observer initiated each trial by a button press (Fig. 2b). A central arrow (attention cue) then appeared for 2 s to indicate which grating (left or right) the observer was to attend to during that trial. Following a 1-s fixation screen, the two flickering gratings appeared. During the subsequent 4.8-s period, the observer voluntarily attended to the cued grating, while maintaining eye fixation at the central fixation marker and attempting to withhold blinks.

We directly manipulated attention by instructing the observers to sustain attention to the cued grating and ignore the other grating. We chose this method, rather than indirectly manipulating attention by using a visual task, so that SSVEP modulations could be attributable to voluntary spatial attention without potential task-related confounding factors. Behavioral^{4,13,43,44} as well as fMRI⁴⁵ results have provided evidence that human observers can reliably allocate attention when instructed to do so. The fact that we obtained substantial attentional boosting of stimulus-selective contralateral SSVEPs provides evidence that our observers successfully allocated attention to the cued grating.

To verify that our manipulation of attention produced behavioral effects that were independent of grating contrast, we conducted the following control experiment. The trials were identical to those in the SSVEP experiment (Fig. 2b), except that we presented a cue instructing the observer to attend to both gratings on half of the trials and we measured the effects of attention using a probe display that was flashed for 100 ms. We presented the probe display (Fig. 8) 500 ms after the grating onset, as the time course of ITPC (Fig. 6b) indicated that observers fully allocated their attention by 500 ms. The target in the probe display was defined by a pair of oblique lines, identical in orientation, that occurred at the location of one of the gratings. The target always occurred at the location of the attended grating when the observer attended to only one grating (cue validity was 100%). Because we presented the targets among feature-matched distractors, they did not attract attention, nor were they easily detectable when the observer distributed attention across the display⁴⁶. Thus, the experiment provided a sensitive measure of attention allocation, where successfully focused attention should have resulted in faster and more accurate target detection at the location of the cued grating. We adjusted the contrast of the probe display for each grating contrast and for each observer so that the target-detection performance in the distributed-attention condition was equivalent for all of the grating contrasts. We tested three of the eight observers who participated in the SSVEP experiment, using 5%, 20% and 80% randomly intermixed grating contrasts, with 384 trials per observer. All of the observers produced both faster response time and greater accuracy in the focused-attention condition (while attending to only one grating) than in the distributed-attention condition (while attending to both gratings) for all of the grating contrasts. Average response times were: 769 ms (focused) versus 982 ms (distributed) for the 5% contrast grating (a 213-ms advantage), 831 ms versus 950 ms for the 20% contrast grating (a 119-ms advantage) and 781 ms versus 972 ms for the 80% contrast grating (a 191-ms advantage). Average accuracies were: 85% (focused) versus 73% (distributed) for the 5% contrast grating

(a 12% advantage), 85% versus 74% for the 20% contrast grating (an 11% advantage) and 89% versus 73% for the 80% contrast grating (a 16% advantage). Thus, these results verified that our instructional manipulation of attention produced similar behavioral effects at different grating contrast levels, suggesting that our observers allocated a comparable amount of attention to gratings of different contrasts.

In the SSVEP experiment, there were 32 trial types: 2 directions of attention (left or right), 2 assignments of flicker frequencies (12.50 Hz on the left and 16.67 Hz on the right, and vice versa) and 8 contrast levels (0.00625, 0.0125, 0.025, 0.05, 0.10, 0.20, 0.40, or 0.80). We ran each trial type 20 times while randomly varying and counterbalancing the 3 factors across trials. We tested each observer for a total of 640 trials in blocks of 160 trials. We initially ran several practice trials and also gave breaks as necessary.

Data recording and analysis. We recorded EEG activity using tin electrodes embedded in an elastic cap at locations distributed relatively evenly across the scalp. For 59 EEG channels, the right mastoid served as the reference. We used four additional channels for monitoring vertical and horizontal electro-oculographic (EOG) activity. We lowered electrode impedances to 5 k Ω , amplified signals with a bandpass of 0.3–200 Hz and digitized them at 1,000 Hz.

We rejected individual trials from further analysis on the basis of blink or muscle-activity artifacts detected by vertical EOG activity. In addition, to retain only the trials in which central eye fixation was maintained, we recursively rejected trials with the highest horizontal EOG activity until the average horizontal EOG activity for each condition (defined by each combination of attention allocation, flicker-frequency assignment, and contrast) for each observer was less than 5 μ V during the entire 4.8-s trial period. This criterion approximately corresponds to maintained central fixation within a visual angle^{22,47} of 0.5°. Following these artifact-rejection procedures, we retained a mean of 89% of the trials.

To exclude the initial transient response to the grating onset, we analyzed EEG waveforms recorded from 526 ms to 4,621 ms after grating onset (except for the time course analysis of ITPC which included the entire trial period). This yielded 4,096 (2¹²) data points per trial. Reducing the number of EEG data points from each trial to a power of 2 is optimal for fast Fourier transform (FFT) analysis. We averaged EEG waveforms from the 59 scalp electrodes separately for each condition and for each observer and then we re-referenced the average waveforms to the average of left and right mastoid recordings.

To extract SSVEP activity that was synchronized to the stimulus flicker, we subjected each re-referenced average waveform (corresponding to a specific condition) from each scalp electrode to an FFT. We then computed the SSVEP amplitude as the Fourier band-power within the range of 0.976 Hz centered at the second harmonic of the stimulus flicker frequency. Because the luminance flicker we used was symmetric about the mid-gray background (Fig. 2), the fundamental-frequency responses (for example, first harmonic) from the non-frequency doubling cortical simple cells would have mostly averaged out in SSVEPs due to the random spatial distribution of the ON and OFF sub-regions of their receptive fields with respect to the flickered stimuli^{2,48–50}. Any remaining power at the fundamental frequencies would then be due to overall unequal activation of the ON and OFF sub-regions, unbalanced amplitudes of ON and OFF responses or both. The effects of attention on such residual responses would be difficult to interpret. In contrast, frequency-doubling responses from cortical complex cells⁵⁰ are largely spatial-phase invariant and they contribute robustly to SSVEPs^{48,49}.

Because the absolute values of EEG signals vary widely from observer to observer, we standardized the data from the eight observers before combining them. Specifically, we z-transformed the SSVEP amplitude from each electrode, in each condition and for each observer based on the observer's overall average and standard deviation of SSVEP amplitudes across all scalp electrodes and across all of the conditions.

ACKNOWLEDGMENTS

This work was supported by a US National Institutes of Health Grant EY14110 to S.S. and by National Institutes of Health Grant NS34639 and US National Science Foundation Grant BCS0518800 to K.A.P.

COMPETING INTERESTS STATEMENT

The authors declare that they have no competing financial interests.

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