Stimulus repetition affects both strength and synchrony of macaque inferior temporal cortical activity.

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Abstract

Repetition of a visual stimulus reduces the firing rate of macaque inferior temporal (IT) neurons. The neural mechanisms underlying this adaptation or repetition suppression are still unclear. In particular, we do not know how the IT circuit is affected by stimulus repetition. To address this, we measured simultaneously local field potentials (LFP) and multi-unit spiking activity (MUA) at 16 sites with a laminar electrode in IT while repeating visual images. Stimulus exposures and inter-stimulus intervals were each 500 ms. The rhesus monkeys were performing a passive fixation task during the recordings. Induced LFP power decreased with repetition for spectral frequencies above 60 Hz but increased with repetition for lower frequencies, the latter because of a delayed decrease in power when repeating a stimulus. LFP-LFP and MUA-LFP coherences decreased with repetition for frequencies above 60 Hz. This repetition suppression of the MUA-LFP coherence was not due to differences in firing rate since it was present when spike counts were equated for the adapter and repeated stimuli. For the frequencies between 15 and 40 Hz, the effect of repetition on synchronization depended on the electrode depth: for the putative superficial layers synchronization was enhanced with repetition, while the LFPs of the putative deep layers decreased their synchrony across layers. The between-sites, trial-to-trial covariations in MUA (“noise correlations”) decreased with repetition, but this might have reflected repetition suppression of the firing rate. This work demonstrates that short-term stimulus repetition affects the synchronized activity, in addition to response strength, in IT cortex.
Keywords

Inferior temporal cortex, multi-unit activity, local field potentials, adaptation, synchronization.
Introduction

The responses of many macaque inferior temporal (IT) neurons decrease with stimulus repetition (Gross et al. 1967, 1969; Baylis and Rolls 1987; Miller et al. 1991a, 1991b; Riches et al. 1991; Sobotka and Ringo 1993; Vogels et al. 1995; Sawamura et al. 2006; McMahon and Olson 2007; Verhoef et al. 2008; Liu et al. 2009; De Baene and Vogels 2010; Kaliukhovich and Vogels 2011). This “repetition suppression” (Desimone 1996) or “adaptation” effect (Ringo 1996) has aroused interest because of the widespread use of adaptation paradigms in fMRI studies (Grill-Spector et al. 2006). Recent studies suggest that adaptation of spiking activity of single macaque IT neurons results from suppression of the input of the neuron and/or synaptic depression (Sawamura et al. 2006; Liu et al. 2009; De Baene and Vogels 2010), at least in paradigms using stimulus presentations of 500 ms or less with inter-stimulus intervals of 1 s or less. This conclusion rests partially on the observation that the amount of the spiking activity to the adapter does not predict the degree of adaptation, as would be expected from firing rate dependent adaptation.

Several studies have demonstrated that the responses of cortical neurons can show synchronized activity at different time scales, which can be oscillatory in nature (Buzsaki 2006). Although the functional consequences of such synchronized activity are still unclear, it can be viewed as an indicator of network activity. Single IT neurons are members of a cortical network, receiving local and distant input, and thus adaptation may reflect and influence network properties. Here, we ask whether stimulus repetition changes the network activity, in particular the synchronization of IT neuronal activity.
Computational studies have made different predictions regarding the effect of adaptation on network activity, suggesting that adaptation increases stimulus-locked synchronized activity in subgamma bands (< 30 Hz; Gotts 2003) or predicting reduced gamma band oscillations with stimulus repetition (Moldakarimov et al. 2010). Recent studies in macaque areas V1 and V4 reported enhanced synchronized activity following adaptation with a short inter-stimulus interval (ISI; 100 ms) for particular frequency bands, including the gamma band (Hansen and Dragoi 2011; Wang et al. 2011). Furthermore, Gutnisky and Dragoi (2008) found decreased trial-to-trial spiking activity correlations following brief adaptation in V1 but such effect was unreliable in V4 (Wang et al. 2011). These findings in early visual areas using short ISIs are difficult to extrapolate to IT, partially because of the typically longer ISIs employed in that region. Moreover, opposite effects of attention on V1 and V4 gamma band synchronization (Chalk et al. 2010) demonstrate that extrapolation of synchrony effects across areas is unwarranted.

To determine whether stimulus repetition not only affects spiking activity but also the degree of synchronized activity in IT, we measured multi-unit spiking activity (MUA) and local field potentials (LFPs), simultaneously, to two successively presented stimuli with an ISI of 500 ms, using a 16-channel laminar electrode. Analysis of the LFP-LFP and of MUA-LFP coherences showed frequency and lamina-dependent effects of stimulus repetition on synchronized activity.
Materials and Methods

Subjects

Two rhesus macaques (Macaca mulatta; male monkey G and female monkey K, weighing 7.2 and 7.6 kg, respectively, both left hemisphere) served as subjects. Before the present study, both monkeys served as subjects in the adaptation study of Kaliukhovich and Vogels (2011). Animal care and experimental procedures met the national and European guidelines and were approved by the Ethical Committee of the K.U. Leuven Medical School.

Details about implants and surgery can be found in Kaliukhovich and Vogels (2011) and will only be summarized briefly. The placement of the plastic recording chamber was guided with a preoperative magnetic resonance imaging (MRI) scan and verified with MRI scans obtained at the beginning and in between recording sessions. Reliable estimations of the recording positions were obtained by the visualization of glass capillaries filled with the MRI opaque copper sulfate (CuSO₄) inserted into the recording chamber grid (Crist Instruments) at predetermined positions. Recording positions were estimated based on the MRI visualization of these markers combined with the microdrive depth readings of the white/gray matter transitions relative to the grid base.

Recordings were made from the lower bank of the superior temporal sulcus (STS). The anterior-posterior coordinates of the estimated recording positions ranged between 16 and 18 mm, and 15 and 17 mm anterior to the auditory meatus in monkeys G and K, respectively. The medial-lateral coordinates ranged between 22 and 24 mm, and
20 and 21 mm lateral to the midline in monkeys G and K, respectively. Based on the MRI, recordings were performed in STS area TEa of Seltzer and Pandya (1978).

Recordings

LFPs and spikes were recorded simultaneously using a 16-channel Plextrode U-Probe (Plexon Inc.). The inter-contact (channel) spacing was 100 µm with electrode sites linearly arranged on a single shaft (outer diameter of 185 µm). The U-Probe was lowered with a Narishige microdrive through a guide tube that was fixed in a Crist grid. The grounded guide tube and metal shaft served as the reference. Recordings were made using a Plexon data acquisition system. Recorded signals were preamplified with a headstage having an input impedance of > 1GΩ. The signals were split into spiking activity (band-passed signal between 250 Hz and 8 kHz) and LFPs (band-passed signal between 0.7 and 170 Hz sampled at 1 kHz). Spiking activity was thresholded online and spike waveforms were saved at 40 kHz. LFP waveforms were saved at 1 kHz. Offline Sorter (Plexon Inc.) was used to remove noise or electrical artefacts from the spiking activity but no further spike sorting was performed. Thus the spiking data reflected MUA.

The U-Probe was positioned so that visually-driven MUA was present on most if not all channels and a visual-driven LFP response was clearly visible for each channel. Monitoring the stimulus-triggered LFPs online proved to be very useful for identifying responsive regions in the STS and positioning the electrode.
After positioning the U-Probe in the STS, we waited for approximately 2 hours before performing the recordings to ensure good recording stability. In addition, this long waiting period usually improved the signal-to-noise ratio of the electrode signal.

Eye position was measured online with an infrared-based eye tracking system (ISCAN EC-240A, ISCAN Inc.; 120 Hz sampling rate). The analog eye movement signal was saved using a sampling frequency of 1 kHz. Eye positions, stimulus and behavioral events were stored for later off-line analysis on a computer which was synchronized with the Plexon data acquisition system.

Stimuli and tests

The stimulus set consisted of 52 color images including human and monkey faces, human and monkey bodies, mammals, birds, fish, snakes, insects, trees, fruits, fractals and manmade objects. The maximum size of the objects was approximately 5° of visual angle. The stimuli were presented on a uniform gray background with their centers of mass positioned in the center of a CRT display (frame rate 60 Hz) located 61 cm from the subject’s eyes.

After a two hour waiting period, the two images to be used during the adaptation test were selected by means of a preliminary test. We presented the 52 images while the animal was performing the passive fixation task. In this preliminary test, a trial started with the onset of a red target square (size: 0.17°), shown in the center of the display, that the monkey had to fixate. After 500 ms of stable fixation, a stimulus was presented for 500 ms. The animal had to maintain fixation during the stimulus presentation and for 475
ms post-stimulus in order to obtain a fluid reward. The different images were presented in
a random order. Based on the spiking responses to the stimuli in the different channels,
we selected two images which elicited a response in several of the channels.

Using the two selected images, A and B, we ran the following adaptation test
(Fig. 1). Two stimuli, adapter and test, were presented for 500 ms each, separated by a
blank screen (ISI) for 500 ms. The stimuli within a trial were either the same (AA or BB
trials; repetition trials) or different (AB or BA trials; alternation trials) images. Subjects
were required to maintain fixation from 500 ms prior to stimulus onset until 475 ms after
the test stimulus ended. Continuous fixation in this 2475 ms interval was followed by a
fluid reward. Any break in fixation during this interval aborted the trial. The fixation
window sizes ranged from 1.1 to 1.8° horizontally and 1.6 to 2.6° vertically across
monkeys. Aborted trials were not analyzed further. The time interval between the test
stimulus end and adapter stimulus onset for the next trial or, in the case of aborts,
between the end of the aborted stimulus and the beginning of the adapter stimulus of the
next trial varied across trials since it depended on the oculomotor behavior of the animal.
The medians of these time intervals ranged from 3326 to 3494 ms across monkeys, with
minima ranging from 2856 to 2923 ms. These values are well above the 500 ms ISI of a
stimulus sequence. The order of the 4 different trial sequences (AA, BB, AB and BA)
was pseudorandomized with the constraint that the adapter image of a trial always
differed from the last presented image of the preceding un aborted or aborted trial. The
proportion of AA, BB, AB and BA un aborted trials was similar. The mean number of
trials per condition was 123.5 (minimum = 86 trials, maximum = 156 trials).
Data analysis

Spiking activity

A site was considered to be responsive to a particular stimulus (A or B) if the mean firing rate to that stimulus as adapter or test was significantly greater than the mean baseline firing rate (two-sided Wilcoxon matched pairs test, $P < 0.05$). The baseline firing rate was measured within a 200 ms time window that started 140 ms before adapter stimulus onset. Firing rates for the adapter and test stimuli were computed within 500 ms windows starting 60 ms after stimulus onset. Only those combinations of sites and stimuli for which there was a significant response were used in the further analyses, except stated otherwise. The use of only responsive sites assured that the analyzed sites were located in responsive cortex. Using this criterion, 6.9 and 28.1% of the stimulus x site combinations were removed from the recorded dataset in monkeys G and K, respectively.

Since preliminary analyses showed that the adaptation was stronger in the early than in the late phase of the response to a stimulus, we employed in most analyses two analysis windows for each stimulus: an early window from 60 till 310 ms poststimulus onset and a late window from 310 till 560 ms. Note that response in the following text refers to gross firing rates, unless otherwise stated.

Local Field Potentials

LFPs were filtered offline with a digital 50-Hz notch filter (48-52 Hz fourth-order Butterworth FIR filter; Fieldtrip Toolbox, F.C. Donders Centre for Cognitive
Neuroimaging, Nijmegen, The Netherlands; http://www.ru.nl/fcdonders/fieldtrip). Trials in which the signal was < 1 or > 99% of the total input range were excluded (median % removed trials across all conditions and animals: 0.4%). We employed two methods for spectral analysis of the LFPs: Morlet wavelet based – as by De Baene and Vogels (2010), and Kaliukhovich and Vogels (2011) – and multitaper spectral estimation methods. By convolving single-trial data using complex Morlet wavelets (Tallon-Baudry et al. 1997) and taking the square of the convolution between the wavelet and signal, the time-varying power of the signal for every frequency was obtained. Averaging spectral maps (power as a function of frequency and time) across trials for a given site produces a spectral map of that site. The complex Morlet wavelets had a constant center frequency-spectral bandwidth ratio \( \left( \frac{f_0}{\sigma_f} \right) \) of 7, with \( f_0 \) ranging from 1 to 170 Hz in steps of 1 Hz. The spectral maps of sites were normalized at each frequency by the average power within the baseline window of 200 ms before adapter onset for each condition.

Multitaper methods (Percival and Walden 1998) were used to estimate the spectrum and cross-spectrum for computation of the coherency (see below). We employed 1 and 5 discrete prolate spheroidal sequence tapers (Slepian functions) for the frequencies from 1 till 30 Hz and from 30 to 170 Hz, respectively, with a duration of 350 ms given a spectral resolution of ±2.9 and ±8.6 Hz. The spectra were estimated in steps of 10 ms and 2.9 Hz. Before performing the multitaper spectral analysis, the average LFP for a condition and site was subtracted from the LFP waveform of each trial of that site and condition.
Coherency analysis

LFP-LFP and MUA-LFP coherencies were computed for pairs of sites. For the calculation of coherencies, both signals were always from different sites. LFP-LFP and MUA-LFP coherencies were computed using the multitaper-based estimates of the spectra and the cross-spectrum of the two signals following the method of Jarvis and Mitra (2001) using Chronux software (http://www.chronux.org). Coherence was defined as the absolute value of the coherency. A coherence value of 1 indicates that the two signals have a constant phase relationship and amplitude covariation, and a value of 0 indicates no phase relationship. Computation of MUA-MUA coherences produced low unreliable values in both animals, which were not analyzed further.

Although MUA-LFP coherence is a power-normalized measure, it can depend on the number of spikes that enters its computation. To control for the contribution of spiking rate differences when comparing the coherence values for two different stimuli, e.g. adapter and test stimuli, we equated the firing rates for the two stimuli before computing the spectra (Gregoriou et al. 2009; Verhoef et al. 2011). For each site and condition, we equated the average firing rate computed in 1 ms bins within an interval of 1000 ms that started 250 ms before stimulus onset by randomly removing spikes of the corresponding bin for the stimulus with a larger firing rate at that bin. The result of this procedure was that the average peri-stimulus time histograms (PSTHs) were equal for the two stimuli within the 1000 ms interval at 1 ms resolution. Thus, possible differences in MUA-LFP coherences between, for example, adapter and test stimuli cannot be due to differences in spiking rate between these stimuli. When equating the responses to the test
stimuli (e.g. A) in repetition (AA) and alternation (BA) trials, we also equated the number of trials in both conditions. This avoids possible differences in computed coherence levels (bias) due to a different number of trials. Note that since adapter and test stimuli occurred in the same trial these stimuli have automatically the same number of presentations.

A second control ensured that the coherence reflected within-trial synchronization and not stimulus-evoked changes in response locked to stimulus onset. The latter evoked responses should be present on all trials and thus can be isolated by computing coherency for signals of different trials of the same condition. This shuffle-correction permutes the order of trials for one of the two signals, recomputes the coherence for the permuted data and then subtracts the shuffle-based coherences from the original coherence values. Thus, the shuffle-corrected coherence is the pure within-trial synchrony of the two signals.

Before subtracting the shuffled coherences from the original ones, we transformed the coherence values using the Fisher transform (arctanh(coherence)) which stabilizes coherence variance (Bokil et al. 2007). All coherence values shown in the present paper are shuffle-corrected.

Statistical analyses

For each stimulus x responsive site combination, we computed adaptation indices for the different analysis windows as follows:

$$ AI = \frac{S1 - S2}{S1} \cdot 100, $$

where $S1$ and $S2$ are the mean net responses (baseline firing rate subtracted) to the adapter and test stimuli. To have a fine-grained analysis of variations in the degree of
adaptation as a function of time, we computed for each 10 ms wide bin an adaptation contrast (AC) index (Kaliukhovich and Vogels 2011), defined as:

\[ AC = \frac{S_1 - S_2}{S_1 + S_2}, \]

with \( S_1 \) and \( S_2 \) being the raw spiking response or normalized power for the adapter and test stimuli, respectively. In the case of spectral power, the AC indices were computed for each frequency and time bin. The AC index has the advantage that it is symmetrical around zero, i.e. equal absolute indices when the relative differences in signals to both stimuli are of the opposite sign.

For statistical testing of differences in coherences between adapter and test stimuli for different frequency bands and early and late response phases, we averaged the coherences within each response phase and each of the following frequency bands: 8.6-11.4 Hz (labeled “alpha”), 14.3-28.6 Hz (“beta”), 31.4-57.1 Hz (“low gamma”), 60.0-97.1 Hz (“middle gamma”) and 100.0-168.6 Hz (“high gamma”). These analyses were performed on the shuffle-corrected Fisher transformed coherences. Analyses using non-transformed coherences produced highly similar results. Note that the frequency band labeled here as “middle gamma” corresponds to the “high gamma” band of De Baene and Vogels (2010), and Kaliukhovich and Vogels (2011). For each analysis window (early and late; see above) and frequency band we concatenated the mean coherence values of the responsive pairs for stimuli A and B. We performed a two-way repeated measures ANOVA on these coherence values for each monkey separately, with frequency band and adapter x test stimuli as factors. In addition, we performed comparisons of the coherence values of the adapter and test stimuli, averaged for each frequency band, using a randomization test. For each analysis window (early and late) and frequency band we
concatenated the mean coherence values of the responsive pairs for stimuli A and B and
computed a paired t-test for the coherence values of the adapter and test stimuli across
pairs. To correct for the multiple comparisons across frequency bands we followed the
procedure of Fries et al. (2008). Briefly, for each pair of sites we randomly assigned the
adapter or test label, recomputed the t-score for each frequency band and then kept the
minimum and maximum t-score across frequency bands. This was done 1000 times so
that we obtained a “null” distribution of 2000 t-scores (1000 minima and 1000 maxima).
An observed t-score was deemed significant (corrected \( P < 0.05 \)) when it was larger than
the 97.5th or smaller than the 2.5th percentile of the “null” distribution. The same
statistical procedure was employed to test whether the coherences for a test stimulus (e.g.
A) following the same (A) versus a different (B) adapter image differed significantly.

**Analysis of eye movements**

We analyzed the saccadic frequencies and their amplitudes using the same
method as Kaliukhovich and Vogels (2011), following Engbert and Kliegl (2003). In
brief, horizontal and vertical eye position traces were low-pass filtered (< 40 Hz, 5th
order Butterworth filter, Matlab; Fries et al. 2008) to remove high-frequency noise and
then differentiated in time to obtain eye velocity. An eye movement lasting at least 16 ms
and of which the velocity exceeded 3 standard deviations of the eye velocity distribution
of the trial computed within the time interval of -500 to 1975 ms with respect to adapter
onset was classified as a saccade. The additional constraint was that any 2 successive
saccades had to be separated by a time interval of at least 50 ms (Ayzenshtat et al. 2010)
to avoid noisy fluctuations over the eye movement signal. Otherwise the second saccade
was discarded in favor of the first. We analyzed both the saccadic rates and amplitudes that were detected in the same analysis windows as those used for the spiking data analysis. In agreement with previous studies (Engbert and Kliegl 2003; Martinez-Conde et al. 2009; Kaliukhovich and Vogels 2011) saccadic peak velocities correlated with saccadic amplitudes for each combination of animal and condition (all Pearson correlation coefficients $r > 0.85$, all $P$-values $< 0.001$).
Results

We recorded, simultaneously, spiking activity and local field potentials using a laminar electrode (16-channel Plextrode U-Probe) located in the ventral bank of the rostral STS during an adaptation paradigm in which repetitions of the same images (AA or BB sequences) were randomly interleaved with successive presentations of different images (AB or BA sequences). We made 21 and 11 penetrations in monkeys G and K, respectively, yielding 319 and 149 sites responsive to either A or B (see Materials and Methods) in G and K, respectively.

Adaptation of multi-unit activity

Figure 2 shows the MUA and mean LFP for the AA and BB trials of one exemplar penetration in monkey G. The MUA was responsive for all 16 sites and decreased when repeating a stimulus within a sequence, i.e. an adaptation effect. The MUA response, averaged across all sites in which there was a significant response to at least A or B, decreased upon repetition of the same image (AA and BB trials; Fig. 3A,B) in each monkey. This adaptation effect was already present at the early phase of the response. The overall activity, including baseline, was higher in monkey K probably due to the lower setting of the threshold during recordings. The adaptation effect was stimulus-selective: the reduction in activity was less in the AB and BA sequences than for the AA and BB sequences, in agreement with previous studies that employed either familiar (De Baene and Vogels 2010) or novel (Kaliukhovich and Vogels 2011) stimuli.
This stimulus dependency of the adaptation proved to be significant in each animal for the first 250 ms of the response (60-310 ms window; two-way ANOVA on the mean responses to A and B presented as the adapter or test stimuli in repetition and alternation trials; interaction repetition x alternation and adapter x test factors: $P < 0.00003$ in each animal). During the later part of the response (310-560 ms window), monkey G did not show repetition suppression (ANOVA; no main effect of adapter x test factor; no interaction between the two factors), while monkey K showed weakly significant greater responses to the test stimuli in repetition compared to alternation trials (ANOVA: interaction $P < 0.05$).

For each stimulus x responsive site combination, we quantified the degree of adaptation in repetition trials by an adaptation index (AI), using the net responses in an analysis window of 500 ms (see Materials and Methods). The distributions of the AIs are shown for each monkey in Figure 3C,D. The median AIs were significantly larger than 0 in each animal (two-sided Wilcoxon signed rank test, $P < 10^{-28}$ in each monkey) and highly similar in the two animals: 33.6 and 34.7% in monkeys G and K, respectively. These values compare well with the median AI of 37% obtained by De Baene and Vogels (2010), who also used familiar stimuli but with a shorter stimulus presentation duration (300 ms) and inter-stimulus interval (300 ms). The large majority of the considered stimulus x responsive site combinations showed a decreased response with repetition (AI > 0 in 91.4 and 87.7% of the combinations in monkeys G and K, respectively). Note that the only selection criterion we employed in this analysis was the requirement for a significantly greater response to the stimulus (A or B), presented either as adapter or test.
Thus, the data of this unbiased sample show that adaptation is a highly common phenomenon in macaque IT.

Closer inspection of the population PSTHs of Figure 3 suggests that the adaptation effect was mainly present in the first half of the response. To assess this response time dependency of the adaptation effect, we computed AIs for the first and second half of the 500 ms window (see Materials and Methods). The median AIs for the early window were 50.5 and 48.0% in monkeys G and K, respectively, and were as expected significantly larger than 0 (two-sided Wilcoxon signed rank test, \( P < 10^{-36} \)). The median AIs for the late window were only 3.0 and 7.3% in each animal, and differed not significantly from 0 (two-sided Wilcoxon signed rank test, \( P > 0.27 \)).

**Adaptation effects on LFP power**

The LFPs of the example penetration of Figure 2 showed robust responses on all channels and as expected when recording from different layers the waveforms depended systematically on the channel depth. Also note the overall increase of the LFP amplitude with increasing depth, which was a typical observation and is consistent with Schroeder et al. (1998). The LFP waveform depended on the stimulus (A versus B) and differed between adapter and test stimuli. Since the adaptation effect of the LFP in IT depends on spectral frequency (De Baene and Vogels 2010; Kaliukhovich and Vogels 2011), we performed a spectral analysis of the LFPs. Figure 4A,B shows the mean normalized power as a function of time and frequency, computed using multitaper methods (see Materials and Methods), for all repetition trials (AA and BB; monkey G: \( N = 626 \)).
stimulus x responsive site combinations; monkey K: N = 253). Unlike in our previous studies, we subtracted the mean LFP of each condition from the LFP waveform of each trial of that condition before computing the spectral power. This was done to compute coherency (see below) and affects the power at the low frequencies.

Both monkeys showed a stimulus-driven increase in LFP power for the frequencies above 60 Hz, i.e. in the middle and high gamma bands. For lower frequencies, both animals showed a stimulus-driven decrease in power with respect to baseline for the frequencies between approximately 15 and 40 Hz and, in addition, an enhanced power at frequencies around 6 and 9 Hz in monkeys G and K, respectively. To examine the adaptation effect as a function of frequency and time in detail, we computed an adaptation contrast (AC) index for each frequency x time bin. Positive AC indices indicate repetition suppression, and negative AC indices indicate repetition enhancement. Except for frequencies below 15 Hz, the pattern of the AC indices as a function of time and frequency was similar in the two animals (Fig. 4C,D). Both monkeys showed repetition suppression at frequencies above 60 Hz mainly in the first half of the response, which fits the strong adaptation seen for the MUA in the early response window. This profound repetition suppression in the middle and high gamma bands agrees with De Baene and Vogels (2010) and Kaliukhovich and Vogels (2011). At frequencies between 15 and 40 Hz, both animals showed repetition enhancement, again only in the first half of the response. Inspection of Figure 4A,B shows that this enhancement is due to the later onset of the stimulus-induced decrease of power for the test compared to adapter stimulus. At frequencies below 10 Hz, repetition suppression is present.
To compare the temporal evolution of the adaptation effects for the LFP power and MUA we computed the Pearson correlation coefficients $r$ between the AC indices for the MUA and the AC indices of the LFP power at each frequency (both AC indices were computed in bins of 10 ms; Fig. 4C,D). In each animal, these correlation coefficients approximated 0.80 for frequencies above about 50 Hz and were strongly negative at the lower frequencies (Fig. 4C,D). These strong and significant correlations are due to the presence of repetition effects in the first half of the response and their absence in the later part of the response in both types of signals.

Coherence of LFP – LFP signals

To determine whether stimulus repetition affects the synchronization of LFPs, we computed LFP-LFP coherences for all possible pairs of simultaneously recorded sites. Following Takeuchi et al. (2011) we will restrict initially the analyses to those sites that were at least 300 µm apart (e.g. channels 1, 4, 7 etc.) with the constraint that the MUA of those sites needed to be responsive (ensuring within-cortex recordings). The mean shuffle-corrected Fisher transformed coherences for these selected pairs are plotted as a function of time and frequency for each monkey (G: N = 545 pairs; K: N =203 pairs) separately in Figure 5A,B. These are average coherences obtained in repetition trials (computed for conditions AA and BB separately), pooled across responsive site pairs. In both animals, LFP-LFP coherence decreased with spectral frequency. For the frequencies above 60 Hz, the LFP–LFP coherence increased during the stimulus presentation, especially in the first part of the stimulus periods. This is poorly visible in Figure 5B.
(monkey K), due to the color scale, but this increase in coherence upon presentation of the adapter in this animal can be appreciated much better when examining the time course of the LFP-LFP coherence (Fig. 6A). For lower frequencies, the pattern was more complex, although in both monkeys there was a tendency towards an increase in the beta range. Importantly, the increase in coherency appears to be stronger for the adapter compared to test stimulus. This can be seen clearly for the high frequencies, e.g. around 100 Hz, in Figure 5A.

To test quantitatively whether the LFP-LFP coherences differed between the adapter and test stimuli in repetition trials, we averaged shuffle-corrected Fisher-transformed coherence values in 5 different frequency bands for both the early and late response windows. For the early response window, a two-way ANOVA (see Materials and Methods) showed in each animal a significant main effect of the adapter x test factor \((P < 0.001\) in each animal) and a significant interaction between frequency band and adapter x test \((P < 0.001\) in each animal). In both animals (G: \(N = 545\) pairs; K: \(N = 203\)) the LFP-LFP coherences decreased significantly with repetition for all bands (randomization test; see Materials and Methods) during this response period, except for the low gamma band in monkey G which showed a significant increase of coherence with repetition (Fig. 6A). In monkey G, there was a pronounced stimulus-driven decrease in average LFP-LFP coherence in the low gamma band which was not present in the average coherences of the other animal. However, further analysis indicated that each animal could show a stimulus-driven decrease or increase in the low gamma band coherence depending on the depth of the analyzed channels. Indeed, the stimulus-driven decrease of the low gamma coherence was present when averaging coherences for the
upper 10 channels in monkey G and for the 5 upper channels in monkey K. Monkey K showed an increased stimulus-driven low gamma coherence when averaging the 10 deepest channels and this increase was also present in monkey G when averaging his 5 deepest channels. Thus, the apparent difference between animals can be explained by a combination of laminar effects on LFP-LFP coherence in this band and deeper recordings in monkey K compared to G. For the late response window, repetition suppressions were smaller and in two cases even failed to reach statistical significance (Fig. 6A), and for the high gamma band the coherence values for the test stimulus were significantly higher than for the adapter in monkey G and didn’t reach statistical significance in the other animal. Nonetheless, the interaction between frequency band and adapter x test factors was still highly significant ($P < 0.001$ in each animal). Examination of the time course of the coherence values for the different bands (Fig. 6A) indicates that in both animals the decrease in coherence with repetition for the frequencies above 60 Hz and in the beta band are not due to prestimulus differences in baseline coherence between the adapter and test stimuli. Note that the stimulus-driven changes in the computed coherence before stimulus onset in Figure 6 (and other Figures showing time courses of coherence) results from the 350 ms long window that was employed to estimate the spectra and cross-spectra.

To assess whether these effects on synchronization depend on adapter and test stimulus identity, we assessed whether the LFP-LFP coherences differed between a test image following the same image (repetition trials: A following A or B following B) compared to the same test image following a different image (alternation trials: B following A or A following B; monkey G: $N = 545$ pairs; monkey K: $N = 203$). For the
early response window, a two-way ANOVA with factors frequency band and repetition x alternation trials showed in each animal a significant main effect of the latter factor ($P < 0.001$ in each animal) and a significant interaction between the two factors ($P < 0.001$ in each animal). Randomization tests (see Materials and Methods) showed that the frequencies above 60 Hz showed a significant decrease in LFP-LFP coherence for the early period of the test stimuli in repetition compared to alternation trials (Fig. 6B). For the frequencies below 60 Hz, stimulus-specific repetition effects were significant for the beta band in monkey G and the alpha and low gamma bands in the other animal (Fig. 6B). This is in line with the higher coherence values for the adapter compared to test stimuli for these frequency bands in these animals (Fig. 6A). Examination of the time course of the coherence values (Fig. 6B) indicates that the latter stimulus-specific decreases in coherence with repetition and those for frequencies above 60 Hz are not due to prestimulus differences in baseline coherence between the adapter and test stimuli. Again, effects were smaller in the late response period (Fig. 6B), although the interaction of frequency band and repetition x alternation trials was significant in each animal (G: $P < 0.0001$; K: $P < 0.02$).

Overall, these data show that stimulus repetition affects significantly the degree of synchronization of LFP signals and such effects are mainly present in the early phase of response, as was the case for the effect of repetition on power and MUA.
**Coherence of MUA – LFP signals**

LFPs reflect mainly synaptic input, especially for lower spectral frequencies, while MUA corresponds to the output of neurons. Thus, MUA-LFP coherency informs about synchronization of synaptic input and neuronal output. We computed MUA-LFP coherence on the MUA and LFPs for the same pairs of sites (at least 300 µm apart) for which we computed the LFP-LFP coherence. The mean MUA-LFP coherences of those pairs are shown in Figure 7 for each monkey separately (G: N = 1090 pairs; K: N = 406). The Fisher transformed coherence values shown in that figure are shuffle-corrected and computed on the MUA that was equated for the adapter and test stimuli (see Materials and Methods). The mean coherence values are much lower than for LFP-LFP signals, which is not surprising given the more local nature of the MUA compared to the LFPs. There is an increase in coherence in the middle and high gamma range with stimulus presentation which appears to be stronger for the adapter compared to test stimulus in each of the two animals. Noteworthy is also the strong coherence after stimulus presentation in the beta and low gamma range. Interestingly, coherence decreases during stimulus presentation in this range, and this drop is delayed and weaker in the test compared to adapter stimulus. This is seen most clearly in monkey G between 20 and 40 Hz.

To obtain a quantitative measure of the MUA-LFP coherence values for the adapter and test stimuli, we again averaged the shuffle-corrected Fisher transformed MUA-LFP coherences in 5 frequency bands and for the early and late response periods (Fig. 8A). For the early response window, a two-way ANOVA showed in each animal a
significant interaction of frequency band and adapter x test stimuli (monkey G: $P < 0.0001$; monkey K: $P < 0.02$). MUA-LFP coherences in the high gamma band in monkey G and in the high and middle gamma bands in monkey K were significantly greater (randomization tests) for the adapter compared to test stimuli (Fig. 8A). These reductions in MUA-LFP coherences with repetition were not due to prestimulus differences in baseline (Fig. 8A). For the beta and low gamma bands, the opposite effect, i.e. an enhanced synchronization with repetition, was present which reached statistical significance in monkey G but not in K (randomization tests; Fig. 8A). This difference was already present well before stimulus onset, which at least partially reflects the increased coherence during the inter-stimulus interval in these bands. The increased coherence during test compared to adapter presentation in these bands also reflects the stronger decrease of coherence for the adapter compared to the test stimulus. This is seen most clearly for the low gamma of monkey G (Fig. 8A) and can also be appreciated in Figure 7. ANOVA showed a significant interaction of frequency band and adapter x test stimuli for the late response period in monkey G ($P < 0.002$) but not in K and effects were weak.

An ANOVA comparing the MUA-LFP coherence to the same test images in repetition and alternation trials for the 5 frequency bands showed a significant interaction between the two factors in monkey G for the early response period ($P < 0.0001$). Randomization tests showed significantly greater coherence values in the beta and low gamma bands for the test stimuli in repetition compared to alternation trials in the early response period and this is not due to baseline differences in coherence (Fig. 8B). In addition, there was a significant decrease of coherence in the alpha band in repetition compared to alternation trials (Fig. 8B). Unlike for the other bands, this difference was
also present before stimulus onset and since no difference before test stimulus onset is expected between repetition and alternation trials, this decrease in coherence should be interpreted with caution. No significant effects were present for the frequencies above 60 Hz, although examination of the time course of the coherences suggested a decrease of MUA-LFP coherence with repetition for the high gamma band (Fig. 8B). For the late response period, no effects were statistically significant.

The ANOVA showed neither a main effect of the repetition x alternation trials factor, nor an interaction effect in the early period in monkey K. However, the randomization test showed a significantly greater coherence for the test stimuli in alternation compared to repetition trials in the middle gamma band (Fig. 8B). This was not due to baseline differences in coherence and fits the significantly greater coherence for the adapter compared to test stimuli in this animal (Fig. 8A). For the later response window, ANOVA did show a significant main effect of the repetition x alternation trials factor ($P < 0.005$) and a significant interaction of the two factors ($P < 0.01$). This interaction mainly resulted from the significant increased coherence (randomization test) in the alternation compared to the repetition trials in the alpha band (Fig. 8B).

Overall, these data show that stimulus repetition affects significantly the degree of synchronization of LFP and spiking activity in IT.

Effects of channel depth on MUA and LFP responses

Although the STS is not perfectly horizontal and, thus, our penetrations were not perfectly orthogonal to the cortex, the upper sites were located on average in more
superficial lamina than the lower sites. Given the absence of histological verification of laminar recording positions in these animals and that Current Source Density analysis of the STS LFP data did not show a clear mid-lamina focus (data not shown), in agreement with Schroeder et al. (1998), we did not attempt to assign electrode contacts to different lamina. Nonetheless, we analyzed the effect of channel depth, averaged across penetrations, reasoning that strong and consistent laminar effects should show up in such analysis. To determine whether the responses differed as a function of channel depth, we classified each responsive site as belonging to either one of 3 groups: group U - upper channels 1-5, group M - middle channels 7-11, and group L - lower channels 12-16. The mean MUA of each of the 3 groups showed stimulus-selective repetition suppression in each animal in the early response window (two-way ANOVA on the mean responses to A and B presented as the adapter or test stimuli in repetition and alternation trials; interaction repetition x alternation and adapter x test factors: $P < 0.002$ in each animal). The baseline-corrected, net responses tended to be higher in the U compared to the L group (mean net responses to adapter (500 ms long window) in the U and L groups were 20.0 and 12.3 spikes/s, respectively, in monkey G and 17.1 and 4.5 spikes/s in monkey K). However, one needs to be prudent in interpreting this difference in response strength since we cannot exclude it reflects a possible bias to select stimuli using the upper (U) channels.

We found systematic differences in the LFP power as a function of spectral frequency between the different depth groups of sites. Figure 9 shows Morlet wavelet based time-frequency plots of the power for the 3 different groups. Note that in this spectral analysis, the power is computed for each trial and without subtracting the
average LFP (unlike the spectra shown in Fig. 4). We show separately the low and high
frequencies for the sake of clarity. Interestingly, the power in the alpha/beta range
increased with recording depth. The two monkeys differ with respect to the changes in
power across the three depth groups (Fig. 9), especially for the low frequencies, but this
apparent inter-animal difference decreases when one accepts deeper penetrations in
monkey K compared to G. Figure 10 shows the multitaper based spectral plots in which
the average LFP per condition was subtracted from each trial of that condition for the 3
depth groups. In both animals there was a shift of the gamma peak to lower frequencies
with increasing depth. In monkey G the stimulus-induced decrease in power between 20
and 40 Hz became somewhat more pronounced with depth while in monkey K there was
an increase in the alpha band (and lower). Notably, stimulus repetition effects were
present in the LFP power in each of the 3 depth groups for each animal, for both high and
low frequencies.

Effects of depth and distance between sites on LFP-LFP coherences

Above we analyzed sites that differed by at least 300 µm and ignored the position
of a site on the laminar electrode. Previous studies in early visual cortical areas suggested
that coherence can depend on the lamina (Bollimunta et al. 2008; Maier et al. 2010;
Hansen and Dragoi 2011; Buffalo et al. 2011) and decreases with inter-electrode distance
(Maier et al. 2010; Hansen and Dragoi 2011; Ray and Maunsell 2011). We have already
noted that differences between the two animals in some of the repetition effects
diminished when one accepts deeper recordings in monkey K compared to monkey G.
Changes in coherence effects with depth may also explain other observed inter-animal differences. Thus, we felt it was important to assess the effect of electrode position and inter-electrode distance on the changes in LFP-LFP coherence with stimulus repetition. To address this issue, we computed the shuffle-corrected Fisher transformed LFP-LFP coherence for all possible electrode pairs and these were averaged within the 5 frequency bands and across penetrations in each animal. Since adaptation effects were the strongest in the early response period we will show the coherences for this period.

Figures 11 and 12 show the mean shuffle-corrected Fisher transformed LFP-LFP coherences for all possible electrode pairs for the adapter and test stimulus in repetition trials (AA and BB) in monkeys G and K, respectively. Several points are noteworthy. First, as expected from previous studies in early visual cortical areas, LFP-LFP coherences decreased with increasing electrode distances at all examined frequency bands. Second, coherences at short electrode distances were stronger for the deeper compared to superficial sites for all frequency bands. Third, the overall effect of inter-electrode distance and electrode location is similar for adapter and test stimuli.

Nonetheless, robust effects of stimulus repetition were present when plotting the t-scores that resulted from a paired t-test contrasting the Fisher transformed coherences for the adapter and test stimuli (Figs. 11 and 12, third row) in repetition trials. A positive t-score indicates a greater coherence for the adapter compared to the test stimulus, i.e. repetition suppression, while a negative t-score indicates repetition enhancement. In monkey G the coherences among the upper sites showed repetition enhancement for the alpha, beta and low gamma frequencies, while coherences for electrode pairs that involved at least one of the deeper sites showed repetition suppression instead. The other
animal showed mainly repetition suppression, although enhancement was also present for the uppermost sites in the beta and low gamma bands. For the frequencies above 60 Hz, both animals showed strong repetition suppression and this for most distances and sites, with stronger effects for the deeper sites and smaller electrode distances (especially in K). In line with the inter-animal differences in effect of depth on spectral power (see above), monkey K middle sites were similar to the deep sites of monkey G. Indeed, the distribution of the adapter-test t scores with depth and inter-electrode distance of channels 7-16 of monkey G qualitatively fits those seen for channels 1-10 for monkey K. Thus, a reasonable explanation of the inter-animal differences in the depth effects on spectral power and coherence is a difference in penetration depth of about 600 μm between the recordings in the two animals. According to the anatomical MRIs, the penetrations were about 20° more oblique with respect to the cortex in monkey G compared to K. However, this difference in penetration angle cannot fully explain a 600 μm difference. Recordings in G were at the maximum reachable depth given his recording chamber, microdrive and electrode length which may also have contributed to the seemingly less deep recordings in that animal. Additional factors may have been the uncontrollable inter-animal differences in tissue dimpling when lowering the guide tube/electrode and movement of the cortex during the 2 hours waiting time.

These stimulus repetition effects were also present in both animals when contrasting the coherences for the test stimuli in repetition and alternation trials (Figs. 11 and 12, fourth row). This can be demonstrated directly by correlating the t-scores between the adapter-test and alternation-repetitions comparisons across all possible electrode pairs (excluding same-electrode pairs; Table 1). These correlation coefficients
were highly significant, ranging between 0.66 and 0.95 across animals and bands. These high, significant correlations demonstrate that the repetition effects on LFP-LFP coherence are real since the repetition effects obtained in two independent measures (comparison of adapter versus test stimuli and comparison of test stimuli in alternation and repetition trials) were correlated. Thus, stimulus repetition produces a drop in LFP-LFP coherences for all frequency bands, except for an increase in local coherence for lower frequencies in probably superficial layers.

Effects of depth and distance between sites on LFP-MUA coherences

Figures 13 and 14 show the mean shuffle-corrected Fisher transformed MUA-LFP coherences for all pairs (except same-electrode pairs) for the 5 frequency bands in monkeys G and K, respectively. Again, we will concentrate on the early response period. Although repetition effects were less pronounced in monkey K, overall qualitatively similar distributions of MUA-LFP coherences across electrode distance and depth were observed in the two monkeys if one allows again a depth shift of 600 µm. For instance, the MUA-LFP coherence distributions for the beta and low gamma bands in monkey K are similar to the corresponding coherence distributions in monkey G allowing a depth shift of 600 µm. In upper (monkey K and G) and middle (monkey G) channels, we observed repetition enhancement for the beta and low gamma bands. Frequencies >60 Hz showed significant repetition suppression in both monkeys. Similar trends were present when contrasting the MUA-LFP coherences for the test stimuli in alternation and repetition trials (Figs. 13 and 14, fourth row). As shown in Table 1, the correlations
between the t-scores of the adapter-test and alternation-repetitions comparisons were lower than in the case of LFP-LFP coherences, ranging between 0.07 and 0.42. Nonetheless, 4/5 (beta and higher) and 2/5 (low and middle gamma) frequency bands demonstrated a significant correlation in monkey G (range: 0.3 – 0.42) and K (0.14-0.36) respectively, indicating that these repetition effects in MUA-LFP coherences are real. A noteworthy feature of the MUA-LFP coherences in the low frequency bands is that these are asymmetrical with respect to which member of a pair contributes MUA or LFP. This is especially visible for the coherences to the test stimuli in monkey G for the beta and low gamma bands (Fig. 13): the coherence for a MUA-LFP pair (a, b) is stronger than for the (b, a) pair when a is larger than b. Given that for these low frequencies the LFP mainly represents synaptic activity (Ray and Maunsell 2011), this asymmetry suggests that the synaptic input is synchronized with action potentials of neurons of which the soma are located at the same level or deeper in the cortex than the input and this appears to hold only for the superficial recordings. This synchrony between synaptic input and action potentials is enhanced with repetition, while high frequency synchronizations are depressed by repetition.

Noise correlations

We assessed the trial-to-trial covariations in MUA, i.e. noise correlations, in the A and B stimuli repetition trials. We correlated the responses for all pairs of responsive sites. The mean noise correlations, computed using responses for the early analysis window, decreased significantly with inter-site distance in each animal (ANOVA, main
effect of inter-site distance: $P < 0.001$; monkey G: mean Pearson correlations ranging between 0.22 (distance 100 $\mu$m) to 0.03 (distance 1.5 mm); monkey K: 0.16 (100 $\mu$m) to 0.05 (distance 1.5 mm). In each animal, noise correlations were significantly larger for the adapter (mean across distances: G: 0.14; K: 0.10) compared to test stimulus (mean across distances: G: 0.11; K: 0.08; ANOVA, main effect of adapter x test: $P < 0.0001$ in each animal). However, this decrease of the noise correlations with repetition did not survive stratification of the noise correlations according to the response strength (mean, geometrical mean or minimum response strength; see Cohen and Kohn 2011) for the sites of a pair. Thus, the lower noise correlations for the test compared to adapter stimulus might be due to the lower response strength to the test stimuli. Similar (negative) results were obtained when analyzing the late and full response windows.

**Eye movements**

Both monkeys had to fixate in small windows and given the relatively large receptive field size of IT neurons (Op de Beeck and Vogels 2000) it is very unlikely that differences in stimulation due to eye movement differences between the adapter and test periods caused the differences in response and coherence. Nonetheless, we analyzed the eye movement data of both animals, computing frequency and amplitude of (micro)saccades in the same analysis windows as used for the neural data analyses. In both animals the microsaccade frequency was significantly lower for the test (monkey G: 0.82 Hz; monkey K: 0.86 Hz) compared to the adapter stimuli (monkey G: 1.12 Hz; monkey K: 1.04 Hz) in the early analysis windows (ANOVA, main effect of adapter x
test variable: \( P < 0.003 \) in each animal). However, in neither animal was there a significant interaction between the adapter x test and the repetition x alternation trial variables (ANOVA) and thus this difference in microsaccade frequency between adapter and test cannot explain differences in adaptation effects between repetition and alternation trials.

In monkey K, the mean microsaccade amplitude was significantly reduced in test (mean: 19 minarc) compared to adapter (mean: 16 minarc; ANOVA, \( P < 0.0001 \)) stimuli in the early analysis windows, but again this reduction was the same in repetition and alternation trials (ANOVA, interaction adapter x test and repetition x alternation trial variables: n.s.). In monkey G there was no significant main effect of adapter x test on mean saccadic amplitude, but a significant interaction between the adapter x test and the repetition x alternation trial variables (ANOVA: \( P < 0.05 \)). In this animal, mean saccadic amplitude increased with repetition in repetition trials (18 minarc versus 19 minarc), which is opposite to that seen in the other animal, and decreased by 0.5 minarc in alternation trials. Given the opposite effects in both monkeys, these small eye movement differences between the adapter and test stimuli cannot explain the consistent neural adaptation effects seen in both animals. On the other hand, the dependency of the difference in eye movement amplitude on repetition versus alternation trials in monkey G suggests that this monkey was attending the stimuli.
We demonstrated that stimulus repetition does not only affect the response strength of IT neurons but also the synchronization of their activity. For frequencies > 60 Hz, stimulus repetition resulted in decreased LFP-LFP and MUA-LFP synchronization. At lower frequencies, the effect of repetition on synchronization depended on the electrode depth within the cortex: for depths likely corresponding to the superficial layers we found a local enhancement of synchronization with stimulus repetition, while the LFPs of the putative deep layers decreased their synchrony across layers.

The changes in coherences with repetition reflect changes in within-trial neural synchrony and not in stimulus-evoked transients since we subtracted shuffled, across-trials coherence values. The concern that changes in MUA-LFP coherence reflect changes in firing rate instead of synchrony was addressed by equating spike counts for the adapter and test stimuli. This implied the removal of a considerable amount of spikes, reducing the sensitivity of the coherence computation. However, this was necessary in order to conclude that changes in MUA-LFP coherence reflect changes in synchrony. Since LFP-LFP coherence computation is less susceptible to changes in power, we believe that the drop in LFP-LFP coherence with repetition for the high frequencies is not merely due to decreased power. In fact, the changes in power with repetition did not always correlate with the changes in coherence. For instance, the decrease in coherence observed for the beta/low gamma range in the first half of the stimulus period was opposite to the relative increase in power with repetition at these frequencies.

In agreement with our previous studies (Sawamura et al. 2006; De Baene and Vogels 2010; Kaliukhovich and Vogels 2011) suppression of the response to the test
stimulus was present from the beginning of that response. The time course of coherence changes also suggests fast repetition effects on coherence. These observations together suggest that at least part of the repetition-induced changes in response reflect bottom-up driven changes, either pre- or postsynaptically. This fast onset of repetition effects was present at all depths (Figs. 9 and 10), fitting anatomical studies that indicate that bottom-up input to IT is mainly columnar (although emphasizing granular and supragranular layers; Saleem et al. 1993, 2000) and agrees with the Current Source Density data analysis of the ventral bank of the STS (Schroeder et al. 1998) which failed to show a clear mid-lamina focus. Notably, adaptation effects of both MUA and LFP power increased after response onset, peaking at 150-250 ms after stimulus onset after which it declined to zero, which fits rather well Liu et al. (2009). These authors suggested that this particular time course of adaptation results from recurrent connections and perhaps input from extra-visual regions coming into play later during the response. The similar temporal evolution of adaptation across depths can be explained by extensive interlaminar connections in IT (Fujita and Fujita 1996). Further studies are required to determine whether the temporal evolution of adaptation is dictated by recurrent processing intrinsic to IT, top-down influences, and/or the temporal evolution of suppression mechanisms at the level of individual neurons during the course of the prolonged stimulus presentation.

The present study extends the previously reported dissociation between repetition effects on the power above versus below 60 Hz (De Baene and Vogels 2010) twofold. First, the pure induced power (mean LFP-subtracted) showed repetition suppression at frequencies above 60 Hz while the beta and low low-gamma bands showed repetition
enhancement due to a delayed drop in power with respect to baseline in the test stimulus. Second, high frequencies showed suppressed synchronization with repetition while low frequencies showed a more complex pattern depending on the electrode depth.

The similar behavior of high gamma LFP power and spiking activity in several cortical areas (Liu and Newsome 2006; Belitski et al. 2008; Gieselman and Thiele 2008; Ray et al. 2008; De Baene and Vogels 2010; Ray and Maunsell 2011) suggests that the power at such frequencies relate to MUA in the neighborhood of the electrode (Ray and Maunsell 2011). Thus, the repetition suppression in LFP-LFP and MUA-LFP coherences for the frequencies above 60 Hz likely reflects decreased spiking activity synchronization with repetition (Ray et al. 2008). Synchronization at such high frequencies requires relatively precise timing of the spikes (100 Hz implies a 10 ms period) which we suggest is disrupted by repetition. Oscillations at these high frequencies likely results from reciprocal interactions between inhibitory interneurons and excitatory pyramidal cells (Cardin et al. 2009; Sohal et al. 2009; Wang 2010). Thus, adaptation may alter the excitatory-inhibitory balance within these local networks so that the high frequency oscillations are reduced (for mechanisms of how changes in excitatory-inhibitory networks can affect synchronization see Brunel 2000 and Middleton et al. 2012). One cannot exclude the possibility that the reduction in synchrony at these high frequencies reflects a reduced synchrony of the input to IT and is not generated within IT.

The increase in LFP-LFP and MUA-LFP coherence with repetition for frequencies between 15 and 40 Hz in the superficial sites is due to less desynchronization with respect to prestimulus baseline in the test compared to the adapter stimuli. Indeed, there was an enhanced synchronization in this band after the adapter stimulus
presentation followed by desynchronization which decreased with repetition. This is reminiscent of the stimulus-driven desynchronization between LIP and IT activity observed by Verhoef et al. (2011) in the beta band during a depth discrimination task, which increased with stimulus strength. Thus, the greater beta/low gamma desynchronization for the adapter compared to the test stimulus might reflect a greater saliency of the former stimulus. It has been proposed that beta band oscillations decrease when the current state is disrupted by an unexpected event (Engel and Fries 2010). In our paradigm repetition and alternation trials were equiprobable implying that the cognitive expectation of repetition equaled that of novelty. Thus, to fit the “status quo signaling” interpretation of the beta band oscillations one needs to assume that the system has a default expectation or assumption of repetition. Interestingly, the relative increase in coherence in the lower frequency bands was seen locally in the upper sites. Also, LFPs of the upper sites tended to be enhanced in synchronization in these bands with the MUA of deeper sites. This might reflect synchronization of apical dendritic potentials with spikes at deeper located soma of pyramidal neurons. STS area TEa indeed contains prominent layer III pyramidal neurons (Seltzer and Pandya 1978). The circuit mechanism of the beta rhythm might be similar to those of higher frequencies, i.e. based on local interactions of interneurons and pyramidal neurons (Wang 2010). Beta oscillations have also been implicated in long-distance communications between areas (Bushman and Miller 2007; Verhoef et al. 2010) for which they are well suited given the longer time delays involved. Since some prefrontal areas (e.g. ventrolateral 45A) project mainly to superficial layers of TEa (Gerbella et al. 2010), it is possible that these low frequency synchronization changes seen in the upper layers reflect top-down oscillatory signals. Indeed, a recent
study in macaque V1 and V4 suggests that low frequencies are involved in feedback
signals while high frequencies relate to feedforward processing (Van Kerkoerle et al.
2011, Society for Neuroscience Abstract). In both monkeys LFP-LFP coherences that
involved deep recording sites showed suppression of the synchronization in the beta and
low gamma bands, suggesting that coherence effects are layer-dependent. Layer-
dependent differences in coherences have also been observed for attention (Buffalo et al.
2011) and fast adaptation effects (Hansen and Dragoi 2011) in early visual cortex.

The effects of adaptation on synchronized IT activity differ from recent reports of
an enhancement of synchronization in alpha to gamma frequencies in the supragranular
layers in V1 (Hansen and Dragoi 2011) and around 60 Hz in V4 (Wang et al. 2011).
Stimulus repetition synchronization effects, like attention effects (Chalk et al. 2010), may
differ between areas, which is possible since synchronization depends on circuit, synaptic
and cellular (e.g. ion channels) properties (Wang 2010). The V1 and V4 experiments
used a short ISI of 100 ms compared to our 500 ms. Especially in V4, such short ISIs can
produce an overlap between the response to the adapter and test stimuli (Motter 2006).
This complicates the interpretation of differences between responses to a test stimulus as
a function of the preceding adapter stimulus (in the V1 and V4 studies only AA and BA
sequences were employed). Aside from these methodological issues, mechanisms of
adaptation may well differ between short and long ISIs.

Gotts (2003) proposed that stimulus repetition enhances low-frequency
synchronized responses, time-locked to stimulus onset. This computational model was
supported by human MEG data using a priming paradigm (Gilbert et al. 2010). Our IT
data showed a repetition-induced evoked power (Morlet wavelet analysis of averaged
LFPs per channel for repetition trials) increase around 25 Hz, but this only occurred in one monkey (K; data not shown). Thus, our data do not fully support the relevance of Gotts’ computational scheme for the short-term repetition effect in IT cortex.

In conclusion, the present work demonstrates that short-term stimulus repetition affects synchronized activity in addition to response strength in IT. The effects on synchronized activity appear to depend on frequency band and lamina. A mechanistic understanding of the rich phenomenology of repetition suppression – of spiking activity, LFP power and the synchrony of these signals – will require more knowledge and modeling of the cortical circuits, their elements (e.g. synaptic channels) and their input and how these change as a result of repetition. The impact of the changes in synchronized activity on the responses of regions to which IT projects and on behavior needs to be addressed in future studies.
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We declare no conflicts of interest, financial or otherwise.


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Figure 1. Adaptation paradigm. The adaptation test was run using two stimuli selected based on the responses of the neurons in a preceding search test. The two selected stimuli (A and B) were presented in succession with an ISI of 500 ms. Trials were either a repetition of the same stimulus (AA and BB sequences; repetition trials) or a successive presentation of A and B stimuli (AB and BA sequences; alternation trials). Monkeys were required to fixate a small target point (shown here not to scale) during the entire trial. The original stimuli were in color. The approximate size of the stimuli was 5° of visual angle.

Figure 2. MUA and LFPs in an example penetration (monkey G). Peri-stimulus time histograms of the MUA for the 16 channels of the laminar electrode are shown in the left column for the AA and BB repetition trials. Bin width is 10 ms. Channel 1 was the uppermost channel. The right column shows the mean LFPs obtained in the same trials. Stippled lines indicate stimulus on- and offsets. 0 ms corresponds to the onset of the first stimulus of a trial. Number of trials (N) is indicated for each stimulus condition. Stimuli were a fractal pattern and white raisins.

Figure 3. Adaptation of MUA. A, B. Population peri-stimulus time histograms of the mean MUA activity of all sites in which there was a significant response to at least A or B for repetition (AA and BB) and alternation (AB and BA) trials in monkeys G (A) and K (B). N indicates the number of responsive sites. Bands indicate within-site standard error of the mean, i.e. computed by removing the between-sites variance in response (Loftus and Mason, 1994). Bin width is 20 ms. Stippled lines indicate stimulus
on- and offsets. 0 ms corresponds to the onset of the first stimulus of a trial. \textbf{C,D}, Distributions of the adaptation indices in monkeys G (\textbf{C}) and K (\textbf{D}). Positive and negative indices indicate repetition suppression and enhancement, respectively. The arrow indicates the median and the vertical line corresponds to an adaptation index of 0% (no adaptation effect). N indicates number of stimulus x responsive site combinations.

\textbf{Figure 4.} Power spectra and Adaptation Contrast (AC) indices in repetition trials. \textbf{A,B}, Time-frequency plot of the averaged normalized power estimated using multitaper methods for monkeys G (\textbf{A}) and K (\textbf{B}), respectively. Stippled lines indicate stimulus on- and offsets. 0 ms corresponds to the onset of the first stimulus of a trial. The power for the frequencies below 30 Hz were computed using 1 Slepian taper, while those above 30 Hz were computed with 5 Slepian tapers. Only MUA responsive site x stimulus combinations were used to average the power. A value of 1 indicates no change in power with respect to baseline. The apparent change in power before stimulus onset is due to the duration of a single taper. \textbf{C,D}, Time-frequency plots of AC indices for monkeys G (\textbf{C}) and K (\textbf{D}), respectively. Positive and negative indices indicate repetition suppression and enhancement, respectively. 0 ms corresponds to stimulus onset. The bottom row labeled MUA shows the AC indices for the MUA of the same stimulus x responsive site combinations. The Pearson correlation coefficient between the AC indices for the power of a given frequency and the MUA is plotted to the right of the time-frequency AC plots.

\textbf{Figure 5.} LFP-LFP coherence in repetition trials: time-frequency plots. Shuffle-corrected Fisher transformed coherence averaged across pairs of MUA responsive sites with a distance of at least 300 $\mu$m. Note that the Fisher transformation can produce values larger than 1. Stippled lines indicate stimulus on- and offsets. 0 ms corresponds to the
onset of the first stimulus of a trial. The power for frequencies below 30 Hz were
computed using 1 Slepian taper, while those above 30 Hz were computed with 5 Slepian
tapers. A, monkey G. B, monkey K.

**Figure 6.** Time course of the mean LFP-LFP coherences as a function of
frequency band. A, Time course of the shuffle-corrected Fisher transformed LFP-LFP
coherence for the adapter and test stimuli, averaged within 5 different frequency bands
(see Results). The values are computed only for pairs of MUA responsive sites separated
by at least 300 μm. Top row: monkey G; bottom row: monkey K. B, Time course of the
shuffle-corrected Fisher transformed LFP-LFP coherence for the test stimuli in
alternation (BA and AB) and repetition (AA and BB) trials. Top row: monkey G; bottom
row: monkey K. In all panels, the stimulus presentation is indicated by the horizontal bar.
Bands indicate within-site 95% confidence intervals of the mean, i.e. computed by
removing the between-sites variance in coherence (Loftus and Mason, 1994). Note the
different scales for the different bands (indicated in bold): there was a marked drop of
mean LFP-LFP coherence with increasing frequency. The significance of the difference
in mean coherence between the two stimuli was tested with a randomization test for the
early and late analysis windows separately. These windows are marked by the stippled
vertical lines and asterisks indicate a statistically significant difference in the
corresponding window ($P < 0.05$; corrected for multiple comparisons).

**Figure 7.** MUA-LFP coherence in repetition trials: time-frequency plots. Shuffle-
corrected Fisher transformed coherence averaged across pairs of MUA responsive sites
with a distance of at least 300 μm. A, Monkey G. B, Monkey K. Same conventions as in
Fig. 5.
**Figure 8.** Time course of the mean MUA-LFP coherences as a function of frequency band. The values are computed only for pairs of MUA responsive sites separated by at least 300 μm. **A**, Time course of the shuffle-corrected Fisher transformed MUA-LFP coherence for the adapter and test stimuli, averaged within 5 different frequency bands. Top row: monkey G; bottom row: monkey K. **B**, Time course of the shuffle-corrected Fisher transformed corrected MUA-LFP coherence for the test stimuli in alternation (BA and AB) and repetition (AA and BB) trials. Top row: monkey G; bottom row: monkey K. Asterisks indicate a statistically significant difference in the 250 ms long early or late analysis windows ($P < 0.05$; corrected for multiple comparisons). Same conventions as in Fig. 6.

**Figure 9.** Time-frequency plots of LFP power in repetition trials computed using Morlet wavelets without subtraction of the mean LFP for the 3 groups of sites sorted according to their depth along the electrode shaft. For the sake of clarity, the scales of the frequencies above and below 40 Hz differ. Power is expressed in units normalized to baseline (power equal to baseline = 1). Time-frequency plots were averaged across all MUA responsive site x stimulus combinations within each group. Site numbers included in each group are indicated. **A**, Monkey G. **B**, Monkey K. Same conventions as in Fig. 4. A.

**Figure 10.** Time-frequency plots of LFP power in repetition trials computed using the multitaper method with subtraction of the mean LFP for the 3 groups of sites sorted according to their depth along the electrode shaft. **A**, Monkey G. **B**, Monkey K. Same conventions as in Figs. 4A and 9.
Figure 11. LFP-LFP coherence and repetition effects for all pairs of MUA responsive sites for 5 different frequency bands: monkey G. Shuffle-corrected Fisher transformed coherences in repetition trials are shown for the early analysis window for all site pairs in the upper two rows: first row: adapter stimulus; second row: test stimulus. Note the different scales for the different frequency bands. A site for a stimulus (A or B) of a particular penetration was included only when the MUA was responsive to that stimulus presented either as adapter or test. The third row shows the t-scores obtained from a paired t-test comparing the coherence for the adapter (first row) and test stimuli (second row) in repetition trials. Positive and negative t-scores indicate repetition suppression and enhancement of coherence, respectively. The fourth row shows the t-scores obtained when comparing the coherence computed for the early period for the test stimuli in repetition and alternation trials. A positive t-score indicates a greater coherence in alternation compared to repetition trials, corresponding to repetition suppression. Changes in coherences that are significantly different from 0 (two-tailed t-test; \( P < 0.05 \)) are indicated by white dots.

Figure 12. LFP-LFP coherence and repetition effects for all pairs of sites for 5 different frequency bands: monkey K. Same conventions as in Fig. 11.

Figure 13. MUA-LFP coherence and repetition effects for all pairs of sites for 5 different frequency bands: monkey G. Same-electrode MUA-LFP coherences (diagonal) were not computed, and those cells were filled in white. Same conventions as in Fig. 11.

Figure 14. MUA-LFP coherence and repetition effects for all pairs of sites for 5 different frequency bands: monkey K. Same conventions as in Fig. 11.
Table 1. Correlations between the t-scores of the coherence changes for the adapter-test stimuli (Figs. 11 and 12) and alternation-repetition trials (Figs. 13 and 14).

<table>
<thead>
<tr>
<th></th>
<th>r LFP-LFP coherence</th>
<th>r MUA-LFP coherence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Monkey G</td>
<td>Monkey K</td>
</tr>
<tr>
<td>Alpha</td>
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<td>0.72*</td>
</tr>
<tr>
<td>Beta</td>
<td>0.95*</td>
<td>0.66*</td>
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<tr>
<td>High gamma</td>
<td>0.78*</td>
<td>0.77*</td>
</tr>
</tbody>
</table>

Table 1 Legend. Correlations are shown separately for LFP-LFP coherences ($r_{\text{LFP-LFP coherence}}$; N = 120) and MUA-LFP coherences ($r_{\text{MUA-LFP coherence}}$; N = 240). Asterisks indicate correlations significantly different from 0 ($P < 0.05$) per frequency band and monkey.