# Bi-directional interactions between visual areas in the awake behaving cat

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The study of the cooperativity among cortical areas is essential to our understanding of brain functioning. Here we investigated the relative contributions of top-down and bottom-up directed interactions between area 17 and area 7 of the cat visual system. Bipolar local field potentials were recorded while the animals performed a go/no-go task or were in a quiet resting state. The data were analyzed by applying measures of interaction based on the Wiener−Granger causality concept. We found that during the visual task top-down directed interactions were of a similar magnitude as the bottom-up component. Second, interareal couplings tended to increase in conditions requiring a discriminative effort. Third, during behaviors not dominated by visual processing non-directed interactions increased. *NeuroReport* 11:1−4 © 2000 Lippincott Williams & Wilkins.

Key words: Bottom-up; Cat; Causality; Cerebral cortex; Feedback; Feed-forward; Local field potential; Top-down; Visual system

## INTRODUCTION

A prominent feature of cortical organization is the high degree of reciprocity in connections between different areas [1]. In particular in the visual system, which can be viewed as a hierarchy of cortical areas [2], feedback connections are present at almost every level [3]. Despite this knowledge, the functional role of the feedback remains a matter of intense debate. Recent research focusing on the visual system testifies the role of top-down interactions in mediating or influencing important cortical functions such as selective attention or figure−ground segregation [4−8]. Here we studied the electrical activity from two cortical areas situated at different levels of the visual system hierarchy in awake behaving cats. To investigate factors that influence the direction and the strength of cortical information flow, we considered measures of the magnitude of top-down and bottom-up interactions in different behavioral situations.

## MATERIALS AND METHODS

*Behavioral experiments and electrophysiology:* The experimental procedures have been described elsewhere [9] and were in accordance with the NIH and institutional guidelines. We investigated three cats, two of which were trained to perform a behavioral visuomotor task. In a modified go/no-go paradigm, the animals were presented with a succession of two visual stimuli (Fig. 1a). The first, preparatory, stimulus was a dark rectangle that moved from left to right on a video screen. In this phase, the task of the animal was to track the stimulus. After a delay uniformly distributed between 500 and 2000 ms, a second behaviorally relevant stimulus emerged gradually from behind the first one. In the case of a cartoon mouse (the go condition), the cat had to press a lever in front of it; in the no-go condition it had to continue tracking a small moving rectangle. The cats were rewarded upon correct performance in either type of trial. At the end of the training period, the animals could perform the task with a certain ease, as indicated by the high fraction of correct responses (> 80%). In the present analysis we considered only trials with correct performance. We also recorded from two of the animals in a quiet resting state.

Recordings of local field potentials were obtained from two cortical areas of the visual system, area 17, which constitutes part of the primary visual cortex and area 7, a visual association area in parietal cortex (Fig. 1b). In each of the two areas, we collected signals at different depths with four microelectrodes of 100−200 kΩ impedance at 1 kHz. Local field potentials were recorded bipolarly with respect to the second shortest electrode in each bundle. Furthermore, potentials at these second shortest electrodes were measured relative to a silver ball electrode placed on the cortical surface at a distance (Fig. 1b). Data were filtered online between 0.5 and 100 Hz. Separate controls
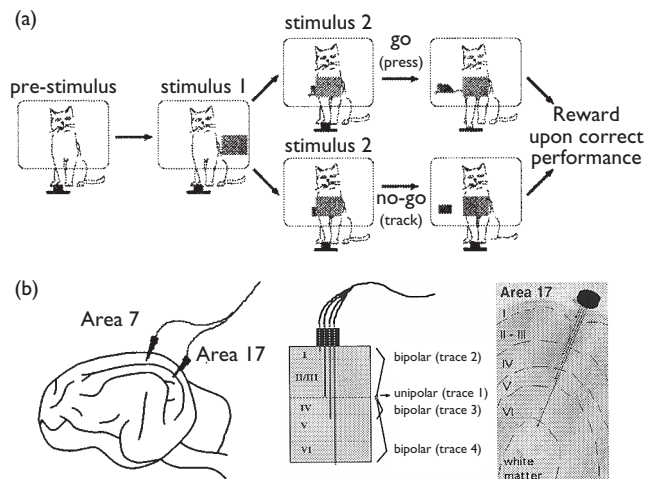
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(a)



(b)



**Fig. 1.** Behavioral paradigm and electrodes position. (**a**) Cats were presented with two successive visual stimuli on a video monitor. The second stimulus was different in go and no-go trials, in which the animal had to press a lever or to continue tracking. (**b**) Position of the two groups of electrodes in the cortex (left figure) and of the four single electrodes of each group in the different layers of the gray matter (center) with the corresponding histological section (right, area 17).

showed that the analog bandpass filters had negligible effects on the frequency bands of interest here. In addition, an analog notch filter was applied to eliminate line frequency artifacts. As a control, parts of the recordings were performed without notch filter. Off-line we applied a symmetrical digital filter (3–100 Hz) and resampled the data at 200 Hz.

*Analysis methods:* Statistical procedures applied are related to the concept of directed coherence [10] and were reported previously [11]. They are based on the Wiener–Granger concept of causality [12], which exploits intuitive properties of dynamic systems, such as 'the past and present may cause the future, but the future cannot cause the past' [12], to infer the direction of interaction among processes. If the past of a time series helps improve the prediction of a second time series compared with the past of the first time series alone, then, under appropriate constraints, causal interactions from the first to the second process is said to be present. In practice we consider measures of interaction between multiple time series that allow a stationary autoregressive representation $x_t = c + A_1 x_{t-1} + ... + A_p x_{t-p} + \varepsilon_t$. Here p is the order of the model, $A_i$ are the coefficients, c is a constant and $\varepsilon_t$ is white noise. The number of channels considered at one time is the dimension of the model and gives the length of vectors $x_t$, $x_{t-1},..., x_{t-p}$. Based on our previous experience [11] we choose p = 7. As proposed by Geweke [13], the total linear dependence (or interaction) $F_{X,Y}$ between two multiple time series X and Y is decomposed into a measure of instantaneous linear feedback $F_{X \times Y}$, which accounts for the fraction of information that moves too fast with respect to our sampling rate or that is caused by common inputs [12], and two directional measures $F_{X \to Y}$ and $F_{Y \to X}$ which account for the interaction directed from X towards Y, and Y towards X respectively: $F_{X,Y} = F_{X \to Y} + F_{X \times Y} + F_{Y \to X}$. These

measures of interaction are normalized with respect to the length of the underlying time series, in order to allow testing of individual trials [13]. In addition, we studied the decomposition of the two directional measures by frequency. Two functions $f_{Y \to X}(\lambda)$ and $f_{X \to Y}(\lambda)$, where $\lambda$ is a frequency, can be derived from the model in such a way that their integral (from $-\pi$ to $\pi$) is proportional to $F_{Y \to X}$ and $F_{X \to Y}$, respectively.

The significance of changes in interaction strength in different conditions was assessed with a paired Wilcoxon test for comparisons of before *vs* after an event and of top-down *vs* bottom-up, and with an unpaired Wilcoxon test in all other cases. $p > 0.05$ was defined as non-significant (n.s.).

## RESULTS

As a first step we investigated the interactions within a cortical area. Using three intraareal bipolar recordings we found interactions directed from infragranular layers towards supragranular and granular stronger than in reverse direction in all three animals. Figure 2a shows a particularly striking example recorded in area 17 with mean dependence value of 0.42 and 0.16 for the opposite direction ($p < 0.001$). However, within a column, in all animals and areas, a major component of the interaction was the instantaneous interaction. Between granular and supragranular layers we found a prevalence of instantaneous interactions, as exemplified in Fig. 2b. These data show the strong coupling within a column, with an asymmetry between supra and infragranular laminae, and will be used to guide our choice of appropriate channels to study interareal interactions.

As a next step we studied interareal relationships by modeling the activity of channels from area 17 and area 7. In all three cats we found that, in general, the two directed components were of a similar magnitude and that the top-down direction contributed significantly to the total interareal interactions (Fig. 3A). When the small differences
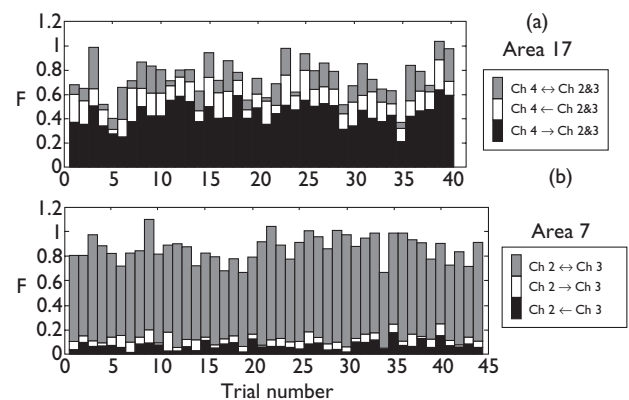


**Fig. 2.** Examples of intraareal interactions. Three bipolar recordings from area 17 are considered in (**a**). Channels 2 and 3 (sampling respectively from the supragranular and granular layers) are modeled against channel 4 (infragranular layers). The height of the white bars reflects the interaction strength from the first set of channels to the second, the black bars represent the opposite direction and gray bars the instantaneous component. In (**b**) we show interactions within area 7, of channel 2 against 3.
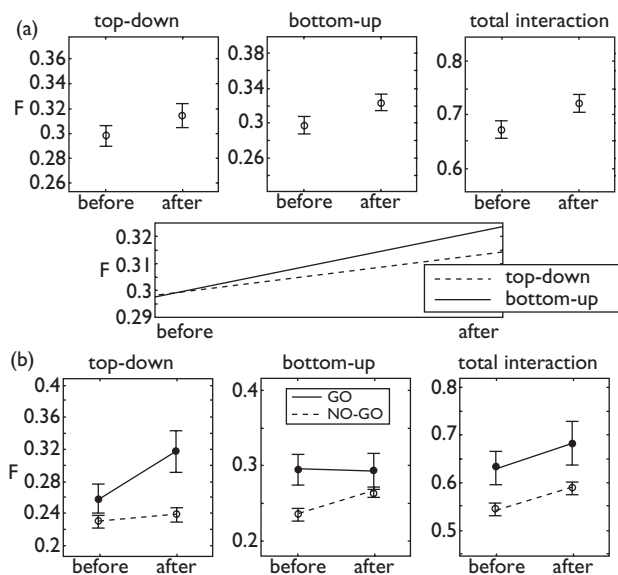
**Fig. 3.** Interareal dependence measures before and after the visual events. **(a)** Changes around the first event (the presentation of the preparatory stimulus) in 110 trials of the first cat. The upper plots illustrate the variation of the two directional components and of the total interactions. The circles indicate the mean values and the length of the whiskers corresponds to the standard error. The lower plot illustrates the change for the two directions. **(b)** Interareal interactions before and after the second visual event in 147 trials.

between the two directions were significant (in 35% of 50 analyzed conditions) it was in all but one case in favor of bottom-up. There was no systematic relationship between these significances and the other variables considered. We can therefore assert that, on average, both interaction components are significant, comparable in size with a slight prevalence of the bottom-up direction.

To assess a dependence of interactions on the behavioral condition of the animal, we compared the measures of interareal relationship immediately before and after the relevant events of the experiments. In each trial the two intervals were of equal length, which was chosen as large as possible (up to 1 s) without including artifacts. For this part of the work, we studied four-dimensional processes. From both areas, traces 2 and 4 were chosen, representing mainly supragranular and infragranular activity. Results for one cat are shown in Fig. 3. For windows positioned before and after the first visual event (Fig. 3a) we found a significant increase in interactions for the bottom-up and top-down directions (+10%, $p = 0.050$ and +6%, $p = 0.004$, respectively). As a consequence, the total interaction also increased (+7%, $p = 0.001$).

In periods around appearance of behaviorally relevant stimuli an increase of the directed interaction between cortical areas was observed (Fig. 3b, +8%, $p < 0.01$, +8%, $p < 0.01$ for the two directions). In the second animal we observed an effect with similar tendency (+9%, top-down, +6%, bottom-up). In these experiments we observed an interesting dissociation of bottom-up and top-down interaction in different types of trials. In go trials a major increase of top-down directed interaction (+22%, $p = 0.004$) was found. In contrast, in No-go trials the increase of

bottom-up interactions was strongest (+12%, $p = 0.001$). This aspect, however, reached significance in one of the two animals only.

To investigate the interareal interactions in non-visually dominated behaviors, we recorded from two of the cats in a quiet resting state. Compared with visually dominated behavior the instantaneous component increased (+40%, $p = 0.041$ with respect to go trials; +59%, $p = 0.006$ with respect to no-go). Simultaneously the directed components decreased (bottom-up: −14%, n.s. with respect to go, −16%, $p = 0.023$ with respect to No-go; top-down: −20%, $p = 0.006$ for go, −15%, n.s. for no-go). In a small number of recordings we had stationary conditions of a sufficient duration to allow the simultaneous analysis of the full set of eight channels. Confirming the previous result, a significant increase in instantaneous interaction in the quiet condition and a slight decrease in top-down and bottom-up interactions was found (+99%, $p = 0.011$; −7%, n.s and −6%, n.s., respectively). Thus, in a quiet state global dynamics are predominant, leading to increased common input and, thus, to increased instantaneous interactions. In contrast, in the behavioral task specifically involving the visual system directed interactions are stronger.

To establish which frequencies contribute most to top-down and bottom-up interactions, we investigated the spectral decomposition of causality relationships. As shown in Fig. 4, the average spectral decompositions display three peaks located at the low frequencies, around 40 Hz and around 80 Hz. Overall, the two directed components show a similar spectral structure. Remarkably, and not seen in previous experiments, an interesting substructure in the γ frequency domain (20–100 Hz) with two separate peaks was observed. This was present in recordings of all three cats investigated, and control recordings without the online notch filter gave qualitatively comparable results. Furthermore, spectra of the individual trials generally display only some of the features of the mean spectra: one or two of the peaks could be missing. This argues against a resonance effect producing the different peaks. Thus, the existence of separate peaks in the γ frequency domain (20–100 Hz) hints at a previously unknown substructure.

## DISCUSSION

The aim of the present project was to study the direction of interactions between cortical areas in cats performing a
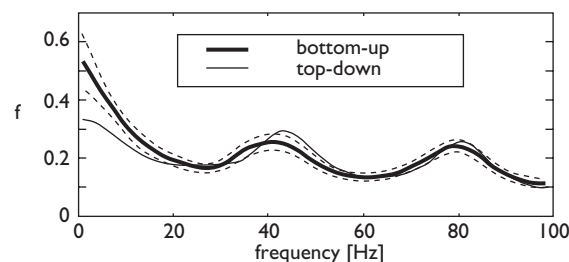


**Fig. 4.** Average interareal dependence spectra. Average of 100 causality spectra, collected around the second event. The bottom-up component is represented by the thick line and is surrounded by its 95% confidence interval (dashed, based on a t-distribution calculated for each point), whereas the top-down component is thin.

behavioral task. Given the high degree of convergence of connections, the influence of any single neuron onto another neuron has to be small. To address this statistical problem we chose to record local field potentials with multiple electrodes, as measures of activity from a moderate number of neurons which, however, maintain sufficient response specificity for the area and layer studied [14]. In addition, such analog data can be conveniently submitted to analysis methods based on the Wiener–Granger causality to investigate the direction of relationships [11–13]. Differences in interaction that were assessed in different experimental conditions, even if highly significant, were relatively small in absolute terms. However, even though we record a spatially averaged signal, we can only capture a modest fraction of the total inputs to a cortical region [15]. As a consequence, the signal from one area can only be partly causal for the activity in the other one, and effects are necessarily small.

Processing of stimuli by the visual system is usually described in terms of a feed-forward architecture. However, in recent years physiological studies of feedback connections found subtle effects on neuronal firing rates [5,6,15,17]. In the present study statistical methods were used which exploit the temporal structure of neuronal activity [11,16]. With these methods we could demonstrate that top-down interactions are on average of the same order of magnitude as bottom-up components.

An insight into possible functions of top-down directed interactions was gathered when comparing interactions during go and no-go stimuli. In stimuli that were associated with a change in behavior, top-down directed interactions dramatically increased. This indicates that internal factors such as the behavioral context have an important influence on cortical processing. The top-down interactions may represent a gating process mediating the behavioral context where sensory-motor representations in higher hierarchical areas influence the activation and dynamics of sensory representations in area 17. Supporting this view, a recent simulation study [18] has shown that cooperative processing of areas on different levels of the processing hierarchy leads to burst firing of neurons integrating top-down and bottom-up signals. Furthermore, depending on the match of the two signals, the network dynamics evolves with characteristic temporal signatures in α and γ

frequency ranges. Although the present data are compatible with such a view, they do not allow a statement on the level of action potentials. Thus, a test of the model is left to ongoing and future experiments.

In the quiet cat, by contrast, instantaneous interactions dominated, presumably as a signature of stronger subcortical drive or of a state with a prevalence of non-visual global interactions. These findings are in line with recent research that assigns a relevant role to cortical feedback processing in the sense that, during periods of increased attention, areas involved in a given task seem to engage in a lively exchange of information [4,5,7,17].

## CONCLUSION

This study of the interaction between cortical areas situated at different levels of the hierarchy of the visual system presents evidence for a systematic tendency towards an increase in the coupling between two visual areas in a visually dominated task. This rise involves both the bottom-up and the top-down components of the interaction.

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