Neural connectivity only accounts for a small part of neural correlation in auditory cortex

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Abstract In order to allow the relation of functional connectivity patterns (inferred from cross-correlograms) to structural connectivity (the anatomical substrate), we analyzed cross-correlogram peaks for spontaneous and stimulated activity in the auditory cortex. It was assumed that the broad correlograms, usually encountered, represent neural connectivity as well as secondary effects such as intrinsic firing patterns, global synchrony related to the ongoing electroencephalographic activity, and stimulus-related effects. Data were collected from 604 neuron pairs recorded under spontaneous conditions in primary auditory cortex of seven juvenile (30–70 days) and nine adult cats. Three hundred and six pairs (51%) had a peak cross-correlation coefficient significantly different from zero. For 113 neuron pairs out of this subgroup, correlations were calculated also for spike trains recorded during click stimulation. After a combined burst-correction and deconvolution procedure was carried out, the correlation peak strengths were not significantly changed for spontaneous activity, but peak width was narrower for single-electrode pairs than for dual-electrode pairs, suggesting a better synchronization for neighboring neurons. Under click stimulation conditions, overall peak synchronization strength was independent of interelectrode distance, whereas, after correction for secondary and stimulus effects, peak synchronization was significantly lower for dual-electrode pairs. However, the primary peak width for single-electrode pairs under stimulus conditions was no longer different from that of dual-electrode pairs. This implies that both under spontaneous and stimulus conditions secondary effects largely obscure any underlying correlation produced by anatomical connectivity. The secondary effects may be the result of intrinsic as well as network properties in auditory cortex and may functionally be more important than the weak primary effects resulting from anatomical connections.

Cross-interval analysis suggests that the correlations in auditory cortex are dynamic and may show random switching between states of stronger and weaker synchronization.

Key words Auditory cortex · Cross-correlograms · Cross-interval histograms · Burst-firing · Neural interaction · Cat

Introduction

Several studies in visual cortex (Ts’o et al. 1986; Krüger 1991; Nelson et al. 1992) and auditory cortex (Vaadia et al. 1991; Eggermont 1992; Brosch and Schreiner 1995) have reported long-distance correlations between the firings of individual units. These correlations may be signs of interconnected neural groups or of neural synchrony between cortical subfields. The correlograms obtained in these cases were often rather broad, with peaks centered around zero lag. The first cross-correlation studies in auditory cortex (Dickson and Gerstein 1974) already showed this preponderance of broad symmetrical correlograms straddling the origin. The occurrence of these broad correlogram peaks has subsequently been confirmed for striate cortex (Krüger and Aiple 1988; Nelson et al. 1992), sensorimotor cortex (Fetz et al. 1991) and auditory cortex (Abeles 1982; Eggermont 1992; Brosch and Schreiner 1995). The larger the distance between the units in the pair, the broader the peaks tended to be (Nelson et al. 1992) but broad peaks were commonly found for single electrode pairs as well (Eggermont 1992). Nelson et al. (1992) attributed the wide correlograms for neurons in separate areas (A17 and A18) in visual cortex to corticocortical interactions. Pairwise intracellular studies in somatosensory cortex (Thomson and Deuchars 1994) have shown that excitatory postsynaptic potentials (EPSPs) evoked in pyramidal cells by neighboring pyramidal cells with horizontal separations up to 100 μm tended to be relatively large and fast, whereas those with larger horizontal separations...
tended to be slower and smaller. Since common-input correlogram peaks tend to mimic the correlation of the EPSPs of the two cells, this will give rise to broader correlogram peaks with horizontal separation of the cells (Perkel 1970; Eggermont et al. 1993).

Burst-firing has been implicated as a cause for broad central peaks in cross-correlograms at the level of the retinal ganglion cells (Mastronarde 1983), in the medial geniculate body (MGB, Heierli et al. 1987), and in the infratemporal cortex (Gochin et al. 1991). Krüger (1991) attributed the broad cross-correlograms in visual cortex to a retinal origin and thereby indirectly to bursting at the ganglion cell level. Heierli et al. (1987) found that in MGB the common-input cross-correlograms between bursting cells had broader central peaks (mean 32 ms) than those between cells that did not burst (mean 23 ms). Gochin et al. (1991) found that broad peaks in shared-input cross-correlograms occurred in correspondence with burst activity of at least one neuron of the pair in all but 5 out of 49 pairs examined. Since there is a tendency of cortical cells to burst in synchrony (Legéndy and Salcman 1985; Eggermont et al. 1993), this may be a specific form of correlation induced by covariation in firing rate.

The need to relate structural connectivity patterns (from anatomical tracings) to functional connectivity patterns (inferred from the cross-correlogram) has resulted in a few studies in the striate cortex that report nearly exclusively narrow correlation peaks, either restricted to short distances (Toyama et al. 1981a,b; Toyama and Tanaka 1984) or, sometimes, extending for several millimeters, albeit in patchy form (Ts’o et al. 1986). This latter pattern was related to the patchy arborizations of layer III pyramidal cell collaterals (for auditory cortex see Wallace et al. 1991). It is thus conceivable that within the broad correlograms found in auditory cortex a narrow correlation peak, representing neural connectivity, is hidden. Thus one needs to separate the more global rate correlation from the local and/or patchy event correlations. A flurry of techniques to extract a correlogram that only reflects monosynaptic correlation, real shared input, or “event correlation,” have been proposed. Among these are deconvolution with the autocorrelogram of the common-input spiketrain (Perkel 1970; Eggermont et al. 1993), removing bursts from the spike record and only calculating correlations between isolated spikes (Eggermont et al. 1993), subtracting a Gaussian fitted to the broad pedestal (Krüger and Mayer 1990), and using the first-order cross-interval histogram instead of the cross-correlogram to distinguish contributions from cortical network properties (Eggermont et al. 1993; Rotter et al. 1993). These methods potentially remove some contributions from the correlograms that are common to the firing of both cells. Under the assumption that the effects of a global synchronization and the effects of neural connectivity to the total neural synchrony are additive, these correction procedures yield useful results. A comparison of these techniques on the same large data set under spontaneous conditions may provide us with a way of parceling out what constitutes and underlies a cross-correlogram in cortex. This, we feel, is a mandatory first step in studies that aim at further investigating whether plastic phenomena in cortex such as those putatively induced by intracortical microstimulation (Recanzone et al. 1992) are the result of connectivity changes, i.e., changes in synaptic efficacy, or rather result from changes in synchrony or changes in intrinsic firing properties of the cells. Analyzing the various contributions to synchronized neural activity in cortex would help to elucidate the purported substrate of these synchronizations as a mechanism of feature linking (Singer 1993). Aertsen and Arndt (1993) suggest that “coherence coding is a natural candidate in the context of lateral and feedback networks” such as are occurring in cortex. Understanding what mechanisms contribute to this coherence may allow further distinctions between modulated firing rate codes and temporal codes in cortex.

Under stimulus conditions, inferred neural correlation strengths are often smaller than under spontaneous conditions (Gerstein 1970; Vaadia et al. 1989; Eggermont 1994). This has been interpreted as a possible artifact from a correction procedure that falsely assumes additivity of the correlation from neural connectivity and from stimulus synchrony (Eggermont 1994). It has also been explained as a consequence of shifting the working point of each neuron from the expansive part to the compressive part of the response function (Melssen and Epping 1987). Because the response function of neurons is generally nonlinear, this also reflects nonadditivity. In the light of the recent finding that certain forms of stimulation may disrupt bursting modes of firing (reviewed in McCormick and Feeser 1990; Bowman et al. 1995), it is also possible that the neural correlations obtained under spontaneous conditions were artificially enhanced by the presence of burst firing. In order to explore the relative contributions of burst firing and stimulus synchrony on the neural correlation, we have also applied the burst-correction procedure and the deconvolution procedure to neuron pairs recorded under click stimulation.

The evaluation of correlation theories about the brain (von der Malsburg 1981) or brain theories emphasizing temporal coding (Hopfield 1995) necessitate a stable foundation of techniques to quantify the various aspects of “correlation” and to delineate the various mechanisms that cause neural activity in cortex to become synchronized. As suggested earlier (Eggermont and Smith 1995a,b) strong global synchronizing effects that dominate the cross-correlogram might imply that long-range structural connections were none existent. Dynamic structures such as the cortex probably are reflected in dynamical relationships between neurons; the correlation between neurons is probably different when they partake in the same neural assembly or when they are members of a different assembly. As von der Malsburg (1981) suggested, these relationships may change over very short time frames, giving rise to the idea of dynamic functional connectivities and therefore dynamic correlations.

The aim of this study is therefore to identify and isolate the numerous sources of synchrony and correlation