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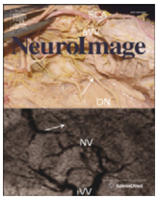

Technical Note

A DCM study of spectral asymmetries in feedforward and feedback connections between visual areas V1 and V4 in the monkey

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ABSTRACT

This paper reports a dynamic causal modeling study of electrocorticographic (ECoG) data that addresses functional asymmetries between forward and backward connections in the visual cortical hierarchy. Specifically, we ask whether forward connections employ gamma-band frequencies, while backward connections preferentially use lower (beta-band) frequencies. We addressed this question by modeling empirical cross spectra using a neural mass model equipped with superficial and deep pyramidal cell populations—that model the source of forward and backward connections, respectively. This enabled us to reconstruct the transfer functions and associated spectra of specific subpopulations within cortical sources. We first established that Bayesian model comparison was able to discriminate between forward and backward connections, defined in terms of their cells of origin. We then confirmed that model selection was able to identify extrastriate (V4) sources as being hierarchically higher than early visual (V1) sources. Finally, an examination of the auto spectra and transfer functions associated with superficial and deep pyramidal cells confirmed that forward connections employed predominantly higher (gamma) frequencies, while backward connections were mediated by lower (alpha/beta) frequencies. We discuss these findings in relation to current views about alpha, beta, and gamma oscillations and predictive coding in the brain.

Introduction

This paper is about the asymmetries in effective connectivity among different levels of the visual cortical hierarchy. These asymmetries were quantified in terms of the spectral characteristics of sources, as measured with electrocorticographic (ECoG) local field potential (LFP) data from an awake-behaving monkey performing a visuospatial attention task. We used dynamic causal modeling to assign underlying neuronal activity to specific cell populations elaborating forward and backward connections among cortical areas. This enabled us to estimate the frequencies conveying forward and backward influences between sources at different hierarchical levels. In brief, we confirmed that forward connections are mediated by gamma frequencies, while backward connections appear to be conveyed by alpha/beta frequencies. These results rest upon two recent developments in the modeling of electrophysiological data: the first is the introduction of dynamic causal modeling for complex data, such as the complex cross spectra summarizing dependencies among recordings from different sites (Friston et al., 2012). The second development is the introduction of a neural mass model (based on a canonical microcircuit) that distinguishes between cell populations that give rise to forward and backward extrinsic connections. This model has been motivated from a theoretical perspective of predictive coding in Bastos et al. (2012). In addition, empirical evidence for a dissociation between gamma and beta in feedforward and feedback transmission in the visual system was recently demonstrated by Bastos et al. (2011, 2015). Given this theoretical and empirical motivation, we use dynamic causal modeling of empirical cross spectra to address, specifically, spectral differences between forward and backward connections and their underlying generative mechanisms.

This paper comprises four sections. The first section briefly reviews the empirical evidence for dissociations in the neuroanatomy, physiology, function, and frequency content of forward and backward message passing, and how these dissociations may be understood in terms of neuronal computations and distributed processing during perceptual inference. The second section then considers the more pragmatic issue of how to quantify asymmetries using mesoscopic and macroscopic electrophysiological measurements. This section constitutes a brief review of the empirical and theoretical motivation for the canonical

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microcircuit model used in the subsequent section for dynamic causal modeling. We then briefly review dynamic causal modeling, with a special focus on models of cross-spectral densities acquired under steady-state assumptions. The final section presents an analysis of empirical data that first establishes the face validity and the predictive validity of the model and then presents our results in terms of population-specific spectral behavior and directed connectivity in terms of transfer functions. We conclude with a discussion of these results in the light of current theories about inter-areal communication, oscillations, and message passing in the brain.

Functional asymmetries in hierarchical connections

The importance of asymmetries between forward and backward connections has been established for several decades and yet the *in vivo* electrophysiological evidence for systematic differences has until recently remained somewhat indirect. Perhaps the most well-known asymmetry between feedforward and feedback connections was established by a series of seminal tract tracing studies (e.g., Rockland et al., 1979) reviewed by Felleman and Van Essen (1991). In this review, the authors examined patterns of anterograde and retrograde anatomical tracing studies made in several different areas of the macaque visual cortex and concluded that three canonical patterns of anatomical connectivity emerged across the many areas studied, which they termed feedforward, feedback, and lateral connections (Felleman and Van Essen, 1991). Feedforward connections canonically derived from the superficial pyramidal cells of the source area and targeted the granular layer of the recipient area, while feedback connections derived from the infragranular layers of the source area and terminated outside the granular layer of the recipient area. This observation led these authors to propose a hierarchical model of cortical processing organized into approximately ten levels, starting with area V1 at the bottom of the visual (cortical) hierarchy. This pattern of connectivity has recently been extended, with the observation that not all feedforward connections derive strictly from the supragranular layers. Instead, it appears that the ratio of projection neurons located in supragranular layer to projection neurons located in infragranular layers can be used as a rough marker for how stereotypically feedforward or feedback a given connection is—areas that are nearby to one another in the hierarchy will have a weaker supra—to infragranular asymmetry compared to areas that are separated by multiple hierarchical levels (Barone et al., 2000; Markov et al., 2013; Vezoli, 2004).

Physiologically, there is a variety of evidence for asymmetries in the functional characteristics of feedforward versus feedback projections. These asymmetries are clearest in the first-order thalamic nuclei such as the lateral geniculate nucleus (LGN), whose afferents can be separated into two classes—feedforward input from the retina and feedback from layer 6 of the first visual cortical area. These connections differ from each other in several ways: feedforward connections display strong initial EPSPs (excitatory postsynaptic potentials), use exclusively ionotropic glutamate receptors, and have depressing synapses to paired-pulse stimulation (Sherman and Guillery, 1998). Feedback connections terminate on the distal part of the dendritic arbor, evoke weaker EPSPs, are more modulatory in the sense that they employ both ionotropic and metabotropic synaptic components, and show paired-pulse facilitation (Sherman and Guillery, 2011). In addition, geniculocortical feedforward and corticogeniculate feedback functional connectivities have recently been shown to be asymmetric in the frequency domain: beta-band frequencies signaled in the feedforward (geniculocortical) direction and alpha-band frequencies signaled in the feedback (corticogeniculate) direction (Bastos et al., 2014a). One possible explanation for this dissociation of the faster frequency for feedforward communication and the slower frequency for feedback communication is that it may be due to the differences in synaptic physiology of the two directions.

In contrast to the LGN afferents, the evidence about the synaptic physiology of corticocortical connections is much more mixed. Two recent studies that examined the synaptic characteristics between mouse V1–V2 and A1–A2 found essentially no evidence for asymmetries in any of the properties that were previously discovered to discriminate feedforward and feedback connections at the level of the LGN (Covic and Sherman, 2011; De Pasquale and Sherman, 2011). At the level of single neurons, it is known that forward connections between V1 and higher cortical areas establish the basic receptive field characteristics of those higher areas because when V1 is experimentally cooled or lesioned to silence its activity, areas V2, V3, V3A, V4, and MT are either strongly reduced in their activity or activity is completely abolished (Girard et al., 1991, 1992; Girard and Bullier, 1989). This is consistent with a strong, driving role for the feedforward connections. In contrast, when the feedback connections are silenced, activity in earlier cortical areas appears to be only weakly affected, and the sign of the effect appears to depend on whether the extraclassical receptive field is stimulated or not (Bullier et al., 1996; Hupé et al., 1998). This indicates that feedback connections are more modulatory or nonlinear and may interact with activity in earlier areas in a complex way. A nonlinear, modulatory role for corticocortical feedback is also consistent with an early neuroimaging study that modeled fMRI responses to visual stimulation, and found that feedback connections between V2 and V1 were more modulatory in relation to the feedforward connection from V1 to V2 (Friston et al., 1995).

Another dissociation between feedforward and feedback connections is their valence (functionally excitatory or inhibitory). Feedforward connections are thought to produce the main excitatory drive to neurons in the visual system, while feedback connections have been associated with contextual processing that can often inhibit neuronal activity of earlier areas (for example, extraclassical receptive field effects). Although extrinsic, i.e., inter-areal, connections in the cortex are often to be exclusively excitatory (but see Melzer et al., 2012), an effective (polysynaptic) inhibitory effect could be mediated through several distinct corticocortical pathways, such as synaptic feedback termination in layer 1 and layer 6 (reviewed in Bastos et al., 2012). Corticocortical feedback connections terminate heavily in these layers (Shipp, 2007), and both layers appear to have an inhibitory influence on pyramidal cells in layers 2 to 5, presumably mediated by intrinsic, i.e., local, inhibitory interneurons (Meyer et al., 2011; Olsen et al., 2012; Shlosberg et al., 2006). This hypothesized inhibitory role for corticocortical feedback is consistent with a large literature in the neuroimaging field that has established that when neuronal responses are more predictable, neural activity in earlier areas tends to decrease, consistent with a predictive role for feedback connections (Alink et al., 2010; Garrido et al., 2009; Summerfield et al., 2008, 2011). Furthermore, a study using dynamic causal modeling (DCM) for induced responses measured with MEG documented a greater suppressive effect of feedback compared to feedforward connections, and this suppressive effect was specific to higher frequencies in higher cortical areas suppressing lower frequencies of lower cortical areas (Chen et al., 2009). The authors interpreted this (somewhat unexpected) result along the following lines: "Heuristically, this means that gamma activity in low-level areas induces slower dynamics at higher cortical levels as prediction error is accumulated for perceptual synthesis. The concomitant high-level gamma activity (due to intrinsic nonlinear coupling) then accelerates the decay of evoked responses in the lower level that are manifest at, the population level, as damped alpha oscillations" (Chen et al., 2009, p461). Importantly, (Chen et al., 2009) modeled induced responses phenomenologically. In the current paper, we build on these findings by modeling the neuronal dynamics that give rise to feedforward and feedback effects such as those reported by Chen et al., 2009. In other words, we try to account for the basic phenomena (asymmetric spectral coupling) in terms of biophysically plausible neuronal processes. Note that the current application of DCM does not require fluctuations in spectral responses; it operates directly on the relative expression of different frequencies in the cross spectra. In contrast, DCM for induced responses (e.g., Chen et al., 2009) models time-dependent changes in cross spectra induced by a stimulus.

This points to another emerging dissociation between forward and backward connections: their frequency content (Wang, 2010). Several