Cortical activity influences geniculocortical spike efficacy in the macaque monkey

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Thalamocortical communication is a dynamic process influenced by both presynaptic and postsynaptic mechanisms. In this study, we recorded single-unit responses from cortical neurons that received direct input from the lateral geniculate nucleus (LGN) to address the question of whether prior patterns of cortical activity affect the ability of LGN inputs to drive cortical responses. By examining the ongoing activity that preceded the arrival of electrically evoked spikes from the LGN, we identified a number of activity patterns that were predictive of suprathreshold communication. Namely, cortical neurons were more likely to respond to LGN stimulation when their activity levels increased to 30-40Hz and/or their activity displayed rhythmic patterns (30 ms intervals) with increased power in the gamma frequency band. Cortical neurons were also more likely to respond to LGN stimulation when their activity increased 30-40 ms prior to stimulation, suggesting that the phase of gamma activity also contributes to geniculocortical communication. Based on these results, we conclude that ongoing activity in the cortex is not random, but rather organized in a manner that can influence the dynamics of thalamocortical communication.

Keywords: V1, LGN, lateral geniculate nucleus, spike rate, coding

INTRODUCTION

Multiple external and internal factors contribute to the dynamics of spike production in the cerebral cortex. Between the lateral geniculate nucleus (LGN) and visual cortex, there is a significant filtering of spikes as LGN neurons typically produce many more spikes than their postsynaptic targets (Alonso et al., 2001; Usrey et al., 2000). Although previous work indicates that much of this filtering can be accounted for on the basis of preceding patterns of presynaptic activity (Levine and Cleland, 2001; Mastronarde, 1987; Rowe and Fischer, 2001; Sinich et al., 2007; Usrey et al., 1998; Usrey et al., 2000; Weyand, 2007), it is also likely that postsynaptic activity patterns play a role. For instance, correlated cortical network activity with increased power in the gamma frequency band and/ or the dynamics of ongoing activity in the cortex could influence the efficacy of thalamocortical communication (Anderson et al., 2000; Arieli et al., 1996; Fiser et al., 2004; Friedman-Hill et al., 2000; Fries et al., 2001a; Fries et al., 2001b; Ramcharitar et al., 2006; Taylor et al., 2005; Tsodyks et al., 1999; Womelsdorf et al., 2006; Womelsdorf et al., 2007).

Along related lines, cortical responses to thalamic input may depend on the depolarized/hyperpolarized or Up/Down state of the cortical neuron’s membrane potential (Bruno and Sakmann, 2006; Haider et al., 2007; Hasenstaub et al., 2005; McCormick et al., 2003; Rigas and Castro-Alamancos, 2007; Rudolph et al., 2007; Sachdev et al., 2004; Shu et al., 2003a; Shu et al., 2003b).

In this study, we examine the influence of prior cortical activity on the transfer of spikes from the LGN to visual cortex in macaque monkeys. To do so, we electrically stimulate the LGN with brief shocks while recording neuronal responses from cortical neurons that receive monosynaptic LGN input. We then compare cortical activity patterns that precede shocks that successfully evoke cortical responses to those that fail to evoke responses. Our results show that electrically evoked spikes in the LGN are more likely to drive suprathreshold responses when the activity of cortical neurons rises to 30–40 Hz. Cortical neurons are also more responsive to LGN input when they are experiencing rhythmic patterns of activity with increased power in the gamma frequency band. These results demonstrate that prior patterns of cortical activity can have a deterministic influence on the transfer of spikes between the LGN and visual cortex.

MATERIALS AND METHODS

Seven adult male macaque monkeys (Macaca mulatta) were used in this study. All surgical and experimental procedures conformed to NIH guidelines and were approved by the UC Davis Institutional Animal Care and Use Committee.

Surgical preparation

Animals were initially anesthetized with ketamine (10 mg/kg, IM) and maintained with sufentanil citrate (3–6 μg/kg/hour, IV) and isoflurane (0.4%) in nitrous oxide and oxygen (2:1). Animals were intubated, placed in a stereotaxic apparatus and wrapped in a thermostatically controlled heating blanket. Throughout the experiment, temperature, expired CO2, electrocardiogram (ECG), electroencephalogram (EEG), heart rate, and SP02 were monitored continuously. Proper anesthetic depth was
assessed by monitoring the EEG for changes in slow-wave/spindle activity, the ECG, and the expired CO₂. If changes in any of these measures indicated a decreased level of anesthesia, additional suxamethonium was given and the rate of infusion increased. A midline scalp incision was made, wound edges were infused with lidocaine, and craniotomies were made over the LGN and V1. Once the dura was reflected, craniotomies were filled with 2% agar in saline. The eyes were dilated with 1% atropine sulfate, fitted with contact lenses and focused on a tangent screen located 172 cm in front of the animal. Following the completion of all surgical procedures, animals were paralyzed with vecuronium bromide (0.2 mg/ kg/hour, IV). Animals were euthanized at the end of each experiment with an overdose of sodium pentobarbital (80 mg/kg).

Data acquisition, electrical stimulation, and neuronal identification

Single-unit recordings were made from V1 neurons using tungsten-in-glass microelectrodes (Alan Ainsworth, London, UK). Neuronal responses were amplified, filtered, and recorded to a PC equipped with a Power 1401 data acquisition system and the Spike2 software package (Cambridge Electronic Design, Cambridge, England). Suction isolation was based on waveform analysis (on-line and off-line) and presence of a refractory period, as indicated by the autocorrelogram.

Neurons in the LGN were electrically stimulated via two platinum/iridium microelectrodes (Frederick Haer and Co., Bowdoinham, ME) implanted in regions of the LGN that were in retinotopic register with recording sites in V1. The exposed tips of the stimulating electrodes were oriented toward 2 standard deviations from the mean level of spontaneous activity. For each neuron, the proportion of spike rates in 10 Hz bins.

RESULTS

We recorded single-unit activity from V1 neurons in the macaque monkey that received monosynaptic input from the LGN to determine whether prior patterns of cortical activity affect the efficacy of geniculocortical spike transfer. Cortical neurons with monosynaptic LGN input were identified by their responses to electrical stimulation in the LGN. This was accomplished by first identifying neurons that followed a brief (0.2 ms), electrical shock with a short-latency response with little temporal jitter (Figure 1A). A collision test was then performed to determine whether the recorded neuron received feedforward input from the LGN and/or provided feedback input to the LGN. In a collision test, the electrical shock is triggered by a spontaneous spike from the recorded neuron. If the recorded neuron receives feedforward input from the LGN, the spike resulting from the shock will propagate to the cortex and drive a postsynaptic spike (Figure 1A). If, however, the recorded neuron is a feedback neuron that projects to the LGN, then the antidromic spike resulting from the shock will collide with the spontaneous spike and the antidromic spike will not reach the cortex (Briggs and Usrey, 2005; Briggs and Usrey, 2007). Using these criteria, we identified 20 V1 neurons that received monosynaptic input from the LGN. Receptive fields of these neurons were located within the central 20 degrees. Based on the relative location of recording sites, these neurons were believed to be located in layers 4C and 6. Across the sample, the average latency for electrically evoked spikes to propagate from the LGN to the cortex was 3.8 ± 0.3 ms (Figure 1B). Similar conduction latencies have been reported previously (Briggs and Usrey, 2007; Bullier and Henry, 1980).

Once we identified a cortical neuron that received direct LGN input, we delivered a shock to the LGN every 5 seconds and examined whether the ability of the shock to evoke a postsynaptic spike was influenced by prior activity from the cortical neuron. For each neuron, shocks were sorted according to whether or not they were successful in evoking a postsynaptic spike. Across our sample of neurons, 51% of all shocks were successful in evoking postsynaptic spikes. More importantly, the pattern of cortical activity that preceded successful trials differed significantly from that which preceded unsuccessful trials (Figure 2). In particular, there were two time intervals prior to the shock (−120 to −130 ms and −30 to −40 ms) where activity preceding successful trials exceeded two times the standard deviation of spontaneous activity (assessed 2 seconds after each shock). For the −30 to −40 ms interval, activity preceding successful trials was significantly greater than activity preceding unsuccessful trials (p < 0.02, t-test).
Cortical activity following electrical stimulation also displayed several noteworthy patterns (Figure 2). As expected, during the first 10 ms following a shock, successful shocks evoked significantly greater activity from recorded neurons than unsuccessful shocks ($p \ll 0.0001$; t-test). Following this time, cortical activity dipped briefly at $\sim 30$ ms for both successful and unsuccessful trials before showing a pronounced elevation between $\sim 40$ and 70 ms. Activity levels for both trial types then decreased for a prolonged period from $\sim 100$–350 ms, which included a period from 150–200 ms where activity levels decreased below spontaneous levels, before returning to baseline levels.

Having found that prior cortical activity can influence the transfer of electrically evoked spikes at geniculocortical synapses, we next asked whether other features of prior activity influence the efficacy of geniculocortical spike transfer. In particular, we wished to determine whether specific spike rates and/or spike correlation patterns preceded successful trials. To study the possible influence of prior spike rate, we calculated spike rates within a 130 ms window immediately preceding successful and unsuccessful trials compared to unsuccessful trials (Figure 3A, red and blue traces, left axis; $p < 0.03$; t-test). An examination of the distribution of preceding spike rates shows that 30–40 Hz occurred significantly more often in successful trials compared to unsuccessful trials (Figure 3A, red and blue traces, left axis; $p < 0.03$; t-test). These results indicate that preceding spike rate, in addition to spike timing, can influence the transfer of spikes at geniculocortical synapses.

To determine whether preceding spike-correlation patterns differed for successful and unsuccessful trials, we generated cumulative autocorrelograms for spikes occurring within a 1-second window prior to electrical stimulation. Across our sample of cortical neurons, autocorrelograms from successful trials contained peaks at $\sim 30$ ms that were not evident in autocorrelograms from unsuccessful trials (Figures 3B and 3C). As a final analysis, we calculated the integral of the power spectrum within the gamma frequency range (20–80 Hz) for each autocorrelogram. Compared to autocorrelograms made from unsuccessful trials, there was 40% more power in the gamma frequency range for autocorrelograms made from successful trials. The analogous comparison made from spontaneous activity measured 2 seconds after successful and unsuccessful trials yielded a difference of less than 4%. Because cortical neurons are more likely to respond to LGN stimulation when their activity increases 30–40 ms before stimulation (Figure 2), it seems likely that the phase of gamma activity is also important for geniculocortical communication.

**DISCUSSION**

We combined single-unit recordings from neurons in the primary visual cortex with electrical stimulation in the LGN to address the question of whether ongoing patterns of cortical activity affect the ability of LGN inputs to drive cortical responses. Our results show that high frequency and/or rhythmic activity can increase the efficacy of geniculocortical communication. In particular, cortical neurons are more likely to respond to LGN stimulation when their activity levels increase to 30–40 Hz and/or their activity displays rhythmic patterns (30 ms intervals) with increased power in the gamma frequency band. Our results also show that cortical neurons are more likely to respond to LGN stimulation when their activity increases 30–40 ms prior to stimulation, suggesting that the phase of gamma activity contributes to geniculocortical communication. Here, we consider the potential mechanisms that underlie these results as well as their functional implications.
Geniculocortical communication and cortical gamma band activity

Recent work demonstrates that ensembles of cortical neurons often display periodic episodes of oscillatory activity in the gamma frequency band (20–80 Hz). This type of activity has been observed across visual cortical areas and is frequently associated with neuronal and behavioral responses to stimuli. Given this, it is tempting to speculate that these periods of increased activity occurred during neuronal Up states. For instance, recordings from brain slices show that neurons in prefrontal cortex and visual cortex are more sensitive to afferent input during Up states (Bruno and Sakmann, 2006; MacLean et al., 2005; Rigas and Castro-Alamancos, 2007; Shu et al., 2003a). Accordingly, we found a consistent increase in the spiking responses of cortical neurons for approximately 70 ms following brief (0.2 ms) electrical stimulation in the LGN. As activity in thalamocortical circuits ultimately affects activity in the cortex, it is tempting to speculate that these periods of increased activity are also likely to influence the temporal properties of spike trains.

In closing, patterns of presynaptic activity in the LGN have been shown to influence the efficacy of geniculocortical communication (Usrey, 2002a; Usrey, 2002b). Here we demonstrate that geniculocortical transmission is enhanced during a specific epoch or phase of the gamma cycle, as predicted from recent modeling efforts and consistent with intracortical communication (Fries et al., 2007; Womelsdorf et al., 2007).
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