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Thalamocortical Conduction Times and Stimulus-Evoked Responses in the Rat Whisker-to-Barrel System

Daniel J. Simons,[1] George E. Carvell,[2] Harold T. Kyriazi,[1] and Randy M. Bruno[1]
[1]*Department of Neurobiology, University of Pittsburgh School of Medicine; and* [2]*Department of Physical Therapy, University of Pittsburgh School of Health and Rehabilitation Sciences, Pittsburgh, Pennsylvania*

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Simons DJ, Carvell GE, Kyriazi HT, Bruno RM. Thalamocortical conduction times and stimulus-evoked responses in the rat whisker-to-barrel system. *J Neurophysiol* 98: 2842–2847, 2007. First published September 5, 2007; doi:10.1152/jn.00800.2007. Studies of the rodent whisker system indicate that somatosensory cortical circuitry operates at a millisecond timescale to transform sensory afferent signals from the thalamus. We measured axon conduction times and whisker-evoked responses of 48 thalamocortical (TC) neurons in the rat whisker-to-barrel pathway. Conduction times were derived from spike-triggered averages of local field potentials evoked in layer 4 cortical whisker-related barrels by the spontaneous firing of individual topographically aligned neurons in the ventral posterior medial thalamus. Conduction times varied fourfold, from 0.31 to 1.34 ms, and faster conducting TC neurons responded earlier and more robustly to controlled whisker deflections. Early arrival of highly responsive TC inputs, thought to contact inhibitory barrel neurons preferentially, could prime the cortical network, rendering it more selective for later-arriving signals.

INTRODUCTION

Experimental and theoretical investigations at both the cellular and the network levels increasingly emphasize the critical role of spike timing in cortical function. An emerging view is that convergence of sparsely firing neurons can serve as the basis for robust stimulus coding, provided that the input neurons fire synchronously (Salinas and Sejnowski 2001). Processing of somatosensory information during active touch is rapid and, as in other sensory systems, the earliest arriving spikes are likely to be particularly important for sensory coding (VanRullen et al. 2005). Rapid perception of tactile stimuli on the human hand depends strongly on the earliest impulses evoked in populations of sensory afferent neurons (Johansson and Birznieks 2004). One implication of these latter findings is that central somatosensory circuits operate at a fast timescale to transform afferent signals that propagate through the posterior column–medial lemniscal system.

The rat whisker-to-barrel pathway is a lemniscal-like system that mediates discriminative touch from the face (Simons 1995). Animals are capable of detecting small differences in texture that are presumably signaled by responses of primary afferent neurons to rapid accelerations and decelerations of whisker hairs as the animal sweeps them across an object's surface (Carvell and Simons 1990). Trigeminal ganglion neurons respond reliably and at short latency to deflection velocity and/or acceleration (Jones et al. 2004; Shoykhet et al. 2000), and both thalamic and cortical neurons fire most robustly in response to high velocity/acceleration stimuli (Pinto et al. 2000; Temereanca and Simons 2003). Experimental and theoretical studies indicate that fast-acting circuitry within whisker-related layer 4 barrels is preferentially sensitive to initial changes in thalamic input signals (Pinto et al. 2003; Wilent and Contreras 2004). To date action potential conduction within the barreloid-to-barrel circuit has been viewed as being uniform. Indeed, studies of the ventral posterior medial thalamic nucleus (VPm), the main source of thalamocortical inputs to the barrels, indicate that neurons there are morphologically and functionally rather homogeneous (Arnold et al. 2001; Harris 1986), at least in comparison to geniculocortical pathways in cats and monkeys where neurons differ substantially in terms of cellular morphology, laminar location, receptive field properties, and axon conduction velocities (e.g., Dreher et al. 1976; Hoffman et al. 2007; Marrocco 1976).

Working in the rabbit whisker system, Swadlow and colleagues (Swadlow and Gusev 2000; Swadlow et al. 2002) used a powerful method to assess the functional impact of individual thalamocortical axons on cortical circuitry. Local field potentials (LFPs) in the cortex are recorded in response to the spontaneous firing of an individual thalamic neuron, and spike-triggered averages (STAs) are generated from several thousand samples. These STAs consist of complex waveforms having distinguishable pre- and postsynaptic components. The earliest waveform, called the *axon terminal potential* (AxTP), reflects the incoming thalamic spike; the existence of an AxTP is thought to indicate nearby termination of a thalamocortical neuron's axon. Subsequently, Bruno et al. (2003) showed that amplitudes of AxTPs evoked from a single thalamocortical neuron can vary within a cortical barrel and that AxTP size correlated with the angular tuning preference of both the thalamic unit and of nearby barrel cells.

On further examination of the data from the Bruno et al. study, we noticed that there was variability not only in AxTP amplitudes evoked by different thalamocortical units (TCUs) but also in their onset latencies. Moreover, AxTP latency for a given TCU could differ at different recording sites in the same barrel. In the present study, we examine AxTP latencies in detail and investigate possible relationships between thalamocortical axon conduction time and stimulus-evoked response properties. Conduction times vary fourfold, from 0.31 to 1.34 ms, and faster conducting TC neurons respond earlier and more robustly to whisker deflection. Such small asynchrony in the

Address for reprint requests and other correspondence: D. J. Simons, Department of Neurobiology, University of Pittsburgh School of Medicine, E1452 Biomedical Science Tower, 200 Lothrop Street, Pittsburgh, PA 15261 (E-mail: cortex@pitt.edu).

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arrival times of thalamocortical impulses, at the submillisecond scale, could enhance response tuning of neurons at the initial stage of processing by the cortical column.

METHODS

We used averaged cortical LFPs triggered from thalamic spikes to estimate the conduction times of individual thalamocortical axons. Spike-triggered averages were obtained in nine adult female rats using procedures described by Bruno et al. (2003). Briefly, rats were initially anesthetized with halothane (1.5–2.0%) and craniotomies were made in the dorsal skull overlying the ventral posterior medial thalamus (VPm) and the posteromedial cortical barrel field; all wound margins were sutured closed and warm saline was applied to an acrylic dam around the craniotomy. For neural recordings, the animal's head was held by means of a steel post attached to the skull and the rat was maintained in a lightly sedated state using a synthetic opiate agonist [fentanyl, ~10.0 $\mu g \cdot kg^{-1} \cdot h^{-1}$, administered intravenously (iv)]. To prevent spontaneous facial movements, neuromuscular blockade was produced using pancuronium bromide (1.6 $mg \cdot kg^{-1} \cdot h^{-1}$, iv), the core temperature was maintained at 37 °C using a heating blanket, and the animal was ventilated with a positive-pressure respirator (Inspiron, Harvard Apparatus). The animal's physiological condition was continuously monitored using a computer to track femoral arterial blood pressure, pulse rate, electroencephalogram, and tracheal airway pressure waveform. At the conclusion of the experiment, or if normative physiological parameters (see Fraser et al. 2006) could not be maintained, the rat was deeply anesthetized with pentobarbital sodium and perfused transcardially for subsequent histological evaluation of recording sites using cytochrome oxidase (CO) histochemistry.

Extracellular recordings were made using 2- to 6-MΩ electrodes constructed from pulled and beveled quartz-coated platinum–tungsten (90/10%) filaments (Uwe Thomas Recording, Giessen, Germany). Single microelectrodes were advanced into VPm using a hydraulic microdrive (David Kopf Instruments, Tujunga, CA). In eight experiments, cortical LFP recordings were obtained with a multielectrode array consisting of two to four microelectrodes mounted in a Thomas multichannel manipulator and head-stage system. All of the cortical electrodes were positioned within the same barrel (confirmed histologically) at distances of 75–300 μm using a surgical microscope equipped with a reticule, and electrode placements were noted with respect to surface blood vessels. The thalamic electrode was placed in the topographically aligned thalamic barreloid. In one experiment, only a single cortical electrode was used. Thalamic recordings were obtained from well-isolated single units using conventional amplification and filtering (0.3–10 kHz). Cortical LFPs were filtered at 10 Hz and 10 kHz. Analog signals of both the thalamic spikes and the one to four channels of cortical data were digitized at 32 kHz and saved to disk. Histological evaluation verified that all thalamic recording sites were located within the VPm nucleus, as viewed in coronal sections. For cortical recordings, the cortex was removed and sectioned in a tangential plane. The barrel of interest and the overlying blood vessels, visible in the most superficial sections, were aligned. It was not feasible to locate precisely the position of each electrode within the barrel; histology was used only to verify that electrode penetrations were within the barrel center, as defined by CO staining.

For cortical recordings, we identified the principal whisker (PW) as the whisker that evoked the largest multiunit responses elicited by manual whisker deflections; the PW was subsequently confirmed histologically by matching it to the barrel in which the electrodes were placed. Thalamic recordings were obtained from homologous thalamic barreloids determined from similar physiological identification of the PW.

Responses of TCUs to controlled whisker deflections were subsequently obtained using an electromechanical stimulator that deflected the PW in eight randomly interleaved directions in 45° increments (Simons 1983). The electromechanical stimulator was attached to the whisker 10 mm from the skin. Ramp-and-hold deflections of 1.0-mm amplitude had onset and offset velocities of about 125 mm/s and sustained displacements of 200 ms. Batteries of eight deflections were delivered 10 or 20 times (total of 80 or 160 trials). For constructing poststimulus time histograms (PSTHs), spike times were binned at 0.1 ms and examined either at this resolution or after a further recombination using 1.0-ms bins. Responses to stimulus onsets (ON) and offsets (OFF) were measured during a 20-ms epoch that captured the large transient responses; plateau activity was measured during the latter 100 ms of the sustained deflection. Similarly, spontaneous activity was measured for a 100-ms period preceding deflection onset. Angular tuning of ON responses was quantified by a directional sensitivity index (DS) as the ratio of the maximal angle response to the response computed over all eight deflection angles.

Spike-triggered averages

Neural signals from each cortical electrode were acquired on the occurrence of a spontaneous thalamic action potential. Mean spontaneous activity was 15.7 Hz (range 1.5–36.8, median = 13.8, $n = 48$). Cortical STAs were constructed from >2,000 such events. STAs consist of a rapid, short-latency initially positive-going biphasic or triphasic waveform superimposed on a long-duration negative-going potential that peaks variably approximately 3.0 ms after the thalamic spike (see Fig. 1 and following text;, also see Fig. 1 from Swadlow and Gusev 2000). The early waveform (i.e., the AxTP) reflects the incoming action potential, whereas the later negativity, termed the focal synaptic negativity (FSN), is a postsynaptic field response (Bereshpolova et al. 2006; Swadlow and Gusev 2000). In experiments in which the array was used to record cortical activity, we obtained data from 45 thalamic units and 153 cortical recording sites, 109 of which yielded an AxTP. For the remainder of the analyses, AxTP latencies are reported based on a single value, when only one AxTP was present, or on the average value, when AxTPs were observed on two or more of the cortical electrodes. Virtually identical results were obtained when only the fastest (or sole) AxTPs were analyzed. In one experiment only a single cortical electrode was used; this experiment yielded four thalamic units with four AxTPs. Data from 24 TCUs (and accompanying STAs) were taken from the previous study of Bruno et al. (2003).

RESULTS

Figure 1*A* shows three simultaneously acquired STAs recorded within a barrel using three cortical electrodes and

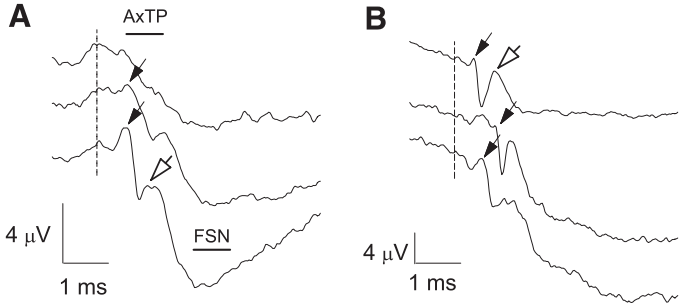

FIG. 1. Simultaneously obtained spike-triggered averages. *A*: this thalamocortical unit (TCU) yielded axon terminal potentials (AxTPs, denoted by solid horizontal bar) on 2 of 3 electrodes. AxTPs were defined by 2 successive positive-going peaks, indicated by solid and open arrowheads. AxTP onset latencies (solid arrowheads in *middle* and *bottom panels*) were both 0.66 ms from the time of the thalamic spike, indicated by the vertical dashed line. *Bottom trace* has a particularly well defined focal synaptic negativity (FSN). *B*: 3 simultaneously recorded AxTPs illustrating the largest observed difference in latencies (0.44 ms in *top trace* vs. 0.91 ms in *middle trace*).

referenced to the spontaneous spikes of a single thalamocortical neuron in the topographically aligned barreloid. As described previously, AxTPs (and FSNs) vary in amplitude across recording sites within the same barrel. The *bottom trace* shows a relatively large AxTP that consists of an initial positive wave that peaks (solid arrowhead) 0.66 ms after the thalamic spike. This peak is followed by a sharp negative transition and, about 0.5 ms later, a second small-amplitude positive-going peak (open arrowhead). The presence of two such well-defined positive peaks separated by a rapid negatively sloped potential was taken as the criterion for identifying an AxTP, and the first peak was taken as its latency. The *middle trace* contains an AxTP as identified by this criterion; the first-peak latency is also 0.66 ms. Although an initial peak can be discerned in the *top trace*, a clear second peak cannot be unambiguously identified and thus no AxTP was measured. Figure 1*B*, from a different experiment, shows three STAs, each with an identified AxTP. In contrast to the recordings in Fig. 1*A*, the three AxTP latencies in Fig. 1*B* differed substantially, ranging from 0.44 ms (*top trace*) to 0.91 ms (*middle trace*); this represents the largest difference observed in our sample. When multiple AxTPs were recorded simultaneously from a single TCU, the mean difference between the fastest and slowest conduction times was 0.13 ms (range 0.0–0.47 ms). Multiple AxTPs referenced to single TCUs were obtained from electrodes within the same barrel. However, it is unclear whether interelectrode distance per se relates to latency differences, when observed, among multiply recorded AxTPs or, for that matter, the likelihood of obtaining them at all.

For a given thalamocortical neuron AxTP latency was correlated with its whisker-evoked response. Figure 2 shows data from three TCUs. The TCU in Fig. 2*A* had a rapid axonal conduction time, as revealed by its short-latency AxTP (0.34 ms), and it responded robustly to whisker deflection as shown by the PSTH below. As illustrated in the polar plot, the TCU was moderately tuned for deflection angle (DS = 1.76). Figure 2*C* shows data from the TCU having the longest AxTP latency (1.34 ms); the cell responded with few spikes to whisker deflection but was well tuned for deflection angle (DS = 2.50). Figure 2*B* shows data from a thalamic cell having intermediate values of AxTP latency and response magnitude (DS = 2.03).

The distribution of mean AxTP latencies is plotted in Fig. 3. The mean value is 0.63 ms with a range of 0.39 to 1.34 (median = 0.60). Note that for Fig. 3 when more than one AxTP was recorded (see METHODS) values are based on average latencies. The shortest single AxTP latency was 0.31 ms; the longest was 1.34 ms. Figure 3*B* shows that response magnitudes evoked by whisker deflection onsets averaged over all eight directions [mean = 1.13 ± 0.67 (SD) spikes per stimulus, median = 1.03] were inversely related to axonal conduction time (Pearson correlation coefficient $R^2 = 0.20$, $P = 0.001$). Similar results ($R^2 = 0.14$, $P = 0.008$; not plotted) were observed for ON responses to each cell's maximally effective deflection angle (mean = 2.12 ± 1.19 spikes per stimulus, median = 1.93). Both the all-angle and maximum-angle correlations remained significant when the two slowest AxTP values were removed ($P = 0.009$ and $P = 0.05$). As plotted in Fig. 3*C*, response magnitudes evoked by stimulus offset averaged over eight directions (mean = 0.92 ± 0.53, median = 0.92) were also inversely related to conduction time ($R^2 = 0.16$, $P = 0.005$); identical correlation values were observed for OFF responses at the maximally effective angle (mean spikes per stimulus = 1.82 ± 1.09, median = 1.60). Again, both relationships remained significant after removal of the two slowest AxTP values ($P = 0.05$ and $P = 0.04$, respectively).

In some experiments, depending in part on the number of cortical electrodes used, multiple AxTPs referenced to a single TCU were obtained. Thus an individual response measure, e.g., maximal angle ON response, could be associated with more than one conduction time measure. To avoid counting such response measures multiple times, we averaged AxTP latencies to arrive at a single value for comparison with other TCUs for which only one AxTP was obtained. Although the mean difference in latency for multiple AxTPs was small, the averaging procedure could conceivably bias the analyses; we therefore additionally analyzed the data set using all individual AxTP latency measures ($n = 109$). All the aforementioned relationships between AxTP latency and response magnitudes remained highly robust, and statistical significance levels were an order of magnitude greater (i.e., smaller P values) when analyses were based on the 109 individual AxTPs versus the 49 averaged (or single) values.

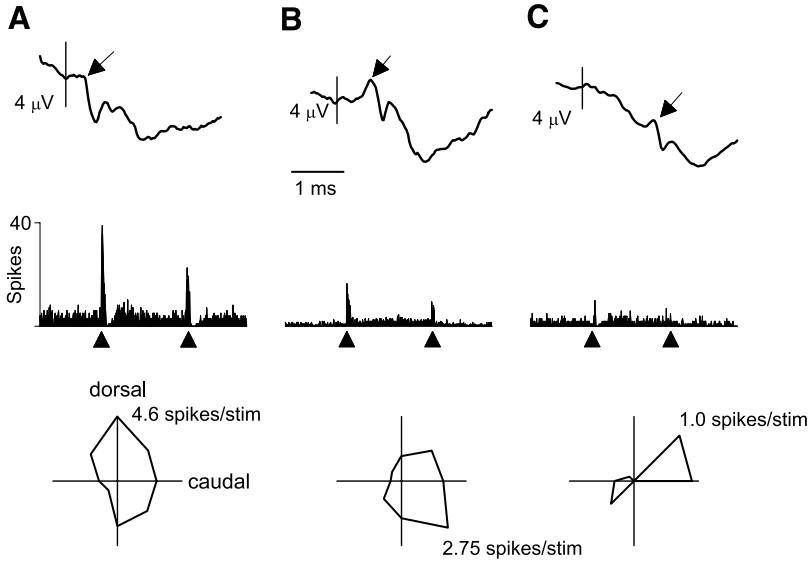

FIG. 2. Representative AxTP latencies and whisker-evoked responses. Each panel shows a spike-triggered average cortical response produced by the TCU whose responses to whisker deflections are shown in the corresponding poststimulus time histogram (PSTH). Each PSTH is based on responses accumulated over all 8 deflection angles, and each is scaled the same. Arrowheads denote stimulus onset and offset. For *top traces* arrows indicate AxTP onset; solid vertical line is the time of the thalamic spikes and the voltage calibration. Data in *A* and *C* are from the TCUs producing one of the shortest (0.34 ms) and the longest (1.34 ms) individual AxTP latencies; *B* is from a TCU having a near-average AxTP latency of 0.65 ms.

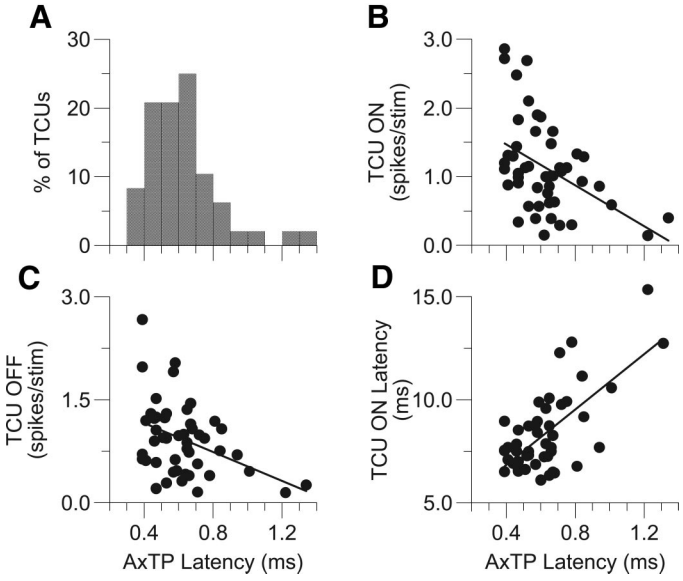

FIG. 3. Axon conduction times and whisker-evoked responses. *A*: distribution of AxTP latencies ($n = 48$) computed as the average across recording sites, when applicable (see METHODS). *B*: scatterplot and regression line of AxTP latencies and responses to whisker deflection onsets (ON) averaged over all deflection angles. *C*: AxTP latencies vs. OFF responses measured over all deflection angles. *D*: AxTP latencies as a function of mean first spike latency evoked by deflection onset at the maximally effective angle (see METHODS).

Strongly responding TCUs are more likely than weakly responding cells to fire at nonpreferred as well as at the preferred (maximally effective) deflection angles; that is, they are more uniformly responsive. We quantified angular tuning by means of a directional sensitivity (DS) index, calculated as the ratio of the response evoked by the maximally effective angle to the response averaged over all eight angles; larger values of DS indicate poorer angular tuning, i.e., more circular polar plots. More strongly responsive TCUs are less angularly tuned (Fig. 4*A*, $R^2 = 0.14$, $P = 0.008$). Consistent with the aforementioned finding that more strongly responsive TCUs have faster conduction velocities (e.g., Fig. 3*A*), faster conducting TCUs tend to display broader angular tuning (Fig. 4*B*, $R^2 = 0.06$, $P = 0.086$). The relationship is more robust when the two outliers having DS values >3.5 are removed ($R^2 = 0.12$, $P = 0.016$), but not when the two cells having the longest AxTP latencies are additionally omitted ($P = 0.24$). The statistical significance of the relationship between DS and AxTP latency ($R^2 = 0.05$, $P < 0.015$) is also greater when the regression coefficient is calculated for all 109 AxTPs rather than average values. To illustrate the combined effects of response magnitude, angular tuning and conduction velocity, we constructed population polar plots for the TCUs having the 10 fastest and 10 slowest average AxTP latencies, i.e., from 0.39 to 0.465 ms and from 0.72 to 1.34 ms. Each individual polar plot was first rotated to a common angle (upward). Figure 4*C* shows that whisker deflection in any direction will evoke, on average, more spikes from the more rapidly conducting population. The population polar plot for the fastest conducting cells is larger and slightly more circular, consistent with the data of Fig. 4, *A* and *B*.

AxTP latency was not correlated with spontaneous activity or evoked activity during the stimulus plateau nor was it correlated with OFF-response angular tuning (data not shown). AxTP latencies were not correlated with AxTP amplitudes. None of the stimulus-evoked response measures examined varied with FSN amplitude.

Fast-conducting thalamocortical neurons having more robust whisker-evoked responses could have a differential effect on cortical circuitry if their signals arrived there earlier, that is, if in addition to faster conduction times they also responded to whisker deflection at the same time as or earlier than the more slowly conducting TCUs. We therefore examined whether conduction velocity of thalamic neurons is related to their whisker-evoked response latencies (Fig. 3*D*). For each TCU we computed the average time of the first spike evoked by a whisker deflection in the cell's preferred angular direction. We examined the maximally responsive deflection angle because TCUs, like trigeminal ganglion cells, often display weak or null responses to stimuli in nonpreferred directions. First-spike latency was positively correlated with AxTP latency ($R^2 = 0.46$; $P \leq 0.0001$); the correlation across all deflection angles was also significant ($R^2 = 0.20$; $P = 0.0003$).

We further examined TCU response profiles by constructing population PSTHs from the 10 fastest and 10 slowest conducting TCUs. Spike times were delayed by each cell's AxTP latency; each population PSTH thus reflects the thalamic signal as it arrives in the barrel neuropil. Response profiles in Fig. 5 confirm the finding that the fastest conducting TCUs have more robust whisker-evoked responses and show, further, that differences in firing rate are most pronounced during the first few milliseconds of the response. We quantified the initial slope of the population firing rate by computing 40% of the total response magnitude (within the response window) and dividing this value by the time required to reach the 40th percentile spike. This yields a population measure of spikes/ms called *temporal contrast* (TC40), which robustly predicts the re-

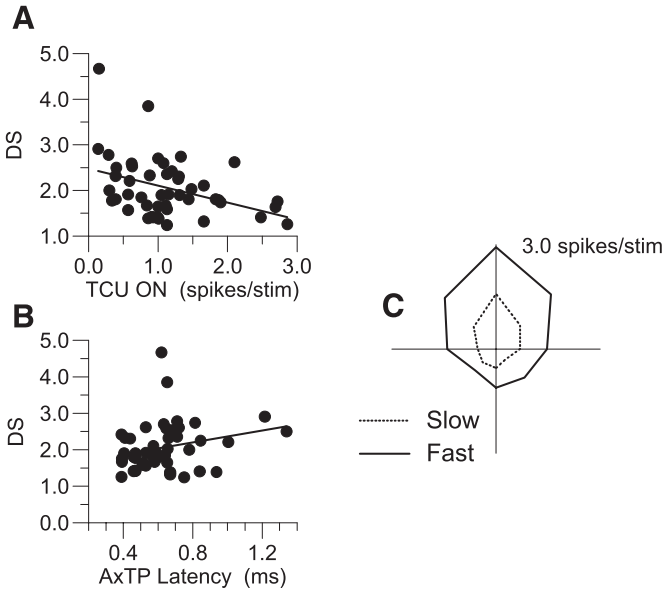

FIG. 4. Relationship between axon conduction time, response magnitude, and angular tuning. *A*: scatterplot and regression line of TCU ON responses (averaged over all deflection angles) and directional sensitivity (DS) calculated as the magnitude of the response evoked by the maximally effective deflection angle divided by the response averaged over all angles. *B*: AxTP latency plotted as a function of DS. *C*: average polar plots constructed from the 10 fastest and 10 slowest conducting TCUs; plots for individual cells were rotated to the same direction, plotted here as up.

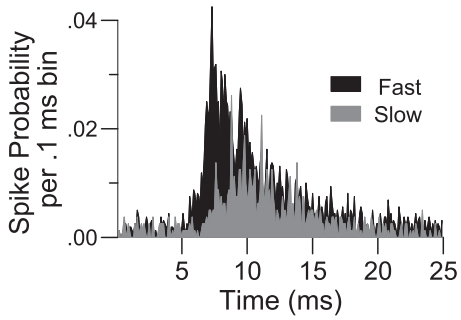

FIG. 5. Population PSTHs constructed from the 10 fastest and 10 slowest conducting TCUs. For each cell, individual spikes were delayed by the corresponding AxTP latency, and spike counts were normalized to the number of whisker deflections. Binwidth = 0.1 ms.

sponses of barrel neurons (Pinto et al. 2000). The population TC40 value for the slowest TCUs is 0.066 spikes/ms, that of the fastest TCUs is 0.192 spikes/ms. Based on the data of Pinto et al. the slow and fast population input signals would evoke cortical responses of approximately 1.1 and 1.7 spikes per stimulus, respectively.

DISCUSSION

We used spike-triggered–averaging approaches to measure conduction times of individual thalamocortical axons that provide input to layer 4 circuits within whisker-related cortical barrels. VPm neurons differ with respect to their axonal conduction velocity, and this parallels differences in both the responsiveness of the neurons to whisker deflection and their stimulus-evoked response latencies. Thus following a whisker deflection faster conducting thalamocortical neurons fire more spikes sooner and do so more broadly with respect to deflection angle. Axon conduction times vary over a range of 1 ms, a brief period but one that is relatively large with respect to the time course of information processing within the barrel circuitry (see following text). With an estimated distance from barreloid to barrel of 5.5 mm, a mean conduction time of 0.63 ms corresponds to a conduction velocity of about 8.5 m/s. By comparison, in rabbits mean VPm-to-vibrissa cortex AxTP latency is 0.71 ms with a range of 0.54–0.92 ms (Swadlow and Gusev 2000); axon distances may be somewhat longer in the rabbit but axons are likely to be of larger diameter. Swadlow and Gusev showed that AxTP conduction times correlate well with independently measured antidromic latencies.

The spike-triggered–averaging approach assumes that the evoked activity in the cortex reflects the influence of the single thalamic neuron that is being recorded (Bereshpolova et al. 2006; Swadlow and Gusev 2000). As noted by Swadlow and colleagues, in the case of AxTPs, the waveforms are so brief that they are unlikely to be produced by multiple cells, which would have to fire virtually simultaneously. Under our recording conditions the synchrony of spontaneous firing is low (Bruno and Sakmann 2006). Nevertheless, to avoid possible contamination in the spike-triggered averages from other synchronously firing thalamocortical neurons, we obtained data only from well-isolated, spontaneous action potentials. Whisker-evoked responses were acquired from cells after we found them to produce an AxTP based on their spontaneous firing. Our sample is therefore biased to TCUs having at least some low level of background activity. However, in our recording conditions almost all barreloid neurons fire spontaneously, and we found no correlation between such firing rates and AxTP latency. We explicitly recorded only in topographically aligned thalamic barreloids and cortical barrels. Although AxTPs may be observed with nonaligned recordings (Swadlow and Gusev 2000), the incidence and strength of the STA activity are small, and we therefore assume that our data reflect the major VPm inputs to single barrels.

Variation in conduction times among thalamocortical axons likely reflects differences in axon myelination and/or diameter. Also, action potential propagation may be slowed at branch points (Debanne 2004). Thalamocortical axons branch extensively within the cortical gray matter and specifically within the layer 4 barrel (Arnold et al. 2001; Bernardo and Woolsey 1987), and therefore local branching patterns might account for our finding that a single TCU can evoke AxTPs differing in latency at different locations within the same cortical barrel. Recording locations associated with longer latencies from a TCU may receive axon collaterals from it that have more local branch points. Similarly, uniformly faster conducting thalamocortical axons may have overall simpler terminal arbors. Anatomical evidence indicates that a given thalamocortical axon may branch more profusely in one part of a barrel than in another (e.g., see Fig. 7 in Arnold et al. 2001). AxTP (and FSN) amplitudes also vary within a barrel, and the pattern of this functional innervation corresponds to the receptive field properties of nearby cortical neurons (Bruno and Simons 2002).

What other properties, related to axon diameter/myelination, might further distinguish VPm neurons? By analogy with other systems (Clamann and Henneman 1976) VPm cells with faster conducting axons may have larger cell bodies. Faster conducting TCUs respond earlier and more vigorously to whisker deflection. Additionally, TCUs that respond more vigorously to PW deflections do so also to deflections of adjacent whiskers (Bruno and Simons 2002), and thalamic neurons having larger somata tend to have larger receptive fields (Harris 1986). These properties do not appear to reflect the cells' receipt of synaptic inputs from similarly rapidly conducting neurons in the brain stem principal sensory nucleus (PrV) because PrV cells having faster conducting axons, measured by antidromic stimulation, are somewhat less responsive to whisker deflection (BS Minnery and DJ Simons, unpublished observations). This latter finding suggests that the robust whisker-evoked responses of fast conducting TCUs reflects greater convergence and/or stronger (e.g., more proximal) trigeminothalamic synapses. Such inputs would be consistent with a requirement for greater spatiotemporal summation by postsynaptic cells having larger somata and/or dendritic fields.

It is presently unclear whether faster versus slower conducting thalamocortical neurons are scattered within a barreloid or whether they are located preferentially in one part of it versus another. One possibility is that fast and slow conducting cells reside in different compartments within a barreloid, such as the side versus the center. Another is that the fastest conducting neurons are located dorsomedially in the barreloid, near the VPm–medial posterior (POm) border. Barreloid cells closer to the VPm–POm border have larger dendritic fields (Varga et al. 2002). Dorsomedial aspects of barreloids stain more darkly for cytochrome oxidase, suggesting higher activity-related metabolism (Land et al. 1995). Neurons there tend to have larger

whisker receptive fields (Sugitani et al. 1990), and thalamocortical cells that fire more robustly to adjacent whiskers also respond more robustly to the principal whisker (Bruno and Simons 2002). Similarly, the slowest conducting, longest latency, and weakest responding TCUs might be preferentially situated in the ventrolateral aspects of VPm where neurons may receive longer-latency inputs from the spinal trigeminal complex as well as from PrV (Pierret et al. 2000). Electrophysiological recordings incorporating single-cell labeling are needed for addressing such fine-scale functional topography within VPm.

In the whisker-to-barrel system thalamocortical conduction is fast, having a mean conduction time of about 0.6 ms. In processing the incoming thalamic signal, barrel circuitry also operates quickly. Rapid, strong, feedforward inhibition coupled with recurrently interconnected local neurons render barrel circuitry highly sensitive to the timing of thalamocortical inputs—on the millisecond scale (Gabernet et al. 2005; Pinto et al. 2003; Swadlow 2003). For example, in response to the approximately 125 mm/s deflections used here, the cortical response is largely determined by the firing rate during the first 2–4 ms of the thalamic response (Pinto et al. 2000). Thus a spread of conduction times of about 1 ms is potentially significant. In this regard, it is interesting that the most strongly responsive TCUs preferentially contact fast-spike units (FSUs; Bruno and Simons 2002), which in the barrel are thought to correspond to GABAergic interneurons. Together with the present findings, these data raise the possibility that FSU/inhibitory interneurons, in contrast to excitatory barrel neurons, may be contacted by a subpopulation of broadly tuned, faster conducting TCUs that respond to whisker deflections more robustly and at shorter latency. Such a specialization within the thalamocortical system would provide yet another mechanism for ensuring that feedforward inhibition is fast and powerful.

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Present address of R. M. Bruno: Columbia University, Hammer Health Sciences Building, 701 West 168th Street, New York, NY 10032.

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REFERENCES

Arnold PB, Li CX, Waters RS. Thalamocortical arbors extend beyond single cortical barrels: an in vivo intracellular tracing study in rat. *Exp Brain Res* 136: 152–168, 2001.

Bereshpolova Y, Stoelzel CR, Gusev AG, Bezdudnaya T, Swadlow HA. The impact of a corticotectal impulse on the awake superior colliculus. *J Neurosci* 26: 2250–2259, 2006.

Bernardo KL, Woolsey TA. Axonal trajectories between mouse somatosensory thalamus and cortex. *J Comp Neurol* 258: 542–564, 1987.

Bruno RM, Khatri V, Land PW, Simons DJ. Thalamocortical angular tuning domains within individual barrels of rat somatosensory cortex. *J Neurosci* 23: 9565–9574, 2003.

Bruno RM, Sakmann B. Cortex is driven by weak but synchronously active thalamocortical synapses. *Science* 312: 1622–1627, 2006.

Bruno RM, Simons DJ. Feedforward mechanisms of excitatory and inhibitory cortical receptive fields. *J Neurosci* 22: 10966–10975, 2002.

Carvell GE, Simons DJ. Biometric analyses of vibrissal tactile discrimination in the rat. *J Neurosci* 10: 2638–2648, 1990.

Clamann HP, Henneman E. Electrical measurement of axon diameter and its use in relating motoneuron size to critical firing level. *J Neurophysiol* 39: 844–851, 1976.

Debanne D. Information processing in the axon. *Nat Rev Neurosci* 5: 304–316, 2004.

Dreher B, Fukada Y, Rodieck RW. Identification, classification and anatomical segregation of cells with X-like and Y-like properties in the lateral geniculate nucleus of old-world primates. *J Physiol* 258: 433–452, 1976.

Fraser G, Hartings JA, Simons DJ. Adaptation of trigeminal ganglion cells to periodic whisker deflections. *Somatosens Mot Res* 23: 111–118, 2006.

Gabernet L, Jadhav SP, Feldman DE, Carandini M, Scanziani M. Somatosensory integration controlled by dynamic thalamocortical feedforward inhibition. *Neuron* 48: 315–327, 2005.

Harris RM. Morphology of physiologically identified thalamocortical relay neurons in the rat ventrobasal thalamus. *J Comp Neurol* 251: 491–505, 1986.

Hoffman K-P, Stone J, Sherman SM. Relay of receptive-field properties in dorsal lateral geniculate nucleus of the cat. *J Neurophysiol* 35: 518–531, 2007.

Johansson RS, Birznieks I. First spikes in ensembles of human tactile afferents code complex spatial fingertip events. *Nat Neurosci* 7: 170–177, 2004.

Jones LM, Depireux DA, Simons DJ, Keller A. Robust temporal coding in the trigeminal system. *Science* 304: 1986–1989, 2004.

Land PW, Buffer JSA, Yaskosky JD. Barreloids in adult rat thalamus: three-dimensional architecture and relationship to somatosensory cortical barrels. *J Comp Neurol* 355: 573–588, 1995.

Marrocco RT. Sustained and transient cells in monkey lateral geniculate nucleus: conduction velocities and response properties. *J Neurophysiol* 39: 340–353, 1976.

Pierret. T, Lavallee P, Deschenes M. Parallel streams for the relay of vibrissal information through thalamic barreloids. *J Neurosci* 20: 7455–7462, 2000.

Pinto DJ, Brumberg JC, Simons DJ. Circuit dynamics and coding strategies in rodent somatosensory cortex. *J Neurophysiol* 83: 1158–1166, 2000.

Pinto DJ, Hartings JA, Brumberg JC, Simons DJ. Cortical damping: analysis of thalamocortical response transformations in rodent barrel cortex. *Cereb Cortex* 13: 33–44, 2003.

Salinas E, Sejnowski TJ. Correlated neuronal activity and the flow of neural information. *Nat Rev Neurosci* 2: 539–550, 2001.

Shoykhet M, Doherty D, Simons DJ. Coding of deflection velocity and amplitude by whisker primary afferent neurons: implications for higher level processing. *Somatosens Mot Res* 17: 171–180, 2000.

Simons DJ. Multi-whisker stimulation and its effects on vibrissa units in rat SmI barrel cortex. *Brain Res* 276: 178–182, 1983.

Simons DJ. Neuronal integration in the somatosensory whisker/barrel cortex. In: *Cerebral Cortex*, edited by Jones EG, Diamond IT. New York: Plenum Press, 1995, vol. 11, p. 263–297.

Sugitani M, Yano J, Sugai T, Ooyama H. Somatotopic organization and columnar structure of vibrissae representation in the rat ventrobasal complex. *Exp Brain Res* 81: 346–352, 1990.

Swadlow HA. Fast-spike interneurons and feedforward inhibition in awake sensory neocortex. *Cereb Cortex* 13: 25–32, 2003.

Swadlow HA, Gusev AG. The influence of single VB thalamocortical impulses on barrel columns of rabbit somatosensory cortex. *J Neurophysiol* 83: 2802–2813, 2000.

Swadlow HA, Gusev AG, Bezdudnaya T. Activation of a cortical column by a thalamocortical impulse. *J Neurosci* 22: 7766–7773, 2002.

Temereanca S, Simons DJ. Local field potentials and the encoding of whisker deflections by population firing synchrony in thalamic barreloids. *J Neurophysiol* 89: 2137–2145, 2003.

VanRullen R, Guyonneau R, Thorpe SJ. Spike times make sense. *Trends Neurosci* 28: 1–4, 2005.

Varga C, Sik A, Lavallee P, Deschenes M. Dendroarchitecture of relay cells in thalamic barreloids: a substrate for cross-whisker modulation. *J Neurosci* 22: 6186–6194, 2002.

Wilent WB, Contreras D. Synaptic responses to whisker deflections in rat barrel cortex as a function of cortical layer and stimulus intensity. *J Neurosci* 24: 3985–3998, 2004.