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Report

Precise Temporal Responses in Whisker Trigeminal Neurons

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Jones, Lauren M., SooHyun Lee, Jason C. Trageser, Daniel J. Simons, and Asaf Keller. Precise temporal responses in whisker trigeminal neurons. *J Neurophysiol* 92: 665–668, 2004. First published March 3, 2004; 10.1152/jn.00031.2004. The ability of rats using their whiskers to perform fine tactile discrimination rivals that of humans using their fingertips. Rats must perform these discriminations rapidly and accurately while palpating the environment with their whiskers. This suggests that whisker-derived inputs produce a robust and reliable code, capable of capturing complex, high-frequency information. The first neural representation of whisker-derived stimulus information is in primary afferent neurons of the trigeminal ganglion. Here we demonstrate that there is a continuum of direction-dependent response profiles in trigeminal neurons and provide the first quantitative analysis of the encoding of complex stimuli by these neurons. We show that all classes of trigeminal ganglion neurons respond with highly reproducible temporal spike patterns to transient stimuli. Such a robust coding mechanism may allow rapid perception of complex tactile features.

INTRODUCTION

Coding of sensory stimuli has been traditionally studied by analyzing changes in mean neuronal firing rates. However, in many sensory systems, stimuli elicit sparse spike trains in individual neurons (Hahnloser et al. 2002; Theunissen 2003; Vinje and Gallant 2000), including the rodent whisker-trigeminal system (Simons and Carvell 1989). The limited numbers of spikes elicited in these systems, combined with the complex stimuli that the systems can distinguish, imply that individual neurons cannot encode stimuli with a rate-based coding scheme. There is mounting evidence that sensory perception involves temporal coding schemes in which the timing of individual spikes encodes information beyond that provided by a rate coding scheme (Dayan and Abbott 2001; Rieke et al. 1997). Temporal coding requires that a sensory stimulus elicit a highly reproducible pattern of spikes. Our goal was to test the hypothesis that in the whisker-trigeminal system, sensory inputs evoke such reproducible spike patterns. We started by analyzing responses in the whisker primary afferents of the trigeminal ganglion, because they necessarily constrain all subsequent processing.

Response properties of whisker-related trigeminal ganglion neurons were previously investigated with the use of ramp-and-hold whisker deflections (Gibson and Welker 1983a,b; Lichtenstein et al. 1990; Shoykhet et al. 2000). In this paradigm, an individual whisker is attached to a computer-controlled piezoelectric device that rapidly deflects the whisker in a specified direction, and maintains the whisker at this deflection angle for tens of milliseconds. This paradigm permits accurate control of stimulus parameters, and studies taking advantage of this approach have elucidated many important response characteristics of trigeminal neurons (Gibson and Welker 1983a,b; Lichtenstein et al. 1990; Shoykhet et al. 2000; see also Szwed et al. 2003). In all of these studies, response properties were characterized based on the neurons' mean firing rates. To test the hypothesis that temporal firing patterns reliably encode stimulus parameters, we focused here on the precise timing of individual spikes in stimulus-evoked spike trains.

METHODS

Data were obtained from nine adult female rats, prepared for electrophysiological recordings as previously described (Lichtenstein et al. 1990). Extracellular recordings of well-isolated single units were obtained under halothane or urethan anesthesia. Spikes were discriminated off-line using amplitude threshold and/or principal component analysis. Autocorrelograms were computed for each unit, and units with interspike intervals <1 ms were discarded. We recorded responses to ramp-and-hold whisker deflections from 85 trigeminal ganglion neurons. As previously described (Gibson and Welker 1983a,b; Lichtenstein et al. 1990; Shoykhet et al. 2000), these neurons had either a phasic response, firing only to stimulus onset and offset, or a phasic-tonic response, firing at stimulus onset/offset and throughout the stimulus hold period (Fig. 1, *A* and *C*). These firing patterns are traditionally used to characterize neurons as either rapidly adapting (RA) or slowly adapting (SA), respectively. However, individual neurons can respond with both RA and SA profiles, depending on the direction of whisker deflection. For example, the neuron depicted in Fig. 1*B* responded tonically (SA response) in five of eight directions, but phasically (RA response) in two of eight directions. Although some cells do respond with an RA or SA profile in every direction of stimulation (Fig. 1, *A* and *C*), we found that 43% of the neurons can respond in either slowly and rapidly fashions, depending on the direction of whisker deflection (Fig. 1*B*).

To quantify this direction-dependent response property, we categorized trigeminal neurons into eight different groups. Category 8 cells respond in a rapidly adapting fashion in all eight directions (pure RA profiles). Category 0 cells respond in a slowly adapting fashion in all eight directions (pure SA profiles). Categories 1–7 respond in a rapidly adapting fashion in one to seven directions and in a slowly adapting fashion (or no spikes) in the remaining directions. For example, the cell depicted in Fig. 1*B* was classified as a category 2 neuron because it responded to two of eight directions in a rapidly adapting fashion. Of the 85 neurons we analyzed, 40% were classified as category 8 (pure RA), and the remaining 60% responded to one or more directions in a sustained, SA-like response (Fig. 1*D*). This finding indicates that trigeminal neurons express a directionally dependent continuum of firing patterns. Gibson and Welker (1983b)

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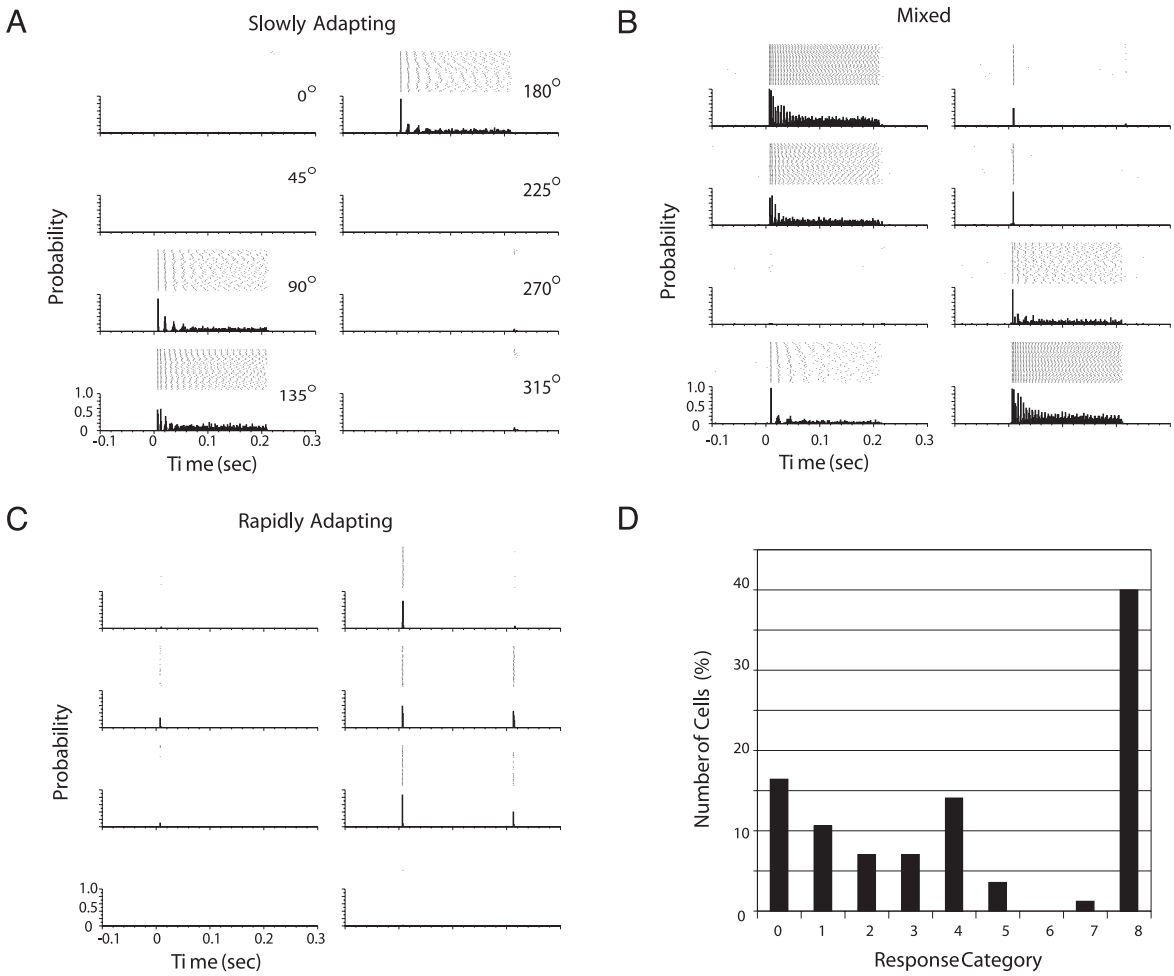


FIG. 1. Direction-dependent response profiles in trigeminal ganglion neurons. *A–C*: peri-event rasters and peristimulus time histograms (PSTHs; 1-ms bins) recorded in response to ramp and hold whisker deflections (200-ms duration), delivered 50 times in each of 8 directions. Neurons that respond with a slowly adapting profile only (*A*) were classified as category 0. Those responding only with a rapidly adapting profile (*C*) were classified as category 8. Neurons with mixed response profiles (*B*) were classified as categories 1 to 7, depending on the number of rapidly adapting response profiles to different deflection angles. *D*: percentage of all cells ($n = 85$) in each response profile category.

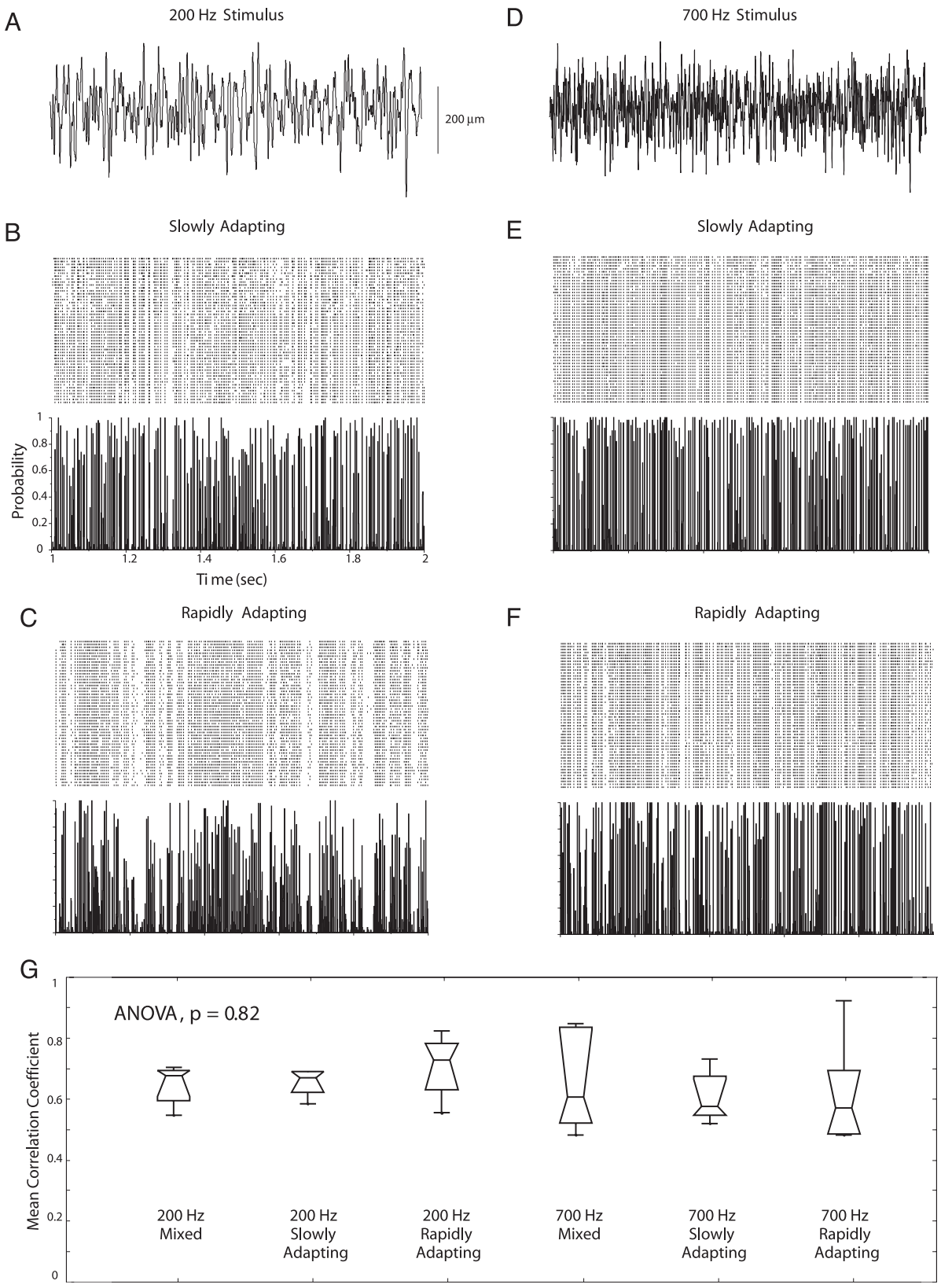
found a similar, amplitude-dependent continuum in sustained responses. Thus this and other classification schemes must take into account the stimulus-dependent response profile continuum—including responses in different directions—of trigeminal ganglion neurons.

RESULTS

In peristimulus time histograms (PSTHs) computed for cells in every category (pure RA, mixed RA/SA, pure SA), the precise timing of the initial spikes was highly reproducible from trial to trial. This reproducibility is evidenced in the early response to the ramp-and-hold stimulus, as seen in Fig. 1. We quantified reproducibility by calculating the time of occurrence of the PSTH bin having the highest probability. For all neurons, the mean peak probability was 89 ± 14% and occurred at 5.6 ± 2.4 ms after stimulus onset. These findings indicate that stimulus transients—such as occur at the beginning of the ramp and hold deflection—produce highly reliable temporal firing patterns in all types of trigeminal neurons.

We then tested the reliability of temporal firing patterns in response to more complex time-varying whisker deflections that may occur during discrimination behaviors (Bermejo et al. 2002; Carvell and Simons 1990; Guic-Robles et al. 1989; Hartmann et al. 2003; Neimark et al. 2003). We deflected an individual whisker in a complex pattern described by a "pink noise" waveform, low-pass filtered at 200 or 700 Hz (Fig. 2, *A*

FIG. 2. Trigeminal ganglion neurons respond to complex noise stimuli with highly reproducible spike trains. *A*: 1-s segment of the 200-Hz pink noise stimulus. *B* and *C*: peri-event rasters and PSTHs recorded in response to 50 presentations of the noise stimulus depicted in *A*. *D*: 1-s segment of the 700-Hz pink noise stimulus. *E* and *F*: peri-event rasters and PSTHs recorded in response to 50 presentations of the noise stimulus depicted in *D*. *G*: notched box and whisker plots (McGill et al. 1978) depicting the mean correlation coefficients among spike trains recorded from each cell class. Lines in each box depict the lower quartile, median, and upper quartile values. The whiskers extending from each end of a box depict the remaining data range. Notches on each box provide an estimate of 95% confidence intervals about the median; that the notches overlap supports the null hypothesis that the true medians in the population are equal.


A
200 Hz Stimulus
200 µm
D
700 Hz Stimulus
B
Slowly Adapting
Probability
Time (sec)
E
Slowly Adapting
C
Rapidly Adapting
F
Rapidly Adapting
G
ANOVA, p = 0.82
Mean Correlation Coefficient
200 Hz Mixed
200 Hz Slowly Adapting
200 Hz Rapidly Adapting
700 Hz Mixed
700 Hz Slowly Adapting
700 Hz Rapidly Adapting

and *D*). We chose these frequency ranges because they encompass the range of frequencies rats are likely to encounter in their environment (Bermejo et al. 2002; Carvell and Simons 1990; Hartmann et al. 2003; Neimark et al. 2003). These waveforms were presented at each cell's preferred direction, as determined from responses to ramp-and-hold stimuli (see preceding text). As expected, individual neurons responded to 700-Hz stimulation with a significantly higher mean firing rate compared with their responses to 200-Hz stimulation (paired *t*-test, $P \leq 10^{-13}$). However, the mean firing rates of the three classes of neurons in response to 200 Hz stimuli (122 ± 57 Hz) were equivalent (ANOVA, $P = 0.70$). Similarly, the mean firing rates of these neuronal classes to 700 Hz stimuli were indistinguishable from each other (273 ± 115 Hz, ANOVA, $P = 0.75$).

Figure 2, *B* and *C*, depicts peri-event rasters and PSTHs in response to 50 presentations of the 200-Hz noise stimulus (Fig. 2*A*), recorded from representative RA and SA units. Figure 2, *E* and *F*, depicts the same for the 700-Hz stimulus (Fig. 2*D*). Note that responses to successive presentations of the same stimulus are highly reproducible, with most spikes—and even multiple spikes within a burst—occurring at precisely the same time in every trial. Highly reproducible response patterns were recorded from all categories of neurons, in response to either 200- or 700-Hz stimuli. Similarly, mechanoreceptors in the cat can precisely phase-lock to high-frequency vibratory stimuli (Gottschaldt and Vahle-Hinz 1981).

To quantify the temporal precision of stimulus evoked spikes, we calculated, for individual cells, the mean correlation coefficient between every pair of the 50 recorded spike trains. Single cell means ranged from 0.50 ± 0.07 to 0.93 ± 0.02, and the group mean across all cells was 0.65 ± 0.11. Figure 2*G* shows means for each cell class (RA, mixed, SA) at each stimulus frequency (200 and 700 Hz). Correlation values computed from responses recorded from all three classes of neuron, in response to either 200- or 700-Hz stimuli, were not significantly different (ANOVA, $P = 0.82$). Thus all classes of neurons respond to complex time-varying stimuli with precise, reproducible temporal patterns of spikes.

DISCUSSION

These findings demonstrate two important characteristics of trigeminal ganglion neurons. First, responses to stimuli mimicking whisker contacts that occur during tactile discrimination are indistinguishable among all classes of neurons. This is evidenced by the similarity in the number and precise timing of spikes evoked in the different classes of neurons, and in the temporal patterns of their evoked responses. Thus the responses of these neurons to static whisker displacements (e.g., RA, SA, or mixed response profile) do not predict their responses to more natural, time-varying stimuli. This is due to the fact that these neurons display a stimulus-dependent continuum of response profiles (Fig. 1*D*) and to the fact that they respond most vigorously (Shoykhet et al. 2000) and reproducibly (Fig. 2) to stimulus transients.

A second important finding is the high temporal precision of responses to repeated presentations of time varying stimuli, including pink noise waveforms and transients in ramp-and-hold stimuli. Because of this precision, a single presentation of a complex stimulus evokes in trigeminal neurons specific and invariant spike patterns. This suggests that a single presentation of a stimulus provides sufficient information to encode complex stimulus features and that these features are encoded equally well in all cell classes. Such a robust coding mechanism may allow faithful detection of rapidly changing, complex tactile features.

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