

Voltage-Gated Na⁺ Channels Enhance the Temporal Filtering Properties of Electrosensory Neurons in the Torus

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Fortune, Eric S. and Gary J. Rose. Voltage-gated Na⁺ channels enhance the temporal filtering properties of electrosensory neurons in the torus. *J Neurophysiol* 90: 924–929, 2003. First published May 15, 2003; 10.1152/jn.00294.2003. Regenerative processes enhance post-synaptic potential (PSP) amplitude and behaviorally relevant temporal filtering in more than one-third of electrosensory neurons in the torus semicircularis of *Eigenmannia*. Data from in vivo current-clamp intracellular recordings indicate that these “regenerative PSPs” can be divided in two groups based on their half-amplitude durations: constant duration (CD) and variable duration (VD) PSPs. CD PSPs have half-amplitude durations of between 20 and 60 ms that do not vary in relation to stimulus periodicity. In contrast, the half-amplitude durations of VD PSPs vary in relation to stimulus periodicity and range from approximately 10 to 500 ms. Injection of 0.1 nA sinusoidal current through the recording electrode demonstrated that CD PSPs and not VD PSPs can be elicited by voltage fluctuations alone. In addition, CD PSPs were blocked by intracellular application of either QX-314 or QX-222, whereas VD PSPs were not. These in vivo data suggest, therefore, that CD PSPs are mediated by voltage-dependent Na⁺ conductances.

INTRODUCTION

Voltage-gated sodium channels are now known to reside in the dendrites of some central neurons (Hausser et al. 2000; Kim and Connors 1993; Magee and Johnston 1995; Turner et al. 1994). Correspondingly, these channels have been implicated in a variety of functions beyond the classical role of generating axonal action potentials (for review, see Reyes 2001). Specifically, dendritic voltage-gated sodium channels may amplify synaptic inputs (Crill 1999; Gonzalez-Burgos and Barrionuevo 2001; Lipowski et al. 1996), actively promote propagation of action potentials into dendrites (Stuart and Sakmann 1994), boost “graded” transmission in nonspiking neurons (Zenisek et al. 2001), and contribute to the bursting properties of central neurons (Magee and Carruth 1999; Turner et al. 1994).

The influences of dendritic sodium channels on the input–output functions of neurons have been investigated primarily in vitro (Hausser et al. 2000). Accelerated by the use of whole-cell patch recording methods (Blanton et al. 1989; Edwards et al. 1989), these studies have provided valuable insight into the distributions of voltage-gated channels and their regional effects on the transmission of electrical signals in dendrites.

Comparatively little is known, however, concerning the roles that these dendritic channels play in the processing of information in vivo. As with in vitro studies, in vivo intracellular investigations of this question have been greatly aided by development of whole cell patch recording methods (Rose and Fortune 1996).

The electrosensory system of gymnotiform fish is an excellent model for exploring the role of voltage-gated sodium channels in information processing in vivo. In social communication, *Eigenmannia* intermittently produce brief interruptions or frequency modulations of their electric organ discharges (EOD) (Hopkins 1974). The brief time course of these signals, coupled with the comparatively long time constants of central neurons, make it likely that amplification processes are needed to ensure transmission of this information to higher centers. Active membrane properties, possibly involving voltage-gated sodium channels, could mediate such amplification. These channels have been found on the apical dendrites of pyramidal neurons in the electrosensory lateral line lobe (first-order central electrosensory area) (Turner et al. 1994), where they contribute to the oscillatory properties of these cells and amplify excitatory postsynaptic potentials (EPSPs) arising from inputs to the apical dendrites (Berman et al. 2001). Little is known, however, about the potential roles of voltage-gated Na⁺ channels in other electrosensory neurons.

Previous whole cell intracellular recordings from neurons in the upper layers of the midbrain torus semicircularis suggest that active membrane properties amplify EPSPs triggered by sensory stimuli (Fortune and Rose 1997a). In these recordings, postsynaptic potential (PSP) amplitude was amplified in an all-or-none fashion at resting potential or with low levels, typically less than –0.2 nA, of negative current clamp. The duration of these all-or-none (regenerative) PSP components was either variable or constant across temporal frequency of stimulation, depending on the cell type. The variable-duration (VD) form principally amplified the responses of cells to low temporal frequencies of stimulation, whereas the constant-duration (CD) type enhanced the responses to higher temporal frequencies. CD all-or-none EPSPs (approximately 20–60 ms in duration, 20–40 mV in amplitude) were often elicited, under negative current clamp, in the absence of spikes. We interpret these findings as indicating that the soma and spike initiation

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zone were sufficiently hyperpolarized to prevent action potential generation, and that the all-or-none CD EPSP components were most likely generated at electrotonically distant sites in the dendrites; current injected at the soma likely produced less hyperpolarization of these dendritic compartments.

In this study, we tested the hypothesis that voltage-gated sodium channels contribute to the all-or-none PSP components of toral neurons by making whole-cell intracellular recordings, *in vivo*, with patch-type pipettes that contained either QX-314 or QX-222. These quaternary ammonium derivatives block voltage-gated sodium channels when applied to the inside of neurons (Narahashi et al. 1972; Strichartz 1973), and have been used in intracellular studies of central neurons (Connors and Prince 1982).

METHODS

Experimental procedures were similar to those described previously (Fortune and Rose 1997a,b; Heiligenberg and Rose 1985; Rose and Call 1993; Rose and Fortune 1999). Fish, approximately 1 yr old, of the genus *Eigenmannia* were used. Animal husbandry, anesthesia, and surgical procedures were performed under the guidelines established by the Society for Neuroscience.

For experiments, a fish's EOD was measured and then attenuated (~1000-fold) by intramuscular injection of Flaxedil (4 µg/g fish). Additional injections of Flaxedil were made during the experiment as necessary to maintain the attenuation of the EOD. The fish's EOD was replaced by a sinusoidal mimic (S1) that was delivered through electrodes placed at the tail and in the mouth. The amplitude and frequency of the S1 were adjusted to approximate the fish's EOD before the injection of Flaxedil. Additional electrosensory stimuli were delivered through an array of carbon electrodes that surrounded the fish. Water temperature was held near 25°C.

At the conclusion of the experiment, not more than 4 h after the first neuron was filled, animals were deeply anesthetized by flow of 4% wt/vol urethane across the gills. Animals were perfused transcardially with saline-heparin solution followed by 4% wt/vol paraformaldehyde in 0.2 M phosphate buffer (pH = 7.4). After perfusion, the brain was removed and stored at 4°C overnight in the paraformaldehyde solution. Sections, 100 µm thick, were cut on a vibratome and reacted using an avidin-biotin peroxidase kit (Elite PK-6100; Vector Laboratories, Burlingame, CA). Sections were dehydrated, cleared in xylenes, mounted on slides, and coverslipped.

Intracellular recording procedures

"Whole cell" recordings were made with patch-type pipettes, as described in detail by Rose and Fortune (1996). Seal resistances of 1 GΩ or more were typically achieved. Intracellular recordings were made from neurons in the dorsal 5 layers of the torus semicircularis of adult *Eigenmannia*. Patch pipettes for intracellular recording were constructed from borosilicate capillary glass (A-M systems No. 5960; 1 mm OD, 0.58 mm ID) using a Flaming-Brown type puller (model P-97; Sutter Instruments). Electrodes were pulled to resistances between 15 and 25 MΩ. Electrode tips were back-filled with a solution (pH = 7.4) consisting of (values in mM) 100 potassium acetate or potassium gluconate, 2 KCl, 1 MgCl₂, 5 EGTA, 10 HEPES, 20 KOH, either QX-314 (bromide salt, 1–40 mM) or QX-222 (chloride salt, 2 mM), and biocytin at a concentration to bring the final osmolarity to approximately 285 mosmol. Biocytin and the QX compounds were replaced by mannitol in the solution used to fill pipette shanks.

Electrodes were mounted in a Plexiglas holder with a "pressure" port. This port allowed the application of pressure pulses (40–80 ms, 40 psi) from a Picospritzer (General Valve) or the manual application of suction or pressure from a 30-ml syringe. The electrode was advanced in 1.5-µm steps (Burleigh 6000 microdrive) through the dorsal 5 layers of the torus. Responses were amplified using an

electrometer (model 767; World Precision Instruments, Sarasota, FL) and stored on videotape at 40 kHz with 16-bit resolution (model 3000; Vetter Instruments).

Initially, recordings were made at several levels of negative holding current (generally less than -0.3 nA). This procedure enabled us to determine whether voltage-dependent conductances contributed to stimulus-driven PSPs; in experiments where QX drugs were placed into the recording electrode, the negative current also limited the diffusion of the positively charged QX compounds into the cell. In experiments without QX drugs, sinusoidal current, 0.1 nA peak-to-peak, was injected into the neuron by the recording electrode. Current sinusoids matched the temporal structure of sensory stimuli, ranging from 2 to 30 Hz. In recordings with QX drugs, the negative holding current was removed after the baseline recording period. Sensory stimulation was continued, thereby eliciting large, all-or-none depolarizations and spiking. These depolarizations appear to accelerate the progression of sodium channel blockade. The amplitude of spikes was monitored to determine the activity of QX drugs in the neuron. In cases where spike amplitude did not drop within 2 min, positive current (<0.2 nA) was applied for ≤1 min to facilitate QX transfer into the neuron. At the conclusion of each intracellular recording, neurons were filled with biocytin by applying 1 to 2 nA of positive DC for 1 to 3 min.

Sensory stimuli

The search stimulus was designed to elicit responses from both ampullary and tuberous neurons in the torus. The ampullary component of the search stimulus was a linear frequency sweep (2–30 Hz, 10-s duration, 1–2 mV/cm at the fish's head) that was added to the S1 and presented through the electrodes in the mouth and at the tail. The tuberous component was the S1 and a sine wave (S2) 4 Hz higher than the S1 frequency. The S2 was delivered concurrently through one pair of the array of carbon electrodes surrounding the fish. Addition of the S2 and the S1 resulted in broad-field amplitude and phase modulations at a rate equal to the difference in frequencies of the S1 and S2; the modulation frequency is known as the "beat rate."

Once a recording was established, the best stimulus (ampullary or tuberous) and the stimulus orientation were determined. Stimulus orientation was chosen to elicit the strongest and most consistent responses from the neuron. The data presented here and in previous reports (Fortune and Rose 1997a,b; Rose and Fortune 1999) indicate that the temporal filtering properties of ampullary and tuberous neurons in the torus are highly similar.

Responses were first recorded while the stimulus frequency (ampullary) or beat rate (tuberous) was linearly scanned from about 2 to 30 Hz. These "sensory scans" were 5 s in duration. Subsequently communication-like stimuli were delivered. These stimuli were generated by "interrupting" an ongoing sinusoidal signal at intervals of about 50 ms. During each interruption, the signal voltage was held briefly at the level that existed when the interrupt command occurred. The "hold voltage" was varied gradually from positive to negative values.

RESULTS

Regenerative PSPs and their functional relations

In a previous study, about 1/3 of neurons recorded in the dorsal 5 layers of the torus showed marked "all-or-none" (regenerative) EPSPs in response to electrosensory stimuli (Fortune and Rose 1997a). In the present study, these PSPs were identified by recording at several levels of negative current clamp (0.0 to -0.4 nA) while presenting an electrosensory stimulus. The stimulus-related PSP amplitude in those neurons with regenerative components dropped dramatically when the negative holding current was increased beyond a particular value; compare recordings at -0.3-nA versus -0.4-nA current

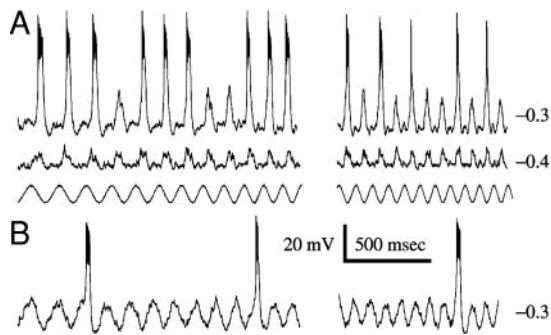


FIG. 1. Activation of "constant-duration" (CD) PSPs. *A*: intracellularly recorded responses of ampullary neuron to frequency-modulated sinusoidal sensory stimulus. Frequency-modulated stimuli were swept from low to high frequencies (2–30 Hz). *Left*: low-frequency sample; *right*: higher-frequency sample (~5–10 Hz shown). The sensory stimulus was presented through 2 carbon rods straddling the fish and oriented at approximately 45° with respect to its longitudinal axis. *Top*: with –0.3-nA holding current; *bottom trace*: –0.4 nA. At –0.3-nA current clamp, full CD PSPs and spikes were triggered on all but 9 cycles of the stimulus; at –0.4 nA the CD PSPs were never triggered. *B*: voltage response of same neuron in response to 0.1-nA sinusoidal current injected intracellularly, –0.3 nA holding current. Frequency of sinusoidal current was similar to that of sensory stimulus above, and is reflected in oscillations of recording trace. Current injection alone was sufficient to trigger CD PSPs, although at this level of holding current they were only occasionally triggered. Resting potential, –70 mV; type b (aspiny) neuron in Lamina III.

clamp (Fig. 1*A*). As in previous studies, regenerative PSPs were divided in two classes, constant duration (CD, Fig. 1) and variable duration (VD, Fig. 2). Stimulus-related PSP amplitudes in neurons without significant regenerative components, however, increased as the level of negative current clamp was increased.

As reported previously (Fortune and Rose 1997*a*), the duration, measured at 1/2 maximum amplitude, of CD PSPs varied little with respect to the periodicity (frequency or beat rate) of the sensory stimulus (Fig. 1). CD PSPs range from 20 to 60 ms across neurons. In contrast, VD PSP duration varied inversely relative to the sensory stimulus periodicity; low stimulus frequencies (~4 Hz) elicited longer-duration VD PSPs (≤ 150

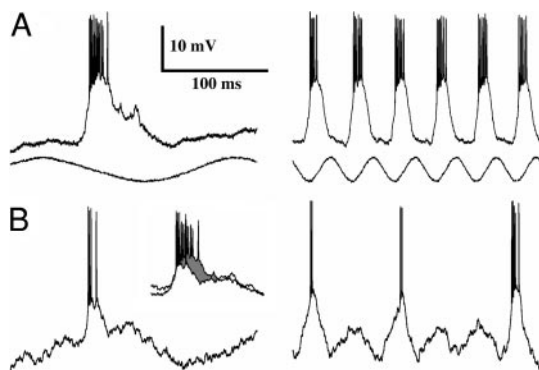


FIG. 2. *A*: intracellular recording from an ampullary-type neuron with both VD and CD PSPs. Sinusoidal sensory stimulus is shown below recording trace. Holding current of –0.3 nA was used. Traces are segments of recording in which all-or-none PSPs were triggered throughout sensory stimulus as it was modulated in frequency from 2 to 30 Hz (lower-frequency sample to the *left*). *B*: voltage response of same neuron in response to sinusoidal current injection, –0.2 nA holding current. *Inset*: traces in *A* and *B* are overlaid; current injection apparently triggers CD PSPs but not VD PSPs in this neuron. Resting potential, –60 mV; type e (giant) neuron in Lamina IV. Sensory stimulus was presented through 2 carbon rods that straddled the fish in transverse orientation; stimulation through mouth-tail electrodes was much less effective.

ms) and high frequencies (~30 Hz) elicited shorter-duration PSPs (~10 ms).

Induction of regenerative PSPs by current injection

To determine whether regenerative PSP components could be elicited by membrane depolarization, sinusoidal current, 0.1 nA peak-to-peak, was injected into three neurons with CD PSPs and three neurons with VD PSPs. Sinusoidal current injection closely matched the temporal structure of the sensory stimuli shown in Fig. 1*A*. The DC offset (holding current) of this sinusoidal signal was between +0.05 nA and –0.4 nA in each experiment.

Sinusoidal current injection into neurons with CD PSPs elicited regenerative depolarizations that appear to be identical to those elicited by sensory stimuli (Fig. 1*A*). Sinusoidal current injection failed, however, to trigger regenerative depolarizations in neurons that showed VD PSPs in response to sensory stimulation.

One neuron appeared to have both VD- and CD-type PSPs (Fig. 2). In this neuron low stimulus frequencies elicited long, variable-duration PSPs, and higher stimulus frequencies elicited shorter, constant-duration PSPs (Fig. 2*A*). Typically, VD PSPs are not elicited by stimulation frequencies of greater than about 10 Hz, whereas CD PSPs are most common at 15 to 30 Hz. Interestingly, subsequent sinusoidal current injection elicited regenerative PSPs with short (~50 ms) durations, even at low stimulation frequencies (Fig. 2*B*), and did not elicit the variable-duration PSPs. Comparison of PSPs elicited by sensory stimulation and voltage responses elicited by current injection suggest that the long-duration PSPs seen in response to low temporal-frequency sensory stimuli were composed of a combination of CD and VD type regenerative PSPs (Fig. 2, *inset*).

Behavioral significance of regenerative PSPs

To determine whether social communication signals ("chirps") elicit CD PSPs, synthesized chirps, short interruptions of a sinusoidal signal, were presented. Such stimuli were effective in eliciting CD PSPs and spikes (Fig. 3). Responses were largest when the interruption consisted of holding the voltage of the stimulating signal at its most negative value (see stimulus traces, Fig. 3). The time course of these PSPs was largely

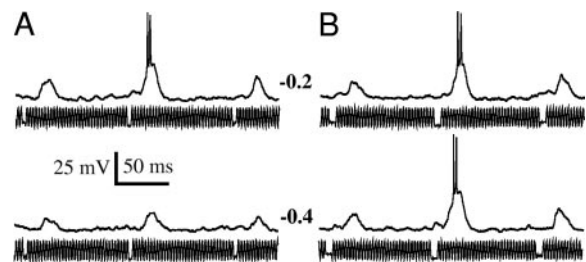


FIG. 3. Enhancement of responses to "chirplike" (communication) stimuli. Recordings were from the same neuron as in Fig. 1, and made at holding currents of –0.2 and –0.4 nA. Sensory stimulus was presented through 2 carbon rods straddling the fish and oriented at approximately 45° with respect to its longitudinal axis. This signal was interrupted every 100 ms by holding voltage constant at the existing value for 2.5 ms (*A*) or 5 ms (*B*). The longer-duration chirps elicited CD PSPs more reliably than shorter-duration chirps. Also, negative-biased chirps were more effective, for this neuron, than more positively biased chirps. Resting potential, –70 mV; same neuron as shown in Fig. 1.

independent of the duration of these stimulus “interruptions” (compare traces in Fig. 3, A and B).

At a current clamp level of -0.2 nA, 2.5- and 5-ms interruptions (stimulus voltage held at most negative value) reliably elicited regenerative PSPs and spikes. At a holding current of -0.4 nA, however, the shorter interruptions failed to elicit spikes on 7 of 8 presentations; a representative recording is shown in the bottom panel of Fig. 3A. At this holding current, 5-ms interruptions triggered regenerative PSPs and spikes on 4 out of 8 presentations. The components of stimulus-driven PSPs that were contributed by active membrane properties that can be viewed by comparing the amplitudes of PSPs that were elicited by the 2.5- and 5-ms interruptions (*bottom panels*).

Previous experiments (Fortune and Rose 1997) demonstrated that low temporal-frequency stimuli, such as those that elicit the jamming avoidance response (JAR), also can elicit VD PSPs.

Effects of QX drugs

QX drugs were applied intracellularly to 17 neurons with regenerative PSP components; 6 cells had CD-type PSPs and 11 had VD types. The QX drugs eliminated spikes in all classes of neurons, including neurons without regenerative PSPs. At 1- to 2-mM concentrations (pipette) of these drugs, spike amplitude and rate diminished over periods from as little as 2 min to more than 20 min in these recordings. Elimination of spikes was accelerated in many neurons when positive current was injected into the cell to increase spiking activity.

In neurons with CD PSPs, there was a concomitant decrease in the amplitude and rate of occurrence of the regenerative

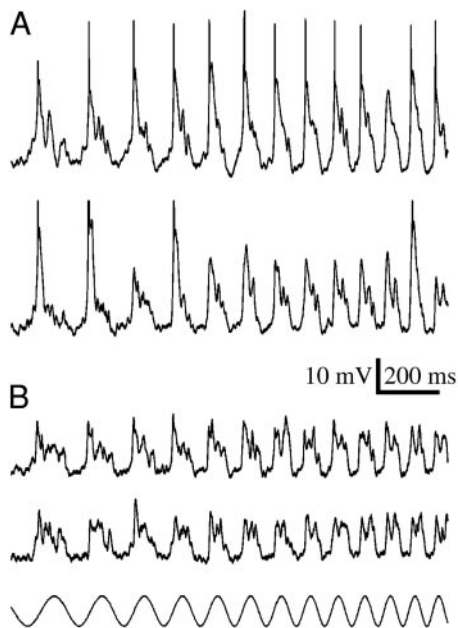


FIG. 4. Effects of QX-222, 2 mM (pipette), on CD-type PSPs. A: intracellular recordings before QX-222 had taken effect. Top: -0.1 -nA holding current; bottom: -0.2 nA. Ampullary sensory stimulus, presented through mouth-tail electrodes, is at bottom of figure. At -0.1 nA most stimulus cycles elicited both a CD PSP and spikes. At -0.2 nA CD PSPs and spikes were infrequently triggered. B: recordings from same neuron approximately 5 min after establishing a stable intracellular recording; CD PSPs and spikes are completely eliminated. Top: -0.1 nA; bottom: -0.2 nA holding current. Resting potential, -50 mV; a poorly filled neuron in Lamina II.

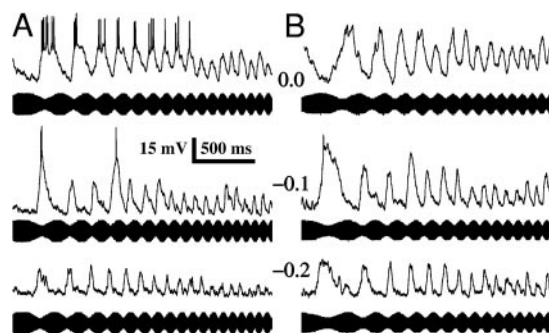


FIG. 5. Effects of QX-222, 2 mM, on VD PSPs. A: recordings before QX-222 had taken effect, and (B) approximately 8 min after establishing the intracellular recording, showing the effects of QX-222. Beat stimuli, shown below each recording trace, were produced by adding S1 and S2, and then delivered through mouth-tail electrodes. Top: intracellular recordings with no holding current; middle: -0.1 nA; bottom: -0.2 nA holding current. With no holding current VD PSPs were triggered by most low-frequency beat cycles; at -0.1 nA VD PSPs were occasionally triggered and at -0.2 nA, were not triggered. QX drugs eliminated spiking but not the VD PSPs. Resting potential, -70 mV; neuron not labeled.

components and spikes. Constant-duration PSPs and spikes were completely, or almost completely, eliminated in all 6 neurons in <20 min (Fig. 4). The shapes of the remaining PSPs were similar to those recorded at negative-current clamp values sufficient for eliminating regenerative PSP components; the latter recordings were made before the QX drugs had taken effect.

In all neurons with VD PSPs, spikes were eliminated but VD PSPs were not (Fig. 5). VD PSPs were qualitatively unchanged after the application of QX drugs. These PSPs were larger, however, after QX delivery, apparently because of a small increase in the cells' input resistance. The durations and the insensitivity to current injection of VD PSPs appeared unchanged in recordings of more than 30 min after the elimination of spikes by the QX drugs. The all-or-none nature of these VD-type PSP components is evident in the recordings at -0.1 -nA current clamp, where they are elicited on some stimulus cycles, but not on others. This amplification of PSP amplitude is absent at -0.2 -nA current clamp.

DISCUSSION

Our earlier intracellular recordings from toral neurons (Fortune and Rose 1997a) revealed prominent all-or-none (regenerative) EPSP components that amplified their low-pass or band-pass temporal filtering properties; hyperpolarization eliminated these components. Such results could be attributed to a positive-feedback network process, requiring the activity of the neuron that was being recorded, or active membrane properties of the neuron itself. Because hyperpolarization also eliminated spiking, it was difficult to distinguish between these two possibilities. On the grounds that regenerative PSPs were often elicited either in the absence of spiking or before the occurrence of spikes, we speculated that they resulted from active membrane properties and not a positive-feedback network.

Intracellular delivery of QX-314 or QX-222 eliminated spiking but failed to attenuate the amplitude of the VD all-or-none PSP components; thus, VD PSPs cannot result from positive feedback. The CD PSPs, however, were eliminated by the

application of QX drugs. This result is consistent with both mechanisms: either a positive feedback network or voltage-gated Na^+ channels. Because the CD PSPs could also be triggered by current injection in the absence of spiking, however, they appear to be the result of active membrane properties (Golding et al. 1999). These lines of evidence thus support the hypothesis that voltage-gated Na^+ channels are responsible for the CD-type PSPs.

Based on the differences in the frequency dependency and time course of regenerative PSPs, we previously proposed to divide these in two distinct physiological classes. This conclusion is strengthened by our present findings that QX drugs eliminated the CD regenerative-type PSPs, but not VD PSPs. These findings also suggest that voltage-gated sodium channels are primarily responsible for CD PSPs.

The validity of this latter conclusion depends on the selectivity of QX compounds for blocking voltage-gated sodium channels. At concentrations of 10 mM, QX-314 has been shown to partially block (<45% of control) low-threshold calcium currents in hippocampal pyramidal neurons (Talbot and Sayer 1996). In other studies, however, QX-314 effectively blocked sodium currents without attenuating calcium currents (Seamans et al. 1997). Although the origins of these differences are unclear, collectively they suggest that these drugs at low concentrations should not appreciably attenuate calcium currents. In our study, QX-314 and QX-222 at concentrations of 1–2 mM completely eliminated the constant-duration, regenerative PSP components. If these depolarizations were primarily a result of the activity of calcium currents, then, at most, only a partial reduction should have been observed. The possibility still remains, however, that high-threshold calcium conductances are also activated by depolarizations that result from the opening of voltage-gated sodium channels (Svoboda et al. 1999); QX agents, in blocking sodium channels, could preclude the normal opening of high-threshold calcium channels. Thus, although we cannot entirely rule out a contribution of calcium conductances, it appears that voltage-gated sodium channels are primarily responsible for generating these large PSP components.

The sodium channel-dependent, regenerative potentials of toral neurons are highly similar to those recorded in vivo from burst-type neurons in the somatosensory cortex of rats (Zhu and Connors 1999). In whole cell recordings in both systems, fast, small spikes often “ride” on much larger regenerative potentials, suggesting that the latter are generated in the dendrites. In vitro studies of cortical neurons suggest that these dendritic, regenerative potentials are mediated by sodium and calcium conductances (Kim and Connors 1993).

What properties of the conductances that result in VD PSPs can we infer from the available evidence? VD PSPs do not likely result from Na^+ conductances because they were not blocked by the application of QX drugs. VD PSPs were also not triggered by voltage fluctuations alone. Evidence from this study and from previous work (Fortune and Rose 2000) demonstrate that VD PSPs are elicited by stimuli that include concurrent synaptic input. We speculate, therefore, that the conductances underlying VD PSPs require both synaptic input and depolarization for activation. These properties are consistent with the hypothesis that *N*-methyl-D-aspartate receptors (NMDARs) generate the conductances that result in appearance of VD PSPs. NMDAR immunoreactivity has been de-

scribed in the dorsal layers of the torus in a related species, *Apteronotus leptorhynchus* (Bottai et al. 1997; Maler and Monaghan 1991;). The hypothesis that VD PSPs are mediated by NMDARs is best tested using in vitro recordings of neurons in living brain slices, where the application of transmitters and receptor agonists can be used to directly assess and characterize the ionic and synaptic bases for the PSPs.

The role of dendritic sodium channels and regenerative potentials

Dendritic sodium channels have been demonstrated in many types of central neurons (for review, see Hauser et al. 2000). These channels are, in many cases, distributed along the dendritic axis in a nonuniform and cell-specific manner, and generate dendritic spikes. There are two schools of thought pertaining to how these dendritic spikes are triggered during information processing. In one model, dendritic sodium channels sustain back propagation of axonal and/or somatic spikes into the dendrites. A competing, although not mutually exclusive, model posits that sodium channel-dependent spikes are triggered by synaptic input and thus serve to amplify relevant patterns of synaptic input. Although these spikes may be generated in vitro after afferent stimulation, it is unclear whether such potentials actually occur in the intact system in response to normal patterns of synaptic input (Kamondi et al. 1998). Ultimately, recordings from these neurons under in vivo conditions of normal information processing are needed to resolve this debate.

In the electrosensory system, these regenerative potentials can be triggered by sensory stimulation and serve to amplify biologically meaningful synaptic input (Fortune and Rose 1997a). This amplification enhances the band-pass temporal frequency selectivity of some electrosensory neurons in the midbrain. Most important, signals that these fish use in social communication (particularly reproductive behavior), for instance, brief cessations of the fish's EODs, are particularly effective in triggering the regenerative, presumably dendritic, sodium “spikes” in midbrain neurons. These in vivo findings thus support the hypothesis that regenerative, sodium channel-dependent dendritic potentials can be elicited by particular patterns of biologically meaningful synaptic input to neurons, and serve to amplify this information.

We cannot ascertain from the in vivo recordings, however, whether voltage-gated sodium channels amplify distal synaptic inputs to dendrites versus those to the proximal dendrites and/or soma. In vitro intracellular recordings with patch-type pipettes are needed to directly identify the distribution of these channels and resolve this issue.

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DISCLOSURES

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