Axotomy- and Autotomy-Induced Changes in the Excitability of Rat Dorsal Root Ganglion Neurons

FUAD A. ABDULLA2 AND PETER A. SMITH1

1Department of Pharmacology and Division of Neuroscience, University of Alberta, Edmonton, Alberta T6G 2H7, Canada; and 2Department of Physical Therapy, Tennessee State University, Nashville, Tennessee 37209

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Abdulla, Fuad A. and Peter A. Smith. Axotomy- and autotomy-induced changes in the excitability of rat dorsal root ganglion neurons. J Neurophysiol 85: 630–643, 2001. The spontaneous, ectopic activity in sensory nerves that is induced by peripheral nerve injury is thought to contribute to the generation of “neuropathic” pain in humans. To examine the cellular mechanisms that underlie this activity, neurons in rat L4–L6 dorsal root ganglion (DRG) were first grouped as “large,” “medium,” or “small” on the basis of their size (input capacitance) and action potential (AP) shape. A fourth group of cells that exhibited a pronounced afterdepolarization (ADP) were defined as AD-cells. Whole cell recording was used to compare the properties of control neurons with those dissociated from rats in which the sciatic nerve had been sectioned (“axotomy” group) and with neurons from rats that exhibited self-mutilatory behavior in response to sciatic nerve section (“autotomy” group). Increases in excitability in all types of DRG neuron were seen within 2–7 wk of axotomy. Resting membrane potential (RMP) and the amplitude and duration of the afterhyperpolarization (AHP) that followed the AP were unaffected. Effects of autotomy were greatest in the small, putative nociceptive cells and least in the large cells. Moderate changes were seen in the medium and AD-cells. Compared to control neurons, axotomized neurons exhibited a higher frequency of evoked AP discharge in response to 500-ms depolarizing current injections; i.e., “gain” was increased and accommodation was decreased. The minimum current required to discharge an AP (rheobase) was reduced. There were significant increases in spike width in small cells and significant increases in spike height in small, medium, and AD-cells. The electrophysiological changes promoted by axotomy were intensified in animals that exhibited self-mutilatory behavior (autotomy group). Increases in excitability in all types of DRG neuron were within 2–7 wk of autotomy. Resting membrane potential (RMP) and the amplitude and duration of the afterhyperpolarization (AHP) that followed the AP were unaffected. Effects of autotomy were greatest in the small, putative nociceptive cells and least in the large cells. Moderate changes were seen in the medium and AD-cells. Compared to control neurons, autotomized neurons exhibited a higher frequency of evoked AP discharge in response to 500-ms depolarizing current injections; i.e., “gain” was increased and accommodation was decreased. The minimum current required to discharge an AP (rheobase) was reduced. There were significant increases in spike width in small cells and significant increases in spike height in small, medium, and AD-cells. The electrophysiological changes promoted by axotomy were intensified in animals that exhibited autotomy. Thus changes in the electrical properties of cell bodies alone may not entirely account for injury-induced spontaneous activity in sensory nerves. The onset of autotomy coincided with alterations in the excitability of large, putative nociceptive neurons. Thus large cells from the autotomy group were much more excitable than those from the axotomy group, whereas small cells from the autotomy group were only slightly more excitable. This is consistent with the hypothesis that the onset of autotomy is associated with changes in the properties of myelinated fibers. Changes in Ca2+ and K+ channel conductances that contribute to axotomy- and autotomy-induced changes in excitability are addressed in the accompanying paper.

INTRODUCTION

Peripheral nerve damage can invoke “neuropathic” pain in humans (Kauppila 1998; Millan 1999). This type of chronic pain is thought to be initiated by persistent spontaneous activity in primary afferent fibers (Nordin et al. 1984; Nystrom and Hagbarth 1981). Experiments using various animal models suggest that ectopic activity originates both from the neuroma that develops at the site of nerve injury and from sensory neuron cell bodies in dorsal root ganglia (DRG) (Babbedge et al. 1996; Kajander and Bennett 1992; Millan 1999; Study and Kral 1996; Waxman et al. 1994). Several laboratories have therefore examined how nerve injury affects the electrophysiological properties of individual DRG neurons (Czech et al. 1977; Gallego et al. 1987; Gurtu and Smith 1988; Kim et al. 1998; Stebbing et al. 1999; Study and Kral 1996; Zhang et al. 1997a). The most consistent finding is that nerve injury reduces the amount of depolarizing current that is required to discharge an action potential (AP) (Gallego et al. 1987; Gurtu and Smith 1988; Kim et al. 1998; Stebbing et al. 1999; Study and Kral 1996; Zhang et al. 1997a). Other observations are less consistent. For example, some authors report clear-cut increases in spike width (Gallego et al. 1987; Kim et al. 1998; Stebbing et al. 1999), whereas others report either small changes (Gurtu and Smith 1988) or no effect (Oyeliese and Kocsis 1996; Oyeliese et al. 1997; Zhang et al. 1997a). This inconsistency likely reflects differences in the response of different types of sensory neuron to axotomy (Abdulla and Smith 1997, 1999; Gurtu and Smith 1988; Kajander and Bennett 1992; Kim et al. 1998; Oyeliese and Kocsis 1996). Variability may also derive from the use of sharp microelectrodes to study DRG in vivo or in vitro in some experiments and the use of patch electrodes to study dissociated cells in others (see Stebbing et al. 1999). Species differences may also be an issue. While some groups have used Wistar rats (Everill and Kocsis 1999; Waxman et al. 1994) or Sprague-Dawley rats (Kajander and Bennett 1992; Xie et al. 1995; Zhang et al. 1997a), Gurtu and Smith (1988) used hamsters, and Gallego et al. (1987) used cats. Even the choice of the strain of rat may lead to inconsistency because the behavioral response of Sprague-Dawley rats to nerve injury is more intense than that of Wistar rats (Carr et al. 1992). Moreover, several different types of nerve injury model have been employed. For example, Wall and Devor...
for the whole DRG population. Zhang et al. (1997a) or identified cutaneous afferent neurons recent voltage-clamp experiments have studied identified un- "large" on the basis of cell body diameter. Some of the more (1996) classified DRG cells into "small," "medium," and long APs and those with short APs, whereas Study and Kral Gurtu and Smith (1988) divided DRG neurons into those with exhibited a "hump" on the repolarizing phase of their APs. This was correlated in the sensory neuron classification criteria used in different subsets (Oyelese et al. 1997). In general, however, differences in the ages of animals used in different studies may have been a factor. Peripheral axotomy promotes much more cell death in the DRG of young animals than it does in older animals (Himes and Tessler 1989).

Most recent studies have used patch-clamp or molecular biological techniques to examine sciatic nerve injury--induced changes in Na\(^+\), Ca\(^{2+}\), and K\(^+\) channel properties and/or expression (Baccei and Kocsis 2000; Black et al. 1997; Cummins and Waxman 1997; Everill and Kocsis 1999; Ishikawa et al. 1999; Rizzo et al. 1995; Sleeper et al. 2000; Waxman et al. 1994). Because of the differences in response of different types of DRG neuron to axotomy (Abdulla and Smith 1997, 1999; Gurtu and Smith 1988; Kajander and Bennett 1992; Kim et al. 1998; Oyelese and Kocsis 1996), changes in AP configuration must be correlated with changes in ionic currents in the same subgroup of neurons. Up until now, few attempts have been made to do this. Oyelese and Kocsis (1996) studied identified cutaneous afferent neurons and showed that sciatic nerve damage reduced the proportion of neurons exhibiting an inflection on their repolarizing phase of their APs. This was correlated with a decrease in the expression of slowly inactivating tetrodotoxin-insensitive Na\(^+\) current in the same identified neuronal subset (Oyelese et al. 1997). In general, however, differences in the sensory neuron classification criteria used in different laboratories (Gallego et al. 1987; Gurtu and Smith 1996) have made it difficult to correlate the older current-clamp data with contemporary voltage-clamp findings. Gallego et al. (1987) studied neurons with conduction velocities >2 m/s, which exhibited a "hump" on the repolarizing phase of their APs. Gurtu and Smith (1988) divided DRG neurons into those with long APs and those with short APs, whereas Study and Kral (1996) classified DRG cells into "small," "medium," and "large" on the basis of cell body diameter. Some of the more recent voltage-clamp experiments have studied identified un-myelinated "C"-type neurons (Cummins and Waxman 1997; Zhang et al. 1997a) or identified cutaneous afferent neurons (Baccei and Kocsis 2000; Everill and Kocsis 1999). As yet, however, no study of the effects of peripheral nerve injury has attempted to correlate current-clamp and voltage-clamp data for the whole DRG population.

We have therefore divided rat L\(_4\) and L\(_5\) DRG neurons into four groups; small, medium, large, and AD-cells and have studied the effect of sciatic nerve section on the "classical" electrophysiological properties of each group. We have used the same cell identification procedure and recording technique in the accompanying paper where we examine changes in K\(^+\) channel currents, Ca\(^{2+}\) channel currents, and Ca\(^{2+}\)-sensitive K\(^+\) conductances (Abdulla and Smith 2001). This approach has also allowed us to apply the same experimental manipulation to similar populations of animals in the two studies and to thereby secure clearer correlation between current-clamp and voltage-clamp data (Abdulla and Smith 2001). Moreover, we are better able to document the differences in magnitude of the effects of axotomy among different groups of DRG neurons.

A second aspect of our work is to study the relationship between nerve injury--induced changes in DRG cells and a self-mutilatory behavior that has been termed "autotomy" (Coderre et al. 1986; Wall et al. 1979). This phenomenon involves biting or gnawing the digits of a denervated limb. Although the appearance of autotomy is regarded, by some, as an appropriate animal model for human neuropathic pain, the exact relationship between the two phenomena continues to be the subject of vigorous debate (Coderre et al. 1986; Kauppila 1998; Rodin and Kruger 1984). As already mentioned, spontaneous activity in damaged sensory nerves originates from both the site of the axon injury and from the cell bodies in the DRG. Wall et al. (1979) suggested that this aberrant activity invokes both autotomy in animals and neuropathic pain in humans. Surprisingly, however, application of local anesthetic to the neuroma that forms at the site of an amputation fails to prevent spontaneous "phantom limb pain" in humans (Nystrom and Hagbarth 1981). This suggests that autotomy is not always directly related to ongoing sensory activity that originates at the site of nerve injury and infers that it may be causally related to aberrant activity originating centrally and/or within DRG (Kauppila 1998). If this is so, the initiation of autotomy should correlate with the onset of alterations in the properties of DRG neuron cell bodies. To test this hypothesis, we have also investigated the possible relationship between axotomy-induced changes in DRG cells and the appearance of autotomy.

**METHODS**

All experimental procedures were in concordance with the recommendations of the International Association for the Study of Pain (IASP) and were reviewed and approved by the University of Alberta animal welfare committee. This committee is responsible for maintaining standards set forth by the Canadian Council for Animal Care. Adult male Sprague-Dawley rats weighing 120–170 g before surgery were housed 2 per cage with free access to food and water under an alternating 12-h light and dark cycle at 23°C. The rats were allowed to adapt to their home cages for 1 wk before use. Rats were anesthe-tized with pentobarbital sodium (50–55 mg/kg ip), and the sciatic nerve was sectioned proximal to its bifurcation into the tibial and the peroneal divisions. A 5- to 10-mm segment of nerve was removed to prevent regeneration. Some of the control animals underwent nerve exploration alone. Operated animals were inspected twice daily for foot mutilation and the degree of autotomy was recorded. Autotomy was scored according to the scale devised by Wall et al. (1979). A score of 1 was given for the removal of one or more nails. The score was increased by 1 for injury to each distal digit, and by another 1 for injury to each proximal digit. Although the maximum score permitted under IASP guidelines is 11, all of our animals were killed before they attained a score of 8. No abnormal behavior or premature deaths occurred in the 7-wk study period. No operated limbs were mutilated by any of the rats. For electrophysiological analysis, rats were
were filtered to within 1 min of establishing whole cell recording. Current-clamp data, generated using 2-ms depolarizing current pulses, were recorded assumed to have reached a "steady state" (see Fig. 4 interspike interval) and the last two APs when the discharge rate was low. To quantify changes in excitability in response to a 500-ms (AHP) that followed the AP was difficult to measure because its minimum amount of depolarizing current that discharged an AP in 50% of trials. Spike width (AP duration) was measured at 50% minimum. Classification of DRG neurons

Control DRG neurons were initially divided into three groups on the basis of their AP waveform: the first group had an AP duration of <3 ms with no deflection in the falling phase, the second group had an AP duration of 3–5 ms with a deflection or shoulder on the falling phase, and the third group had an AP duration of more than 5 ms (Fig. 2A). These differences in AP duration and shape were reflected as differences in cell size as estimated from $C_{in}$. Thus the first group, in which $C_{in}$ was always >90 pF, were defined as large neurons, the second group, in which $C_{in}$ was 70–90 pF, were defined as medium neurons, and the third group, which had the widest spikes and had $C_{in} < 70$ pF, were defined as small neurons. The APs recorded in 16.7% of all control neurons exhibited an afterdepolarization (ADP) rather than an afterhyperpolarization (AHP; Fig. 2A). AD-neurons of this type have been described by White et al. (1989) and Cardenas et al. (1995). Although the $C_{in}$ of most of these cells places them in the medium neuron category, some such cells clearly belonged in the small or large neuron categories. This, and the fact that the AP characteristics of AD-neurons were radically different from small, medium, or large neurons suggested that they should be placed in a fourth, separate category. Because the presence of an ADP often caused AD-neurons to generate bursts of two or more spikes in response to a brief (2 ms) depolarizing current
command (Fig. 2A), we were interested to see whether such cells became more excitable after axotomy.

**Characteristics of control DRG neurons**

Figure 2A illustrates representative recordings of APs elicited in small, medium, large, and AD-neurons by a 2-ms pulse of depolarizing current. Note long duration (broad spike width) of small neuron AP and large ADP in the AD-neuron that promotes the discharge of three APs despite the brevity of the stimulus. The electrophysiological characteristics of 259 control large, medium, small, and AD-neurons are summarized in Table 1.

**TABLE 1. Characteristics of control DRG cells and effects of axotomy and axotomy-induced autotomy**

<table>
<thead>
<tr>
<th>Cell Type</th>
<th>n</th>
<th>RMP, mV</th>
<th>Spike Height, mV</th>
<th>Spike Width, ms</th>
<th>AHP Amplitude, mV</th>
<th>AHP Duration at 25% Repolarization, ms</th>
<th>AHP Duration at 50% Repolarization, ms</th>
<th>AHP Duration at 75% Repolarization, ms</th>
<th>Rheobase, nA</th>
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<tbody>
<tr>
<td>Large cells</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Control</td>
<td>147</td>
<td>-59.1 ± 1.5</td>
<td>100.9 ± 0.9</td>
<td>1.37 ± 0.03</td>
<td>10.33 ± 0.33</td>
<td>19.78 ± 1.31*</td>
<td>42.03 ± 3.20*</td>
<td>85.05 ± 5.39b</td>
<td>0.25 ± 0.03</td>
</tr>
<tr>
<td>Axotomy</td>
<td>100</td>
<td>-57.6 ± 1.8</td>
<td>101.5 ± 0.9</td>
<td>1.46 ± 0.04</td>
<td>9.67 ± 0.42</td>
<td>19.91 ± 1.79</td>
<td>39.66 ± 3.64</td>
<td>81.48 ± 6.49</td>
<td>0.15 ± 0.01c</td>
</tr>
<tr>
<td>Autotomy</td>
<td>50</td>
<td>-58.4 ± 1.6</td>
<td>108.8 ± 0.9c</td>
<td>2.45 ± 0.07d</td>
<td>10.23 ± 0.79</td>
<td>19.76 ± 2.95</td>
<td>38.12 ± 4.78</td>
<td>80.19 ± 8.78</td>
<td>0.10 ± 0.01cd</td>
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<tr>
<td>Medium cells</td>
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<tr>
<td>Control</td>
<td>40</td>
<td>-58.6 ± 1.4</td>
<td>100.7 ± 1.74</td>
<td>3.86 ± 0.10</td>
<td>11.22 ± 0.64</td>
<td>24.90 ± 4.12</td>
<td>49.28 ± 7.94</td>
<td>86.84 ± 10.57</td>
<td>0.27 ± 0.03</td>
</tr>
<tr>
<td>Axotomy</td>
<td>49</td>
<td>-58.2 ± 1.3</td>
<td>106.6 ± 0.95c</td>
<td>4.00 ± 0.09</td>
<td>10.58 ± 0.58</td>
<td>22.14 ± 1.46</td>
<td>43.02 ± 3.96</td>
<td>78.50 ± 7.74</td>
<td>0.15 ± 0.01c</td>
</tr>
<tr>
<td>Autotomy</td>
<td>35</td>
<td>-56.4 ± 1.6</td>
<td>109.9 ± 1.50c</td>
<td>4.46 ± 0.08d</td>
<td>10.47 ± 0.70</td>
<td>22.85 ± 4.55</td>
<td>46.46 ± 3.29</td>
<td>80.95 ± 7.49</td>
<td>0.10 ± 0.01c</td>
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<tr>
<td>Small cells</td>
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<tr>
<td>Control</td>
<td>28</td>
<td>-56.8 ± 1.3</td>
<td>103.8 ± 2.31</td>
<td>6.21 ± 0.24</td>
<td>11.16 ± 0.76</td>
<td>30.70 ± 5.51</td>
<td>60.41 ± 10.37</td>
<td>115.33 ± 16.00</td>
<td>0.30 ± 0.03</td>
</tr>
<tr>
<td>Axotomy</td>
<td>54</td>
<td>-54.6 ± 1.4</td>
<td>111.0 ± 0.89c</td>
<td>7.31 ± 0.18e</td>
<td>9.79 ± 0.38</td>
<td>28.64 ± 2.05</td>
<td>56.81 ± 4.10</td>
<td>100.08 ± 6.63</td>
<td>0.16 ± 0.02c</td>
</tr>
<tr>
<td>Autotomy</td>
<td>37</td>
<td>-55.4 ± 1.5</td>
<td>113.5 ± 1.45c</td>
<td>9.54 ± 0.45d</td>
<td>9.76 ± 0.55</td>
<td>29.53 ± 1.89</td>
<td>60.14 ± 4.80</td>
<td>96.39 ± 7.98</td>
<td>0.11 ± 0.01cd</td>
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<tr>
<td>AD-cells</td>
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</tr>
<tr>
<td>Control</td>
<td>44</td>
<td>-58.9 ± 3.1</td>
<td>117.4 ± 1.74</td>
<td>1.63 ± 0.06</td>
<td>40.16 ± 5.51</td>
<td>60.41 ± 10.37</td>
<td>115.33 ± 16.00</td>
<td>0.30 ± 0.03</td>
<td>0.25 ± 0.02</td>
</tr>
<tr>
<td>Axotomy</td>
<td>44</td>
<td>-59.4 ± 2.8</td>
<td>129.6 ± 1.77c</td>
<td>1.76 ± 0.08d</td>
<td>3.54 ± 0.49d</td>
<td>60.14 ± 4.80</td>
<td>96.39 ± 7.98</td>
<td>0.11 ± 0.01cd</td>
<td>0.09 ± 0.02cd</td>
</tr>
</tbody>
</table>

Values are means ± SE; n is number of cells. DRG, dorsal root ganglion; RMP, resting membrane potential; AHP, afterhyperpolarization; AD, afterdepolarization. *Significantly different from small cells at P < 0.005. †Significantly different from small cells at P < 0.05. ‡Significantly different from control at P < 0.001. §Significantly different from axotomy at P < 0.001. ¶Significantly different from control at P < 0.05.
<0.05 at 25% repolarization). There were no significant differences between the AHP duration of medium neurons and that of large or small neurons (Table 1).

Apart from their spike width, all other electrophysiological properties of control DRG neurons were quite similar. Thus there were no significant differences in the spike amplitudes, rheobase or RMP of large, medium, small, and AD-neurons (Table 1).

Because the ADP of AD-cells is the consequence of activation of T-type Ca^{2+} current (White et al. 1989) and this current is partly inactivated at the typical RMP of DRG neurons (~55 to ~60 mV; Table 1) (see Fox et al. 1987), we injected current into some neurons to see whether they would exhibit an ADP when their membrane potential was hyperpolarized to ~90 mV. By this procedure, we were never able to induce an ADP in a neuron that did not exhibit an ADP when studied at its normal resting potential.

**Effects of axotomy**

The morphological and functional effects of axotomy on DRG neurons start as early as 3 days and continue for more than 15 wk (Titmus and Faber 1990). In the present study, we investigated effects that occur within a period ranging from 2 to 7 wk postaxotomy in age-matched control rats. Initially, we attempted to make a detailed time course study of the electrophysiological changes induced by axotomy; there was, however, little significant difference between groups sampled at successive weekly intervals over the 2- to 7-wk postaxotomy period. We did note, however, that DRG neurons from rats exhibiting autotomy were more affected than those from axotomized rats that did not exhibit autotomy. The division of data into three groups was therefore made without reference to the postoperative time according to the following terminology: 1) data from control animals, 2) data from axotomized animals that did not exhibit autotomy (“axotomized” group), and 3) data from axotomized animals that exhibited autotomy (“autotomy” group).

Because $C_{in}$ is a primary criterion for cell identification, it was important to establish that cell size was not altered by axotomy. Figure 3, A–C, shows distribution histograms for $C_{in}$ for control, axotomized, and autotomy group cells. There are clear cut distributions for small, medium, and large cells, and the peaks do not appear to shift after axotomy or in the autotomy group.

**Effects of axotomy and the appearance of autotomy on spike width (AP duration)**

In previous studies of hamster DRG neurons using sharp microelectrodes (Gurtu and Smith 1988), it was noted that AP duration tended to increase after axotomy, but this increase fell short of attaining statistical significance. In rat neurons, spike width also tended to increase, but the difference was only significant for small cells and not for large, medium, or AD-cells (Table 1). It is possible that changes that occurred in these groups were masked by the pooling of data for statistical analysis. When the data are analyzed in a different way, an
upward trend in all spike widths can be seen. This is illustrated in Fig. 3, D–F, which shows the distribution of spike widths in control neurons, axotomized neurons, and neurons from animals exhibiting autotomy. Figure 3D shows that the peak spike width for the whole population of control neurons falls within the 1- to 2-ms range, and this represents 55% of all cells studied. Figure 3E shows that after axotomy, the peak of spike width between 1 and 2 ms represents only 40% of the population. There are also rather few control neurons with spike widths >6 ms (about 4% of the total neuronal population, Fig. 3D). After autotomy however, about 17% of the cells exhibit spike widths >6 ms (Fig. 3E).

The trend toward broad spike widths is greater in the autotomy group (Fig. 3F). Here, only 8% of the total population have spike widths in the 1- to 2-ms range, and some neurons have spike widths of 15–16 ms. Moreover, the AP duration of small, medium, large, and AD-cells from animals that exhibited autotomy were significantly greater than those of both the autotomy and control groups (Table 1).

The typical recordings of APs from the four types of control neurons in Fig. 2A are compared with those from axotomized neurons in Fig. 2B and with those from neurons in animals that exhibited autotomy in Fig. 2C. Note the very broad APs recorded from neurons in the autotomy group and that the increase in spike width devolved from a slowing of AP repolarization rather than from an increase in time to peak.

**Effects of axotomy and autotomy on spike height (AP amplitude)**

The AP amplitudes of small, medium, and AD-neurons were significantly increased by axotomy (Table 1). Axotomy did not, however, change the AP amplitude of large neurons. By contrast, the AP amplitude of all four cell types in the autotomy group were significantly increased compared with controls. Additionally, the AP amplitude of large neurons were significantly larger in the autotomy group compared with the axotomy group (Table 1).

**Effect of axotomy and autotomy on AHP amplitude and duration**

Although axotomy attenuates the amplitude and duration of the AHP in both frog sympathetic B-neurons (Gordon et al. 

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**FIG. 4.** Effects of axotomy on excitability as determined by neuronal responses to 500-ms current pulses at rheobase strength. A–D: summaries of discharge patterns in control, axotomized, and autotomy group neurons. The graphs show percentages of cells that exhibited 1 AP, 2 APs, or more than 2 APs in response to current. Data from small (A), medium (B), large (C), and AD-cells (D) show that axotomy increased the percentage of cells that exhibited >2 spikes and reduced the percentages of cells that exhibited 1 or 2 spikes. This trend was exaggerated in cells from the autotomy group. E–G: sample recordings of APs discharged by injection of 500-ms depolarizing current commands in a large control neuron (E), an axotomized large neuron (F), and a large neuron from an animal that exhibited autotomy (G). Note the increase in excitability seen in the axotomized neuron and the further increase seen in the neuron from the autotomy group. Arrows labeled First and S-S in E indicate the 1st and the steady-state interspike interval. AP height in G is cropped by the limited sampling rate of the digitizer.
1987) and in cat slow motoneuron (Kuno et al. 1974), it produces little or no change in the AHP of hamster DRG neurons (Gurtu and Smith 1988). Similarly the duration and amplitude of the AHP in rat DRG neurons were not significantly altered in either the axotomy or the autotomy groups (Table 1). In view of the complex shape of the AHP in some large cells, we measured AHP duration in three ways; at 25, 50, or 75% repolarization. Despite this, no significant differences were seen for any measure of AP duration in large, small, or medium cells.

FIG. 5. Summary of alterations in gain seen in the axotomized and autotomy groups. A–D: the relationship between the amplitude of 500-ms depolarizing current commands and discharge frequency as measured from the 1st interspike interval (see Fig. 4E). E–H: the relationship between depolarizing current and discharge frequency as measured from the steady-state interspike interval (see Fig. 4E). A and E show relationships for small neurons, B and F for medium neurons, C and G for large neurons, and D and H for AD-cells. Note that in all cases, the discharge frequencies attained in the axotomized cells are greater than those seen in controls and even higher frequencies are attained in the neurons from animals that exhibited autotomy. Error bars represent SE. Control data from 9 small, 29 medium, 29 large, and 8 AD-cells. Axotomy data from 28, 18, 29, and 18 small, medium, large, and AD-cells, respectively. Data for the autotomy group from 23 small, 18 medium, 22 large, and 7 AD-cells.

FIG. 6. Differential effects of the onset of autotomy on small and large cell gain. Maximum steady-state discharge frequencies evoked in control, axotomized, and autotomy group small and large cells by a 0.75-nA current command. Note that the onset of autotomy invokes a marked increase in the gain of large cells ($P < 0.05$), whereas the increase in gain of small cells is not significantly different from that seen after axotomy (n.s.). Data derived and replotted from the Fig. 5, E and G.
Effect of axotomy and autotomy on AD-cells

AD-cells comprised 16.7% of the control neuronal population, 14.3% of the axotomy population, and 9% of the autotomy population. It is unlikely therefore that cells that exhibited an AHP prior to axotomy developed an afterdepolarization once the sciatic nerve was cut. AD-neurons from control animals occasionally exhibited more than one AP in response to a brief pulse of depolarizing current (Fig. 2). There was no increased tendency for AD-neurons in the axotomy or autotomy groups to behave this way. Thus control AD-neurons cells fired an average of 1.55 ± 0.10 APs in response to brief depolarizing stimuli (n = 44), axotomized neurons fired 1.61 ± 0.10 APs (n = 44), and neurons from rats that developed autotomy fired 1.50 ± 0.15 APs (n = 12). Examination of the data using ANOVA showed that there are no significant differences between the three groups: F(2) = 0.20, n.s.

Spontaneously active cells

A very small proportion of control dissociated neurons (0.4%) and slightly more (2.1%) axotomized cells exhibited spontaneous activity. This spontaneous discharge of APs was not seen in any cells derived from animals that exhibited autotomy. Overall, spontaneously active cells comprised 0.8% of all neurons studied.

Effect of axotomy and autotomy on excitability

Because DRG are thought to be a source of ectopic activity in damaged sensory nerves (Kajender and Bennett 1992; Study and Kral 1996; Wall and Devor 1983; Zhang et al. 1997a), we examined axotomy-induced changes in excitability. Three different types of discharge patterns were seen in response to a 500-ms depolarizing current command. Some control cells exhibited a phasic response in that they discharged a single AP and then accommodated and remained silent throughout the remainder of the depolarizing current command. This occurred in 55.7% of control large cells, 55.6% of control medium cells, 46.2% of control small cells, and 53.6% of control AD-cells. Other cells were slightly more excitable and exhibited two APs before accommodating. This occurred in 14.4% of large cells, 13.9% of medium cells, 19.2% of small cells, and 17.9% of AD-cells. The third group of cells exhibited more than two APs and continued to discharge throughout the application of applied current. The rate of discharge of APs slowed and reached a steady-state frequency after 4 or 5 spikes. This type of sustained discharge occurred in 29.9% of large cells, 30.6% of medium cells, 34.6% of small cells, and 28.6% of AD-cells. These numbers are summarized in Fig. 4, A–D. Figure 4, E–G, shows examples of sustained discharge in large neurons from the control (Fig. 4E), axotomy (Fig. 4F), and autotomy groups (Fig. 4G). The graphs in Fig. 4, A–D, also show that after axotomy, more large, medium, small, or AD-cells tended to exhibit sustained discharge (>2 spikes), whereas fewer cells fired only one or two spikes. Moreover, this trend was exaggerated in cells from the autotomy group, in this situation over 70% of small, medium, large, and AD-cells exhibited sustained discharge, whereas only 10.7% of small cells (Fig. 4A), 8.7% of medium cells (Fig. 4B), 16.7% of large cells, and 11.1% of AD-cells exhibited a single AP and accommodation. Axotomy thus produced an overall increase in excitability, and this effect was exaggerated in cells from the autotomy group.

The effects of axotomy and autotomy on repetitive discharge was analyzed more quantitatively by constructing frequency-current (f-I) curves for the first and steady-state interspike intervals for small, medium, large, and AD-neurons (see Fig. 4E). Cells that discharged only one AP in response to sustained current have an infinite initial and steady-state interspike interval. They were therefore assigned initial and steady-state...
higher gain than those from the axotomy group (Fig. 5, A and E, medium cells from the autotomy group have only are compared with those from the autotomy group. Small and modest differences are seen between control and axotomized cells. This pattern is not preserved, however, when axotomized cells are compared with those from the autotomy group. Small and medium cells from the autotomy group have only slightly higher gain than those from the axotomy group (Fig. 5, A and E, and B and F), whereas the large neurons and AD-cells from animals that exhibit autotomy have a much higher gain than those from the axotomy group (Fig. 5, C and G, and D and H). This important observation implies that the appearance of autotomy is associated with a change in the properties of the larger, nonnociceptive cells rather than with a change in the small cells that are presumably predominantly nociceptive. To underline this point, some data from Fig. 5E for small cells and from Fig. 5G for large cells have been replotted in Fig. 6. The presence of autotomy is associated with a significant alteration in the steady-state discharge frequency of large cells but not in that of small cells.

Effects of axotomy and autotomy on rheobase

The amount of current required to evoke AP generation in all neuronal types was significantly decreased in the axotomy group and was further decreased in the autotomy group. Thus after axotomy, rheobase was lowered by 47% in small cells, by 45% in medium and AD-cells, and by 40% in large cells. In the autotomy group, rheobase was lowered by an additional 31% in small cells, an additional 33% in large and medium cells, and an additional 40% in AD-cells (Table 1). Decreases in rheobase seen in the axotomy and autotomy groups are also illustrated in the typical recordings shown in Fig. 7. The top records are a series of 10 voltage responses induced by the 10-incrementing current commands shown in the bottom records. In the control large cell (Fig. 7A), the first seven current commands produce only passive responses (shaded in gray), and only the three most intense currents elicit APs. In the axotomized large cell (Fig. 7B), only the first four current commands fail to generate APs, whereas in the neuron from the autotomy group (Fig. 7C) all current pulses stimulate the generation of one or even two APs.

Effects of axotomy and autotomy on time-dependent rectification

Many DRG neurons, especially the larger cells, exhibit a time-dependent change in voltage or “sag” in response to hyperpolarizing current (Czeh et al. 1977; Gurzu and Smith 1988; Vilière and McLachlan 1996). In the present experiments, we observed this phenomenon in 49/49 control large cells, 33/37 control medium cells, 14/23 control small cells, and 27/30 control AD-cells. A typical record from a large control neuron is shown in Fig. 8A. The initial transient peak voltage response ($V_{peak}$) settles to a less negative steady-state
level \((V_{SS})\) within 300 ms. This rectification results from the presence of a hyperpolarization-activated, inwardly rectifying, time-dependent, nonsynaptic cation current (H-current, \(I_h\)) (Abdulla and Smith 2001; Jafari and Weinreich 1998; Mayer and Westbrook 1983; Scroggs et al. 1994). The graph in Fig. 8B shows the relationship between peak \((V_{peak})\) and steady-state \((V_{SS})\) voltage responses and hyperpolarizing current commands for control large neurons \((n = 49)\). The time-dependent rectification is pronounced as the peak voltage response to \(-0.5\) nA is over \(-100\) mV, whereas the steady-state voltage response is only \(-60\) mV.

Previous studies in the cat (Czeh et al. 1977) showed that time-dependent rectification in DRG cells was attenuated after peripheral nerve axotomy. Our results show that this also happens in rats. A typical recording from an axotomized large cell is illustrated in Fig. 8C. Note the attenuation of rectification in these records compared with the records from a control neuron shown in Fig. 8A. Not all large axotomized cells exhibited the rectification (23/28), and the response was observed less frequently in medium (16/21), small (10/24), and AD-cells (18/23). Figure 8D illustrates the attenuation of rectification after axotomy in all large cells studied. There is much more difference between \(V_{peak}\) and \(V_{SS}\) in the control large neurons \((n = 23;\) Fig. 8B) than in axotomized large neurons \((Fig. 8D)\).

No further attenuation of time-dependent rectification was seen in cells from the autotomy group. The sample data record from a large cell in an animal that exhibited autotomy (Fig. 8E) is similar to that seen after axotomy (Fig. 8C). The rectification response was still present in 20/25 large cells, 14/20 medium cells, 10/26 small cells, and 8/11 AD-cells. The amplitude of the rectification is illustrated for 20 large cells from the autotomy group illustrated in Fig. 8F is similar to that seen in axotomized cells (Fig. 8D).

**DISCUSSION**

**Classification of DRG neurons**

Both \(C_{in}\) and AP shape were used to distinguish small, medium, and large cells in the control DRG neuron population. Because very few cells exhibited \(C_{in}\) between 61 and 70 pF, the use of 70 pF as a cutoff clearly distinguishes the small and medium cell populations (Fig. 3A). The use of 90 pF as a point of distinction between medium and large cells therefore seems more arbitrary as there is no obvious gap in the size distribution at this point. It was noted, however, that all cells with a clear inflection on their falling phase exhibited \(C_{in} < 90\) pF. The combination of inflection and \(C_{in} > 70\) pF and \(< 90\) pF was therefore used to define medium cells and to distinguish them from large cells in the control DRG neuron preparation. After axotomy, however, spike shape changes (Fig. 2) so that \(C_{in}\) is the only available criterion for cell identification. Nevertheless, the size distinction between small and medium cells is preserved both after axotomy (Fig. 3B) and in the autotomy group (Fig. 3C). In both cases, few cells are distributed in the 61- to 70-pF range. This implies that cell size is unaffected by axotomy. It would therefore seem reasonable to use \(C_{in}\) as the criterion for distinguishing small, medium, and large cells in the axotomy and autotomy groups.

The relationship between cell body size, axonal conduction velocity, functionality, and AP configuration of different types of DRG neuron is a topic of ongoing debate (Harper and Lawson 1985; Ritter and Mendell 1992; Rose et al. 1986; Villière and McLachlan 1996). Sensory neurons are usually divided into three groups: rapidly conducting \(A\alpha/\beta\) cells that transmit nonnociceptive sensory information; \(A\delta\)-cells that are responsible for the relatively rapid transfer of nociceptive stimuli that might be elicited by a pin prick; and slowly conducting \(C\)-cells that transmit longer lasting, “burning” pain that may be associated with inflammation (Bessou and Perl 1969). While it is generally agreed that \(A\alpha/\beta\) cells have the shortest spike width and largest soma diameter (Gallego and Eyzaguirre 1978; Gurtu and Smith 1988; Kim et al. 1998; Koerber et al. 1988; Rose et al. 1986) and that nociceptive \(C\)-cells have the greatest spike width and smallest soma diameter (Gallego and Eyzaguirre 1978), the distinction is not absolute. This is because the soma diameter of some \(A\delta\)-cells fall into the \(A\alpha/\beta\) or \(C\)-cell range (Harper and Lawson 1985; Villière and McLachlan 1996). It is therefore not appropriate to equate the medium cell population used in our study with \(A\delta\)-cells identified in vitro or in vivo. It is likely, however, that nociceptive neurons predominate in the small cell group, whereas nonnociceptive neurons reside within the large cell group.

**Characteristics of dissociated DRG neurons**

One advantage of whole cell recording for comparing the electrophysiological properties of different groups of neurons is that APs can be recorded with high fidelity and there are no problems with “penetration” injury that can be promoted by using sharp microelectrodes (Ikeda et al. 1986). However, APs recorded in DRG with sharp microelectrodes are generally of shorter duration than those recorded with patch electrodes. While our measurements of spike width in control DRG neurons \(1.37 \pm 0.37\) ms for large cells and \(6.21 \pm 0.24\) ms for small cells; Table 1) are similar to those seen in other studies done with whole cell recording (Caffrey et al. 1992; Cardenas et al. 1995; Ikeda et al. 1986), they are considerably shorter than values reported by Villière and McLachlan (1996). Using microelectrodes, these authors observed spike widths as little as \(0.5\) ms in \(A\alpha/\beta\) (large cells), and spike widths in small cells \((C\)-cells\) were always \(< 4\) ms. The experiments of Villière and McLachlan (1996) were done at \(35^\circ\)C, whereas ours were done at room temperature. Since cooling from 37 to 20°C can double AP duration in DRG neurons (Amir and Devor 1996), differences between our data and those of Villière and McLachlan (1996) may be explained, at least in part, in terms of differences in temperature.

Our finding that about 30% of all types of control neurons show sustained discharge in response to depolarizing current (Fig. 4, A–D) also differs from results obtained with microelectrodes. For example, Villière and McLachlan (1996) found sustained discharge in only 4 of 56 (7%) of \(A\alpha/\beta\) neurons studied with microelectrodes at \(35^\circ\)C, whereas we found it in 29.9% of large control neurons studied at 20°C (Fig. 4C). Voltage-insensitive, low-conductance \(g_{K,Ca}^*\) that underlie slow AHPs \((SK_{Ca}\) channels\) limit repetitive discharge in a subpopulation of vagal afferent neurons (Cohen et al. 1994; Cordoba-Rodriguez et al. 1999; Fowler et al. 1985; Moore et al. 1998), but such channels are not seen under our experimental conditions. We saw no effect of the SKCa blocker, apamin, on
repetitive discharge or AP shape of DRG cells studied with patch pipettes at room temperature (M. J. Stebbing and P. A. Smith, unpublished observations). Loss of SKCa function during recording with patch electrodes has been reported in other neuronal types (Zhang et al. 1994; but see also Gold et al. 1996). It is therefore tempting to speculate that the absence of functional SKCa channels in our studies accounts for the observed propensity for sustained discharge (Fig. 4). This does not, however, explain the lack of accommodation seen in 29.9% of control large cells (Fig. 4C) as these cells have relatively short AHPs (Table 1) and do not express SKCa channels (Gold et al. 1996). The presence of other types of channels presumably underlies spike-frequency accommodation in large cells. If these channels were damaged during enzymatic dissociation procedures, this may contribute to both increased excitability and to increased spike width in dissociated DRG neurons.

Changes produced by axotomy

Axotomy tended to increase excitability, spike height, and spike width in all neuronal types, whereas RMP or AHP were unaffected (Table 1). Increases in excitability included increases in gain and decreases in accommodation and rheobase (Figs. 4 and 5). For all AP parameters that were altered, changes were most pronounced in small cells and least pronounced in the large cells. The altered properties of medium and AD-cells laid between those of large and small cells. Thus axotomy promoted a marked increase in the excitability of small cells, less pronounced increases in medium and AD-cells, and small increases in the excitability of large cells. Similarly for changes in spike height. The effects of axotomy were highly significant in the small and AD-cells (P < 0.001), significant at the P < 0.05 level in medium cells yet insignificant in large cells. Axotomy also significantly increased the spike width of small cells, and although its effect on large, medium, and AD-cells did not attain statistical significance (Table 1), there is a clear trend toward wider spikes in the frequency histograms shown in Fig. 3, D–F. Axotomy decreased rheobase in all cell types by the same level of significance (Table 1).

TABLE 2. Summary of effect of axotomy or nerve injury on DRG cells

<table>
<thead>
<tr>
<th>Study</th>
<th>Excitability</th>
<th>Spike Height</th>
<th>Spike Width</th>
<th>Rheobase</th>
<th>RMP</th>
<th>AHP</th>
<th>$R_m$</th>
<th>Time-Dependent Rectification</th>
</tr>
</thead>
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<tr>
<td>This study</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↓</td>
<td>Unchanged</td>
<td>Unchanged</td>
<td>N/A</td>
<td>↓</td>
</tr>
<tr>
<td>Czeh et al. (1977)$^a$</td>
<td>N/A</td>
<td>Unchanged</td>
<td>Unchanged</td>
<td>↑</td>
<td>N/A</td>
<td>Unchanged</td>
<td>Unchanged</td>
<td>N/A</td>
</tr>
<tr>
<td>Gallego et al. (1987)$^a$</td>
<td>N/A</td>
<td>N/A</td>
<td>↑</td>
<td>↓</td>
<td>Unchanged</td>
<td>Unchanged</td>
<td>Unchanged</td>
<td>↓</td>
</tr>
<tr>
<td>Gurtu and Smith (1988)$^a$</td>
<td>N/A</td>
<td>Unchanged</td>
<td>(slight)$^b$</td>
<td>↓</td>
<td>Unchanged</td>
<td>Small</td>
<td>Unchanged</td>
<td>Unchanged</td>
</tr>
<tr>
<td>Study and Kral (1996)</td>
<td>↑$^b$</td>
<td>N/A</td>
<td>Unchanged</td>
<td>↓</td>
<td>Unchanged</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Oyelese and Kocsis (1996)$^a$</td>
<td>N/A</td>
<td>Unchanged or ↑, loss of infection</td>
<td>N/A</td>
<td>Unchanged or small decrease</td>
<td>N/A</td>
<td>Decreased or unchanged</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Zhang et al. (1997a)$^y$</td>
<td>N/A</td>
<td>Unchanged</td>
<td>(slight)$^c$</td>
<td>↓</td>
<td>Unchanged</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Kim et al. (1998)</td>
<td>↑</td>
<td>Unchanged</td>
<td>↑</td>
<td>↓</td>
<td>Unchanged$^d$</td>
<td>N/A</td>
<td>Increased</td>
<td>N/A</td>
</tr>
<tr>
<td>Stebbing et al. (1999)</td>
<td>N/A</td>
<td>Unchanged</td>
<td>↑</td>
<td>↓$^i$</td>
<td>Unchanged</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

For abbreviations, see Table 1. $^a$ In small, medium, and AD-cells; increased in large cells in autotomy group. $^b$ In small cells after axotomy, increased in all cell types in the autotomy group. $^c$ N/A, not applicable (not examined in this particular study). $^d$ Experiments done on cats. $^e$ Experiments done on hamsters. $^f$ Subsignificant trend towards an increase. $^g$ Small increase or decrease depending on cell type. $^h$ Increase in incidence of spontaneously active cells but little change in excitability in terms of numbers of action potentials (APs) produced by current injection. $^i$ Spike width unchanged in cutaneous afferents, increased in muscle afferents. Marked decrease in cutaneous afferents with inflected APs, decreased RMP in muscle afferents. $^j$ In small (C-cells). $^k$ In large cells, slight depolarization in C-cells. $^l$ In large cells identified on basis of conduction velocity.
autotomy group are modest, this is not the case for large cells. There are obvious and significant differences between the properties of axotomized large cells and large cells from autotomy group. This distinction applies to spike height, rheobase (Table 1) excitability (Figs. 5 and 6), and to the changes in certain voltage-sensitive conductances described in the accompanying paper (Abdulla and Smith 2001). The development of autotomy therefore seems to be associated with a change in properties of nonnociceptive cells; i.e., autotomy is initiated without a change in the properties of small, putative nociceptive cells. This finding parallels the observation that destruction of peripheral C-fibers with capsaicin fails to prevent the autotomy induced by a prior nerve injury (Nagy et al. 1986). It is also consistent with the clinical observation that large myelinated afferent fibers seem to signal the mechanical hyperalgesia associated with nerve injury (Campbell et al. 1988). If alterations in the properties of myelinated neurons correlate both with the onset of pain and with the onset of autotomy, this would support the contention that autotomy is a useful experimental model for human neuropathic pain (Coderre et al. 1986).

**Increased excitability but lack of spontaneous activity in axotomized neurons**

Because only 0.8% of the whole population of control, axotomized, or autotomy group neurons exhibited spontaneous activity, changes in the electrophysiological properties of DRG cell bodies may not entirely account for the ectopic activity that originates in injured DRG in vivo (Wall and Devor 1983). It should be noted, however, that the dissociated neurons used in this study lack an axon hillock region that is characterized by low-threshold Na\(^+\) channels. These channels could perhaps drive spontaneous activity in axotomized DRG in vivo. Other mechanisms may also contribute. These include the actions of norepinephrine released from perivascular sympathetic fibers that sprout into DRG neurons after injury (Devor et al. 1994; McLachlan et al. 1993). Although these fibers seem to abut primarily the larger neurons, both small and large neurons start to express excitatory \(\alpha_{1}\)-adrenoceptors (Abdulla and Smith 1997; Birder and Perl 1999; Petersen et al. 1996; Xie et al. 1995; Zhang et al. 1997b). These receptors may be important in generating ectopic activity because stimulation of sympathetic nerves invokes spontaneous activity in axotomized sensory nerves (Devor et al. 1994; McLachlan et al. 1993; Xie et al. 1995). Other potential excitatory mediators include substance P, which is released from the cell bodies of DRG neurons (Huang and Neher 1996) and exerts powerful excitatory actions within sensory ganglia (Dray and Pincock 1982; Inoue et al. 1995). Neuropeptide Y (NPY)—containing axons are also abundant in axotomized DRG (Wakisaka et al. 1991, 1992), and the excitatory actions of this peptide on DRG neurons are increased after sciatic nerve section (Abdulla and Smith 1999). Actions of any or all of these substances may contribute to the chemical cross-excitation that has been reported to occur in axotomized DRG in vivo (Amir and Devor 1996).

Our findings with sciatic nerve section anatomy differ from those of Study and Kral (1996), who showed that about 20% of neurons dissociated from animals that have received chronic constriction injury to their sensory neurons displayed spontaneous activity ex vivo. This may simply reflect methodological differences between our studies and theirs.

**Possible mechanisms for the effects of axotomy**

Although the present current-clamp experiments say little about the specific mechanisms underlying the increased excitability of axotomized neurons, certain possibilities can be ruled out. For example, axotomized cells are not chronically depolarized (see Kim et al. 1998), and AD-cells that tend to generate repetitive action potentials under control conditions do not display this tendency to a greater extent after axotomy (Fig. 2). The maximum discharge rate elicited in AD cells in the autotomy group (Fig. 5, D and H) is no greater than that seen in small (Fig. 5, A and E), medium (Fig. 5, B and F), or large cells (Fig. 5, C and G). Also, time-dependant rectification (Czeh et al. 1977; Villière and McLachlan 1996), which could contribute to increased excitability at certain membrane potentials, is attenuated rather than enhanced after axotomy (Fig. 8).

Axotomy-induced lowering of rheobase (Fig. 7) goes along with increased excitability. The lack of effect of axotomy on AHP amplitude and duration was somewhat unexpected because it occurs in at least two other neuron types (Gordon et al. 1987; Kuno et al. 1974), and increased neuronal excitability is often a consequence of AHP attenuation. On the other hand, no decreases in AHP amplitude or duration were seen in our previous study of the effects of axotomy on hamster DRG neurons (Gurtu and Smith 1988). We show, however, in the accompanying paper (Abdulla and Smith 2001) that axotomy attenuates Ca\(^{2+}\) channel current \((I_{Ca})\), as well as Ca\(^{2+}\) -sensitive \(K_{v}\) conductances \((g_{K,CA})\) that depend on \(I_{Ca}\). Because some types of \(g_{K,CA}\) are voltage sensitive (Pennefather et al. 1985), it is possible that changes in this conductance can alter repetitive discharge without affecting a Ca\(^{2+}\) recorded at a relatively negative membrane potential. This is likely to be the case in rat DRG cells as attenuating influx of Ca\(^{2+}\) through N-type Ca\(^{2+}\) channels with Cd\(^{2+}\) (Abdulla and Smith 1997) or \(\omega\)-conotoxin GVIA or attenuating “maxi” (voltage-sensitive) \(g_{K,CA}\) with charybdotoxin (Abdulla and Smith 1999) or iberiotoxin (Scholz et al. 1998) increases their excitability.

The voltage-clamp studies described in the accompanying paper (Abdulla and Smith 2001) address axotomy-induced changes in various ionic channels in DRG neurons and provide additional information as to how changes in Ca\(^{2+}\) and K\(^{+}\) currents might contribute to the observed changes in excitability of axotomized neurons.

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