Fast and Slow Pyramidal Tract Neurons: An Intracellular Analysis of Their Contrasting Repetitive Firing Properties in the Cat

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SUMMARY AND CONCLUSIONS
1. Intracellular recordings were made from an estimated 500 neurons in the sensorimotor cortex of barbiturate-anesthetized cats. Of those which were antidromically identified from the medullary pyramids, 70 were selected which also exhibited steady repetitive firing to steps of current injected through the recording electrode; 81% were "fast" (conduction velocity greater than 20 m/s) and 19% were "slow." 2. As shown by earlier workers, the spike duration is a function of conduction velocity; a spike duration of 1.0 ms is the dividing line between fast and slow.

3. Of the 57 fast pyramidal tract neurons (PTNs), 14 exhibited double spikes during otherwise rhythmic firing patterns to a step of injected current. These very short interspike intervals (usually 1.5-2.5 ms) were first seen interspersed in a rhythmic discharge (e.g., 50-ms intervals) but, with further increases in current strength, would come to dominate the firing pattern; e.g., double spikes every 40 ms. Further increases in current would typically shorten only the long intervals; e.g., 40-30 ms, but some fast PTNs developed triple spikes, etc.

4. The extra spike appears to arise from a large hump which follows most spikes in fast PTNs; while this humplike depolarizing after-potential can also be seen in slow PTNs, it is small. Extra spikes were seen only in fast PTNs with large postspike humps; in perhaps half of the fast PTNs, extra spikes probably contributed to "adaptation."

5. Slow PTNs often had frequency-current curves which were not repeatable; a "hysteresis" phenomenon could often be seen, where the proportionality constant relating current to firing rate decreased following high firing rates.

6. The B spike was distinguishable from the A spike in differentiated antidromic spikes in 77% of the slow PTNs, in only 14% of the fast PTNs which later exhibited double spikes during current-induced repetitive firing, and in 53% of the other fast PTNs.

7. The antidromic spike heights of doublet PTNs were not significantly different from those of other repetitively firing PTNs.

INTRODUCTION
From both extracellular and intracellular recordings, it has been apparent during the past decade that pyramidal tract neurons (PTNs) with fast conduction velocities (>20 m/s) are quite different from the slow PTNs. We have summarized some of those differences relating to the cell's geometry and electrophysiological properties in Table I. There are, in addition, other interesting features: e.g., the slow PTNs tend to provide recurrent excitation to the fast PTNs (42), and there are marked differences in spontaneous activity (20).

In comparing these differences to the well-studied size spectrum of spinal motoneurons, it is apparent that PTNs (e.g., Koike et al., ref 26) have an even more exaggerated differentiation of cell properties than do motoneurons (e.g., Kuno et al., ref 29). Especially when one views motoneurons and PTNs from the framework of repetitive-firing properties, many features can be noted which go well beyond the usual categorization of fast PTNs as being "harder to fire" but also more "vigorous and variable" when they do fire.

Repetitive-firing properties of CNS neurons have been recently reviewed by Calvin (10). Essentially, a cell generates a spike train in response to various input waveforms using three different modes of repetitive firing: 1) occasional excursions of the membrane potential through threshold give rise to an occasional
TABLE 1. Comparison of properties of fast and slow pyramidal tract neurons

<table>
<thead>
<tr>
<th>Property</th>
<th>Fast</th>
<th>Slow</th>
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<tbody>
<tr>
<td>Conduction velocity (26, 41), m/s</td>
<td>20–76</td>
<td>&lt;20</td>
</tr>
<tr>
<td>Proportion seen intracellularly* (19, 41), %</td>
<td>74–81</td>
<td>26–19</td>
</tr>
<tr>
<td>Proportion seen extracellularly (43), %</td>
<td>52</td>
<td>48</td>
</tr>
<tr>
<td>Proportion predicted from axon count (43), %</td>
<td>4.5</td>
<td>95.5</td>
</tr>
<tr>
<td>Antidromic latency from medullary pyramids (41), ms</td>
<td>0.6–2.3</td>
<td>&gt;2.3</td>
</tr>
<tr>
<td>Spike width at base† (41), ms</td>
<td>0.4–1.0</td>
<td>1.0–2.1</td>
</tr>
<tr>
<td>Time to bottom of afterhyperpolarization (41), ms</td>
<td>6.3–17.9</td>
<td>17.1–37.5</td>
</tr>
<tr>
<td>Input resistance (41), MΩ</td>
<td>1.4–12.1, 1.6–15.1</td>
<td>linearly related</td>
</tr>
<tr>
<td>Time constant (28), ms</td>
<td>12.3</td>
<td>24.2</td>
</tr>
<tr>
<td>Sag from peak $V_m$ following current step (28), %</td>
<td>30</td>
<td>17</td>
</tr>
<tr>
<td>Rheobase (26), nA</td>
<td>1.57</td>
<td>0.53</td>
</tr>
<tr>
<td>Range</td>
<td>0.55–4.50</td>
<td>0.10–2.00</td>
</tr>
<tr>
<td>Latency to first spike following current step to twice rheobase (26), ms</td>
<td>9.8</td>
<td>27.1</td>
</tr>
<tr>
<td>Interspike interval variability during rhythmic firing (26), SD as % of mean</td>
<td>24</td>
<td>9</td>
</tr>
<tr>
<td>f-I curve slopes$,^*$</td>
<td>Greater</td>
<td>Less</td>
</tr>
<tr>
<td>Accommodation to current ramps (28)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Axon collaterals to some subcortical structure (19), %</td>
<td>67</td>
<td>30</td>
</tr>
</tbody>
</table>

* Our data included. † Our data and Takahashi's (41) pooled, several stray points eliminated of 114 total points. ‡ Koike et al. (26) data show factor of 5 or 1.7 times, depending on whether or not current is expressed in rheobase units.

spike mode, 2) sustained depolarizing waveforms which attempt to hold the membrane potential above threshold give rise to a rhythmic firing mode with firing rate proportional to depolarizing current, and there is 3) an extra spike mode where depolarizing afterpotentials (large postspike humps) appear to rise through the falling threshold milliseconds after a spike to give rise to an "extra" spike. This extra-spike discharge is most easily detected when it arises during otherwise rhythmic discharge to a constant depolarizing current, i.e., double spikes in the midst of a rhythmic train of single spikes. In motoneurons, the double spikes were first seen with string galvanometer methods (23); their correlation with the postspike humps has only been more recently established (9, 13). In a preliminary report on our present data (15), we showed that the same phenomenon often occurs in fast PTNs and discussed the striking firing patterns produced, which are similar to those seen in "epileptic" neurons.

**METHODS**

**Experimental procedures**

We anesthetized 23 adult cats with pentobarbital (initial dose, 35–50 mg/kg intraperitoneally, with supplements intravenously to maintain deep anesthesia) and immobilized them with gallamine triethiodide. Arterial pressure was monitored and rectal temperature was automatically maintained by hot pad and heat lamp. The artificial respiration was adjusted to moderately hyperventilate the cats (end-expired CO₂ about 3.5%). A bilateral craniectomy exposed both pericruciate areas; we usually made a small slit in the dura of the right side to aid in CSF drainage and reflected the dura on the left side for recording.

We opened the dura at the cisterna magna, both for CSF drainage and to place a concentric bipolar stimulating electrode in the medullary pyramids via a dorsal approach (an approach at about 45°, about 1 mm left of midline, will intersect the pyramids before their decussation even
with the entry point several millimeters caudal to the obex). We temporarily recorded antidromic surface potentials from the pericruciate gyri with silver ball electrodes while adjusting the position of this stimulating electrode. While this dorsal placement is not as good at eliminating orthodromic driving of PTNs as the more exciting ventral approach to the pyramids, one has little difficulty in distinguishing antidromic from orthodromic activation with intracellular recording if the shock is adjusted to straddle the threshold.

To further reduce cerebral pulsations, we performed a bilateral thoracotomy and held the rib cage in an extended position. We used a thin Plexiglas "pressor foot" of 10 mm diameter, with a central 1-mm hole. This was positioned over the pericruciate area, angled so as to press harder posteriorly and to barely touch at the hole. We observed the surface blood vessels through a dissecting microscope while adjusting the pressure; we avoided signs of pia blanching within several millimeters of the recording site. This pressor foot also contained three Ag-AgCl electrodes embedded flush with the ventral surface of the Plexiglas; we used one to monitor the surface electrocorticogram (ECoG) near the recording site. The other two were occasionally used for attempts (largely unsuccessful) to modify cell responses by bipolar surface stimulation.

**Microelectrode methods**

We used single-barrel micropipettes which we beveled (2) and then back-filled with 2.7 M KCl using drawn-out PE tubing. These micropipettes were capable of transmitting large currents without the usual troublesome resistance fluctuations (1). Our tip diameters were probably about 1 µm and our electrode resistances were usually on the order of 4–8 MΩ when measured with a 1-kHz square wave. We injected various combinations of pulse-, step-, and ramp-current waveforms through the recording microelectrode; we approximately balanced the bridge of the neutralized capacitance amplifier (Bioelectric Instruments, PI) using spike-height and firing-level methods rather than by compensating for the make-and-break discontinuities. We were careful not to overcompensate for capacity. We recorded the injected-current waveform, the microelectrode and ECoG recordings, and various synchronization pulses on an FM tape recorder having a band pass of direct current to 5 kHz. This 5-kHz band pass was capable of resolving the usual components of the differentiated spikes (29) in the playback, even for very narrow spikes from fast PTNs. Other aspects of the experimental methods were analogous to those we have previously described (11, 15, 39).

**Cell selection**

We estimate that we encountered over 500 neurons in the 15 good experiments, i.e., cells where the intracellular penetration would have been至少 good enough to allow for the brief study of synaptic potentials (if not spikes). The reduction of this sample to the present 70 PTNs (14%) is discussed later. We first tested for repetitive firing by injecting a step of current through the recording electrode; if successful, we turned on our tape recorder and tried to obtain antidromic identification. We then used various combinations of injected current to explore the repetitive firing behavior. A typical sequence was 400-ms pulses repeated every 1,200 ms, with the pulse size incremented gradually until very high firing rates were obtained and then gradually decremented to zero.

We typically recorded from area praecentralis gigantopyramidalis (4 y), judging from the maps of Hassler and Muhs-Clement (22). Our microelectrode usually recorded first from surface posterior sigmoid gyrus and then from buried cortex along the cruciate sulcus. We did not typically test synaptic inputs.

**Data-analysis methods**

Some experiments were done with the aid of an on-line computer (LINC-8, Digital Equipment Corp.) which generated current steps and plotted the current against the resulting firing rate so that we could immediately judge the response. A variation of the same program could be used during replay of FM tapes for data analysis off-line. The program also generated plots of instantaneous firing rate (reciprocal of interspike interval) versus time. It plotted frequency-current (F-I) curves using a different alphanumeric symbol (0–9, A–Z) for each successive point to allow reconstruction of the sequence in which points were obtained; this feature was important when attempting to judge shifts in F-I curves, such as in the case of the hysteresis seen in slow PTNs (Fig. 4).

The local variations of the raster method of Wall (44) and the joint interval density of Rodieck et al. (33) have been previously described (4, 7, 8). Spikes were detected using a rate-of-change method within the computer program rather than by using the oscilloscope sweep circuit previously described (8).

**Results**

We have reduced our population of PTNs, for the purposes of this paper, to a total of 70 anti-
dromically identified cells, of which 57 (81%) were fast (antidromic conduction time less than 2.3 ms, following Takahashi, ref 41) and 13 (19%) were slow. The latency spectrum shown in Fig. 1C demonstrates the distribution of latencies across the range 0.78-4.70 ms. These cells were antidromically identified and fired repetitively to steps of injected current; on most, we were able to obtain enough current steps to plot all or part of an f-I curve. Some cortical neurons on which we could not obtain antidromic identification have also been used in selected figures, as noted.

**Spike heights**

The scatter plot of Fig. 1A shows that the spike heights from the slow PTNs were, on the average, larger than those of the fast PTNs, in agreement with spinal motoneuron data (29). The 13 slow PTNs antidromic spikes ranged from 58 to 104 mV (mean and SD, 83 ± 13 mV), while the 57 fast PTNs ranged from 48 to 100 mV (77 ± 13 mV).

For the purposes of Fig. 1 we have included cells down to 48-mV spike heights, provided that they exhibited repetitive firing to injected currents. This serves to demonstrate that fast PTNs exhibiting doublets (15), as shown in Fig. 6, were not preferentially distributed; the doublet fast PTNs are shown as triangles in Fig. 1A and B, and as the shaded areas of the latency histogram in C. It is apparent that doublets occur throughout the entire range of fast latencies; also, they are not concentrated in the low spike heights, as might be expected if injury played a prominent role in their production.

The spike heights shown in Fig. 1A were typically obtained within the first 60 s following penetration. They often improved with time; for example, the 89-mV antidromic spike and 122-mV repetitive spikes in Fig. 2A are from a cell contributing a 76-mV point to Fig. 1A because the heights increased. Of course spike heights more often deteriorated, but this often meant that the cell was discarded from our sample for failure to obtain repetitive firing (see DISCUSSION). Thus, the spike heights in Fig. 1A probably represent an underestimate of our spike heights.

**Spike width**

Fast and slow PTNs can usually be instantly identified from their sound in the loudspeaker; the fast PTN spike can be 2–3 times narrower than those of slow PTNs, as shown in Figs. 1B and 2. The fast PTN spikes range from 0.38 to 1.00 ms in duration, while the slow PTN spikes are uniformly longer than 1 ms. The spikes were measured near their base; while it would seem that the end point of the width measurement might be somewhat arbitrary, the scatter about the least-squares line in Fig. 1B is proportionately no worse than that of a similar plot made with the spike width measured half way up the spike (the width at half-height is about 45% of the base width). Extrapolating our least-squares fit line (Fig. 1B; W = 0.272 + 0.295L) to the 12-ms latencies expected for the

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**Fig. 1.** Properties of 70 pyramidal tract neurons (PTNs) as a function of antidromic latency from the medullary pyramids. Triangles in A and B and shaded areas in C are those cells which subsequently showed double spikes during repetitive firing to injected current steps. For cell selection criteria, see text. A: spike heights from resting potential to the peak of the antidromic spike. B: spike duration (base to base) and least-squares-fit line. C: number of PTN in each 0.2-ms bin. Using the Takahashi (41) fast-slow separation latency of 2.3 ms, there are 57 fast and 13 slow PTNs, of which 14 of the 57 fast PTNs exhibited double spikes during repetitive firing.
slowest PT cells (43) would yield 3.8-ms spike widths, if the linear relationship continued.

**AB components in differentiated spikes**

As Koike et al. (27) have shown for PTNs, the differentiated spikes can show the usual A and B components plus several minor inflections. We were struck with the number of cells in which it was difficult to discern the notch on the rising phase of the dV/dt record which signals the B spike. It is not that it is absent; rather, the B spike seems to arise out of the A spike smoothly unless the cell is stressed by high repetition rates. As tabulated in Table 2, we were able to discern the AB notch in the antidromic spike of only 14% of the fast PTNs exhibiting doublets to current steps, in perhaps half of the other fast PTNs, but in 77% of the slow PTNs.

**Changes in spike height**

In extracellular recordings, changes in spike height are often observed, particularly during high firing rates (11, 12). Synaptic conductance changes may well play a role in some spike-height reductions (18). However, spike heights often change even when the cell is driven by injected current; the PTNs exhibit a spectrum of such behavior. We have scanned a number of different firing rates by injecting a ramp of current into a PTN, and Fig. 3 shows typical behaviors of fast and slow PTNs. The maintenance of the spike peak near or at its maximum value is typical for fast PTNs; the declining spike heights for the slow PTN are also typical of that group. Each spike included in Fig. 3 was differentiated; the superimposed dV/dt records above each ramp illustrate the sequence of changes seen in the slow PTNs. While not even an AB notch (31) can be seen in the dV/dt records from the fast PTN, the B component of the slow PTN spike becomes later and smaller, suggesting a progressive diminution of somatic invasion. While extracellular spikes are not merely proportional to dV/dt (see ref 5 for a discussion), the peak-to-peak excursion of the dV/dt records of Fig. 3 does suggest that slow PTNs will be harder to find extracellularly because of their slower spikes and labile heights.
**TABLE 2. Summary of present data**

<table>
<thead>
<tr>
<th></th>
<th>Fast</th>
<th>Slow</th>
</tr>
</thead>
<tbody>
<tr>
<td>B spike distinguishable from A spike in antidromic dV/dt records</td>
<td>14% of doublet cells, 53% of others</td>
<td>In 77% Graded delay, decrement in B spike</td>
</tr>
<tr>
<td>Spike heights during rapid repetitive firing</td>
<td>Often maintained</td>
<td>Small or no hump</td>
</tr>
<tr>
<td>Postspike humps</td>
<td>Deep notch-hump always</td>
<td></td>
</tr>
<tr>
<td>Extra spikes during rhythmic firing (doublet cells)</td>
<td>In 25%</td>
<td>Never</td>
</tr>
<tr>
<td>Probable extra spikes contributing to adaptation</td>
<td>In about 50%</td>
<td>Never</td>
</tr>
<tr>
<td>Hysteresis in f-I curve</td>
<td>Not seen</td>
<td>Frequent</td>
</tr>
<tr>
<td>Climbing trajectories following current step*</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

* Uncommon in spinal motoneurons.

**Hysteresis in f-I curves**

In motoneurons, f-I curves are seldom dependent on the order in which the points are taken, i.e., there does not seem to be a historical effect on the time scale of the 1.2-s spacing between injected current pulses. This has also been true in our experience with fast PTNs. However, we have been surprised to find that our slow PTNs exhibited a different f-I curve during descent from the maximum firing rates than they exhibited during ascent. Furthermore, as shown in Fig. 4, they could bend over to form a "genu" during ascent. In the absence of experiments specifically designed to investigate historical effects of such time durations and to test for the effects of injecting Cl⁻ ions, we would speculate that long adaptation-time constants may play a substantial role in slow PTNs. It should be noted that it is the fast motor units which are associated with adaptation and "fatigue," not the slow ones (e.g., Burke et al., ref 3).

**Membrane-potential trajectories**

The subthreshold course of the membrane potential between spikes during rhythmic discharge to a constant current shows a very orderly progression of changes in the case of the cat spinal motoneuron (34–37). The lengthening of the interspike interval during the adaptation which follows the step of current was typically due to the early part of the trajectory (the "scoop") becoming deeper with each successive spike; the linear rise of the membrane potential toward the firing level for the next spike (the "ramp") did not alter, surprisingly. During the steeper secondary range of the f-I curve, this ramp began to increase in steepness with

![FIG. 3. Changes in spike height with firing rate. As could be seen in Fig. 2, PTNs may undergo changes in spike height during repetitive firing. In this figure, we have scanned a range of firing rates by using a ramp of injected current (not shown), starting at the beginning of sweeps. The differentiated spikes are shown with a fast sweep, superimposed on the slow sweeps showing the membrane potential (spikes electronically enhanced). For the fast (50.0 m/s) PTN (left) the spike heights are maintained and the differentiated spikes show little change. For the slow (9.2 m/s) PTN (right), the spike heights decline and the differentiated records show that the B component of the spike has changed. It becomes smaller and is delayed, relative to the A component.](image-url)
each additional increment in current, which accounts for the increased "gain" (34).

This convenient phenomenological subdivision of the membrane potential trajectory into scoop and ramp portions is not particularly apparent in the behavior of PTNs. While many slow PTNs would appear to have scoops and ramps, the interspike-interval changes do not correlate with scoop and ramp alterations in the fashion that they do in the cat's spinal motoneuron. In the case of the fast PTN's trajectories, the scoop-ramp categories seem completely inapplicable, perhaps because a large hump and a short afterhyperpolarization obscure such phenomena. As seen in Fig. 2, the subthreshold membrane-potential trajectories are very different in the fast PTN when compared to the slow PTN (or to cat spinal motoneuron; not shown). Characteristically, the falling phase of the fast PTN spike terminates well below the firing level. The voltage then rises sharply, cresting in a hump. This deep notch, separating the falling phase of the spike from the subsequent hump, is a prime identifying characteristic of the fast PTN. While the slow PTN may have small humps (Fig. 2A), there is never the deep notch. The notch is also similar to that seen in various invertebrate preparations (e.g., ref 38).

One distinct difference between motoneurons and both fast and slow PTNs is the nature of the adaptation phenomena following the beginning of the current step. In motoneurons, the bottom of the scoop is at its highest point with the trajectory following the first spike; it becomes deeper with successive spikes. In PT cells, the opposite is typically true; the bottoms of the membrane-potential trajectories typically climb for the first few spikes. In motoneurons, the latency from the beginning of the current step to the first spike is typically very brief compared to the subsequent interspike interval; in PT cells the latent period may be an appreciable fraction of the first interspike interval. In this descriptive regard, they are somewhat like the invertebrate cells described by Conner and Stevens (17). Both the latency differences and the "climbing minimum" lead us to speculate that there is some slow process underlying the

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**FIG. 4.** Frequency-current (f-I) curve for a slow (9.2 m/s) PTN exhibiting hysteresis. Successive current steps were incremented in size with each presentation (400 ms, repeating every 1,200 ms) until high rates were reached, whereupon they were decremented. Unlike cat spinal motoneurons and the fast PTNs of the present experiments, slow PTNs often did not retrace the same f-I curve during decrements. Successive current steps are plotted with different symbols, incrementing from 0 to 9, then from A to Z, then back to 0 again. At about 10 nA during the incrementing series, the f-I curve begins to change (points I-J). Firing rates actually began declining (S-V) with increasing currents, forming a genu. The decrementing series (W-Z) proceeds downward in firing rate, forming an f-I curve of substantially reduced slope and shifted origin.
initial repetitive-firing behavior in both fast and slow PTN which is not prominent in motoneurons; it may be nothing more than the considerable difference between the 12- to 24-ms time constants of PTNs (Table 1) and the 3- to 5-ms time constants of spinal motoneurons.

**Postspike humps**

These “delayed depolarizations” or depolarizing afterpotentials seem to be very common in CNS neurons (10). While vanishingly small in some slow PT cells, they can be seen as a small bump at the bottom of the trajectory in other slow PT cells (Fig. 2A). Fast PT cells invariably demonstrate a hump preceded by a deep notch. The hump may change in size with successive spikes of the train (9; unpublished observations).

**Extra spikes during sustained rhythmic discharge**

A large postspike hump may intersect the falling threshold and elicit an extra spike within several milliseconds following a regular spike (9, 10). In its simplest form, this takes the form of a doublet in the midst of an otherwise rhythmic train of spikes (9, 10, 13, 15). We have not seen these extra spikes in slow PT cells.

Such extra spikes are easily detected in the midst of otherwise rhythmic firing but probably exist during other more irregular spike trains (e.g., Fig. 2C) where they may be studied using the methods of Fig. 7. Whatever the mechanism of the postspike humps (which appear to involve the retrograde invasion of the somadendritic region following spike initiation at the initial segment (cf. ref 10)), it is quite apparent that large humps elicit extra spikes by intersecting the falling threshold near the end of the “relative refractory period” of such neurons (9). Figure 5 shows the subthreshold trajectory of the membrane potential (35) between spikes and an extra spike arising from the hump.

Extra spikes during the sustained rhythmic discharge were seen in 25% of our fast PTNs. As shown in the scatter plots of Fig. 1, they show no apparent correlation with antidromic conduction time, spike height, or spike width. The 14 doublet cells were obtained from eight different cats.

When extra spikes are seen in cat spinal motoneurons (and, inferentially, in cat external cuneate nucleus neurons (11)), they tend to drop out when the average firing rate is increased by raising the current. This phenomenon has been particularly prominent in the doublet firing patterns of some lobster stretch receptors (unpublished data of D. K. Hartline and W. H. Calvin). Exactly the opposite occurs in these fast PT cells (and in other lobster re-

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**FIG. 5.** Subthreshold membrane potential trajectories following a step of injected current. Top: unidentified cortical neuron (probably a fast PTN by 0.5-ms spike width) which shows the usual changes in postspike humps with successive spikes. Bottom: fast PTN (same cell as Fig. 2C) with much larger and longer humps, with extra spike arising from hump following second spike (bottom right). Spikes off scale.
ceptors): the doublet discharge is not seen at low rhythmic firing rates (Fig. 6); sporadic doublets are replaced by unfailing doublets as the current increases further. In a joint interval density (a scatter plot of interval versus preceding interval (33)), a rhythmic discharge appears as a diagonal line when data from a number of different driving currents are pooled (Fig. 7A). Extra spikes tend to appear as points along lines parallel to the axes (at 1–3 ms in the case of Fig. 7). As seen in Fig. 7B–F, the joint interval density for neurons exhibiting doublet discharge has a characteristic “arrow pointing to the origin” shape (15). Short intervals followed by short intervals, e.g., triplets, give rise to the point at the head of the arrow. In some fast PT cells, further increments in current beyond the level at which the doublets appear may give rise to triplets, quadruplets, etc., as shown in Fig. 6B, C. Indeed, in some fast PTNs, a rhythmically recurring burst discharge could be seen (Fig. 6C).

**Extra spikes during adaptation**

Once extra spikes have been identified by their presence during sustained rhythmic discharge, one’s attention is drawn to the changes in spike patterns which occur just after the beginning of the step. In instances involving doublet cells and also in the case of many other fast PTNs, we believe that we can identify extra spikes early in the discharge contributing to the high initial firing rates.

Koike et al. (26) commented on an unusual adaptation pattern where the firing rate first rose, then fell. Interestingly enough, our extra spikes frequently start following the second rhythmic spike rather than the first. In a raster display (4), one can choose to align the second spikes of responses rather than the first.

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**FIG. 6.** Three cortical neurons which exhibit double spikes during repetitive firing in response to current steps. For each cell, responses to four current steps are shown. A: Fast (24.5 m/s) PTN in the top row (also shown in ref 15, Fig. 1A–H) begins to fire rhythmically at about 5 nA and increases its firing rate by about 13 spikes/s for each additional 1 nA until about 9 nA is reached, whereupon double spikes (2-ms interspike intervals) begin to appear during otherwise rhythmic firing. By 11 nA, every spike is double (after the initial transient firing phenomena; see text) and each additional 1 nA increases the firing rate by about 25 spikes/s with little change in the doublet interval itself. The extra spikes arise from the peak of the depolarizing hump following spikes. B: fast (62.1 m/s) PTN in the middle row (see also ref 15, Fig. 1J–M) goes through a similar sequence, except that triple spikes, etc., are seen at higher currents where the depolarizing humps following extra spikes are themselves eliciting additional extra spikes. C: for the unidentified neuron (0.68-ms spike width) in the bottom row, maintained firing was very irregular at the 12-nA current threshold for repetitive firing; the large depolarizing humps can be easily seen following all spikes (except the first) and doublets are common. With 13.6 nA of current, triplets are common, quadruplets by 15 nA, and more sustained high-frequency firing by 19 nA. These three cortical neurons illustrate the range of the double-spike phenomena seen in the 25% of fast PTNs showing double spikes during sustained repetitive firing; since the initial transient firing may also contain double spikes in these cells and others, the total percentage of fast PTNs with double spikes may be much higher (estimated at 50% in Table 2).
FIG. 7. Joint interval densities for six cortical neurons. These scatter plots of interspike-interval duration versus the following interspike-interval pool data from many current steps of different sizes. Changes in mean interspike interval also occur during adaptation in firing rate to a given current step. For a cell which fires rhythmically (A), all points are peridiagonal. For cells with pronounced doublet firing at all interspike intervals shown (B), one sees clusters parallel to axes; the central cluster (short followed by another short) is primarily from adaptation intervals. A combination of features is seen in C, giving rise to an arrow pointing to the origin shape (same PTN as Fig. 6B). The transition from rhythmic firing to doublet firing is made between 10 and 5 ms; the lack of points between the peridiagonal group and the 2-ms clusters demonstrates the lack of gradation of the doublet phenomenon in this cell. The wider peridiagonal spread of points in D and E tends to obscure the rhythmic versus doublet transition. In E, one can also see a tipped arrow because higher currents tend to decrease the interspike interval below the characteristic doublet (3 ms in this cell). The arrow tip is even more pronounced in F because the characteristic doublet is about 4 ms, while high currents can shorten the interspike interval to 1 ms. Cells for B-E are identified fast (44.3, 62.1, 37.7, 53.5 m/s) PTNs; antidromic identification was not obtainable for the cells of A and F but their spike durations (0.8 and 0.55 ms) suggest fast PTNs.

has been done in Fig. 8 (and in Fig. 1F of ref 15) showing that, as current increases, a third spike develops several milliseconds after the second spike, and this interspike interval does not change dramatically with further increments in current which are shortening the "rhythmic interspike intervals" in the usual fashion.

It is not always easy, however, to make a clear distinction between whether a spike corresponds to the "rhythmic-firing mode" or to the "extra-spike mode" (10). Figure 2B illustrates a PT cell with an intermediate conduction time (1.75 ms from the medullary pyramids). There is a distinct change in the firing pattern following the 11th spike at the intermediate current level, tempting one to say that the 10 spikes following the 1st spike are extra spikes and that the cell reverted to ordinary rhythmic firing with the 12th spike. At other currents, this sudden transition is not so apparent.

Less stereotyped long-short interval alternation

For most of the fast PTNs which we have classified as doublet type, the joint interval density shows a distinct cluster of points along lines parallel to the axes and a relative lack of points nearby. This suggests to us that the spikes really do arise from the peak of the post-spike humps and that one may thus speak of extra spikes arising from the depolarizing aftermath of the antecedent spike (9).

It is, however, apparent that there is a less-
stereotyped phenomenon which is probably related. We show in Fig. 7 a series of joint interval densities from six cells; they start with the peridiagonal plots of the neuron in Fig. 7A. Those in Fig. 7B–D produce the stereotyped short intervals which give rise to the arrow pointing to the origin shapes. In Fig. 7E, the filled-in nature of the areas depopulated in Fig. 7C suggests that the excitability of the cell exhibits a much broader peak, extending to at least 10 ms. Figure 7F shows a "tipped arrow" due to the extra spike intervals being at 3–4 ms but with higher currents shortening the initial intervals well below those values.

Long-short alternation is well known from the tendency of afterhyperpolarizations to summate (13, 15). If the interval following a short interval lengthens so the sum of the two intervals becomes twice the average interval, one would expect the point to fall along a line perpendicular to the diagonal. This would considerably broaden the peridiagonal scatter seen in Fig. 7A. Scatter often increases with mean ISI (14, 30); the relatively constant scatter about the peridiagonal seen in Fig. 7C may reflect long-short alternation. The compensatory lengthening from afterhyperpolarization summation does not, however, explain the origin of the shorter intervals; it only references the compensatory lengthening of the next interval.

"Long first-interval" phenomenon

We first described this phenomenon in extracellular recordings from epileptic monkeys (16). Essentially, there is a stereotyped cluster of spikes which follows the second spike of a burst. When the raster display aligns on the second spike of the burst, one can see columns formed by the succeeding spikes of the response, indicating the stereotyped nature of this "afterburst." The first spike stands in front of this stereotyped afterburst at varying times (Fig. 8).

In our intracellular recordings from normal cats, we believe that we can identify extra spikes following the second rhythmic spike of the train (rather than the first) in at least 30% of the doublet-type fast PTNs. However, it is common to see a larger postspike hump following the second spike (unpublished observations). This pattern, whereby postspike humps may not develop until after the second rhythmic spike, is also seen in cat spinal motoneurons (9, 10, 13). This normal property may account for many of the long first-interval phenomena in epileptic cortex (but both Calvin et al. (16) and Wyler et al. (45) describe patterns which may arise from other mechanisms).
DISCUSSION

Our population of PT neurons must be judged by several selectivity factors: 1) the natural selection for larger neurons imposed by the microelectrode, 2) our "discard" criteria, and 3) how any injury in accepted PT cells affected the physiological properties which we report.

Figure 9 shows, using connected data points, a population of 226 PTNs recorded intracellularly, obtained by pooling our 70 PTNs with the 156 PTNs in the Takahashi (42) histogram. The line graph represents the latency distribution of the 640 PTNs extracellularly obtained by Towe and Harding (ref 43, Fig. 3). The bar graph shows their estimate of the latency distribution to be expected from the axon diameter distribution alone, without weighting for cell size; on this basis, the average PTN would have a 5.6 ms latency. Intracellularly, one samples only the fastest 42% of the PTNs (longest latency 5.0 ms); extracellularly, one samples from the fastest 75% (longest latency 6.9 ms). Both extracellular and intracellular samples, however, heavily favor the cells with the fastest axons.

The proportion of the axon fiber spectrum which might be expected to possess anti-dromic conduction times less than 2.3 ms (the fast-slow separation used by Takahashi (41)) is 45% of the total. Our proportion of fast PT cells is 81% and the figure for extracellular recording is 52% (43). Thus the slow PT cells are considerably underrepresented and the slowest 58% of them are never observed intracellularly at all.

In addition to the evaluation of the microelectrode selectivity, one must evaluate experimenter selectivity. Our earlier experience with intracellular recording in spinal motoneurons (9, 13, 14) and cortical neurons (39, 40) led us to conclude that only initially excellent penetrations would ever be useful for repetitive firing studies. Thus, our strategy was to advance our microelectrode at a rapid rate, continuing on through any cell which did not immediately look promising for repetitive firing studies. It has been our impression that a slow approach to a cell does not necessarily yield better penetrations, but that rapid advance yields more penetrations per hour. Interestingly enough, our latency distribution (Fig. 1C) closely matches that of Takahashi (41) who did not impose the repetitive firing selection criterion that we used.

To illustrate the selectivity of the experimenters, we kept tallies of all neurons encountered during 2 of our 15 good experiments; we noted the cell if it was a neuron potentially good enough for studies of synaptic potentials. Of the 71 neurons thus tallied in the two experiments, we judged 27 (38%) good enough to turn on the tape recorder. Extrapolating this 38% to our 194 tape-recorded neurons suggests that we encountered over 500 neurons in the present series. The 194 neurons were reduced to the present 70 by selecting only those on which we could obtain adequate antidromic identification and on which we could obtain repetitive firing. These 70 are less than 14% of the estimated total neurons successfully penetrated. The more rigorous selection criteria needed for detailed repetitive firing studies (13, 14) would reduce the percentage considerably further. It should be noted that excellent recordings were also obtained (perhaps 12 in the present series) in neurons which we were unable to antidromically identify; one can tentatively identify these otherwise good cells as fast or slow using the spike width and checking for the characteristic postspike notch-hump of fast PT cells. There is, however, always the possibility that some of these cells are true non-PT neurons and not merely a problem with the electrode placement in the medullary pyramids.

The third factor, the physiological concomitants of injury, is inextricably linked to the selection criteria. When a previously "healthy" cell begins to deteriorate, one sees transient re-
petitive firing to an intermediate-sized current step; thus one assumes that a cell showing such transient responses on penetration is injured. These cells were always discarded. This problem has been discussed by Kernell (25) and by Calvin (10).

If this feature of the rhythmic firing mode is extremely sensitive to injury, might also the extra spike mode exhibit injury features? Figure 1A shows that our doublet neurons have spike heights which are scattered throughout the observed range; they do not seem to be preferentially distributed in the lower spike heights.

The fast-slow classification may represent nothing more than the extremes of a unimodal spectrum as in the case of spike widths. We have, however, been impressed by the number of differences between fast and slow pyramidal tract neurons as compared to fast and slow spinal motoneurons. Table 1 shows the wide variety of fast-slow contrasts deduced by previous workers. Table 2 summarizes the additional fast-slow contrasts from the present data. The fast-slow subdivision utilized in these tables serves to reinforce the notion that fast PT cells, while requiring more current to activate, respond more vigorously when they do react. It is apparent that part of the vigorous response immediately following a current step is due to the extra spike mode and not merely to adaptation in the usual sense (35). That fast, and not slow, PT cells have the capability for extra spike discharge means that they have the capability for doubling, tripling, etc., the gain of their frequency-current relationship (15).

If one views a PTN spike train from the standpoint of a downstream neuron receiving PSPs, the effect of the extra spikes should be even more striking. Unlike the facilitation associated with la afferents, the corticomotoneuronal EPSPs (in monkeys) exhibit marked increases in second EPSPs; the facilitation peaks at 2 ms (32) which is, interestingly enough, the typical extra spike interval in PTNs (Fig. 7). Since the second EPSP may be twice as large as the first, the average depolarization which the PTN spike train contributes to the motoneuron (6, 10) should increase threefold when the doublets begin, assuming that the EPSP pair data can be applied to a train-type situation.

The association of slow with “resistance to fatigability” which has developed in motor units may not be applicable to PT neurons: the hysteresis which develops in the f-I curve of slow PTNs may well represent a fatigue factor, although further experiments will be required to elucidate this point. We may be dealing with some processes having time constants an order of magnitude greater than the usual $10^{-2}$ s which one associates with the afterpotentials of PT neurons.

At least 64% of cat pyramidal tract neurons (19) have axon collaterals to various subcortical structures in addition to their axon in the medullary pyramid. Considerable time may be consumed for the conduction along these axon collaterals, compared to the faster conduction time of the “parent” axon. This raises the possibility that some axons in the medullary pyramids may be smaller because the “major” branch goes elsewhere. Thus, the antidromic conduction times from the medullary pyramids may exhibit some scatter toward longer times, relative to the time which would be predicted from the original axon size as it left the soma. Similarly, this factor would skew the axon diameter spectrum to smaller values, and thus the unweighted latency prediction of Fig. 9 to longer latencies, ameliorating somewhat the enormous sampling bias noted earlier. Whatever scatter does exist, however, does not obscure a very direct relationship between the antidromic conduction time and such features as spike width, spike afterhyperpolarization duration, and (for fast PT cells) input resistance (41).

Finally, it is interesting to compare these properties of normal PTNs to those of the “epileptic” cortical neurons (11, 16, 21, 45) from the chronic (months, years old) epileptic foci (Fig. 8). All of the cortical neurons in the chronic monkey foci with stereotyped bursts seem to be fast PTNs (21), just as all of our doublet cells turn out to be fast PTNs in normal cats. The stereotyped nature of the epileptic bursts often starts with the second, rather than the first, spike. Our extra spikes often begin after the second rhythmic spike both in PTNs (15) and in motoneurons (8).

While it thus seems likely that the extra spike mode plays a prominent role in the burst firing seen in epileptic foci, it is not clear just what has been altered. Our results, albeit in deeply narcotized cats, suggest that some extra spikes are typical of fast PTN discharges. They suggest that long first-interval bursts are not necessarily abnormal. Why such bursts are plentiful in epileptic foci and not seen by the same workers (E. E. Fetz, personal communication) in normal cortex using identical methods presents interesting possibilities: perhaps the activity in normal unanesthetized monkeys suppresses the extra-spike mode,
perhaps the depopulation in epileptic foci enhances the chances of encountering a fast PTN with an augmented extra-spike mode, etc. As discussed earlier (9, 10), it is possible that the extra-spike mode is sensitive to the history of the cell in a manner analogous to automatic-gain controls: a history of inactivity might augment the extra-spike mechanisms so that whenever a spike occurs, a few extra spikes are produced.

REFERENCES


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