Relationship Between Simulated Common Synaptic Input and Discharge Synchrony in Cat Spinal Motoneurons

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Binder, Marc D. and Randall K. Powers. Relationship between simulated common synaptic input and discharge synchrony in cat spinal motoneurons. J Neurophysiol 86: 2266–2275, 2001. Synchronized discharge of individual motor units is commonly observed in the muscles of human subjects performing voluntary contractions. The amount of this synchronization is thought to reflect the extent to which motoneurons in the same and related pools share common synaptic input. However, the relationship between the proportion of shared synaptic input and the strength of synchronization has never been measured directly. In this study, we simulated common shared synaptic input to cat spinal motoneurons by driving their discharge with noisy, injected current waveforms. Each motoneuron was stimulated with a number of different injected current waveforms, and a given pair of waveforms were either completely different or else shared a variable percentage of common elements. Cross-correlation histograms were then compiled between the discharge of motoneurons stimulated with noise waveforms with variable degrees of similarity. The strength of synchronization increased with the amount of simulated “common” input in a nonlinear fashion. Moreover, even when motoneurons had >90% of their simulated synaptic inputs in common, only ∼25–45% of their spikes were synchronized. We used a simple neuron model to explore how variations in neuron properties during repetitive discharge may lead to the low levels of synchronization we observed experimentally. We found that small variations in spike threshold and firing rate during repetitive discharge lead to large decreases in synchrony, particularly when neurons have a high degree of common input. Our results may aid in the interpretation of studies of motor unit synchrony in human hand muscles during voluntary contractions.

INTRODUCTION

The occurrence of synchronous motoneuron discharge in the muscles of human subjects performing steady isometric contractions has been well documented (e.g., Datta and Stephens 1990; Dietz et al. 1976; Schmied et al. 1993). Although the functional significance of motor unit synchronization remains uncertain (see Yao et al. 2000 for review and references), measurements of synchrony have been used to infer the extent to which motoneurons in the same and related pools share common synaptic input (Bremner et al. 1991a,b; Farmer et al. 1993a; Stephens et al. 1999). This inference is based on the hypothesis that synchronous discharge of two simultaneously active motoneurons is produced by the near-simultaneous arrival of synaptic inputs arising from presynaptic fibers that branch to contact both motoneurons (Datta and Stephens 1990; Kirkwood and Sears 1978). In the case of human hand muscles, it has been proposed that descending pathways from the cortex, including corticospinal neurons, are likely sources of the synchronizing input (Datta et al. 1991).

The principal technique for assessing motoneuronal synchrony has been to compile cross-correlation histograms between the spike trains of concurrently active motoneurons. A short-duration, central peak in the cross-correlation histogram (“short-term synchrony”) (Sears and Stagg 1976) is taken as evidence of synchronized discharge and the size of this “correlogram” peak is thought to vary with the proportion of input that is shared by a pair of motoneurons (Datta and Stephens 1990; Kirkwood and Sears 1978). Thus variations in the average strength of synchronization associated with differences in motor-unit location (Bremner et al. 1991a,b) relative recruitment threshold (Datta and Stephens 1990) and following CNS pathology (Farmer et al. 1993b) are all assessed by measuring the central peak in the cross-correlation histogram.

A number of different procedures have been used to normalize the central peaks in the cross-correlation histograms to produce an “index of synchronization” (see Nordstrom et al. 1992 for review). However, all of these proposed indices depend on the discharge rates of the neurons (Datta and Stephens 1990; Davey and Ellaway 1988; Nordstrom et al. 1992) and thus must be interpreted with caution (J. R. Rosenberg, personal communication). Moreover, the actual relationship between the extent to which two motoneurons share common synaptic input and the degree of synchrony in their spike trains has not been determined directly. It is this latter issue that we have addressed in the present study.

To examine the relationship between synchronization and common input, we injected current noise composed of the sum of several independent random signals into cat spinal motoneurons. Each motoneuron was tested with a number of different waveforms. Some of the current-noise waveforms were completely independent, while others shared common subcomponents. Crosscorrelation histograms were then compiled between the different discharge records in which motoneurons were activated with noise waveforms of variable degrees of similarity. We found that the relationship between the various indices of synchronization and the amount of shared input was nonlinear and that the apparent relationship between synchroniz-
pendent on which index was used. Further, using a simple neuron model, we found that small variations in spike threshold and firing rate during repetitive discharge lead to large decreases in synchrony, particularly when neurons have a high degree of common input. Our results may be useful in the interpretation of studies of motor-unit synchrony in man where inferences on shared synaptic input have been drawn from the analysis of cross-correlation histograms (e.g., Bremner et al. 1991a). A preliminary account of some of these results has been presented (Powers and Binder 1999).

METHODS

Experimental preparation

Intracellular recordings from lumbar motoneurons were obtained from 10 adult cats. Some of the data collected from these animals were used in our recent study on the relationship between motoneuron afterhyperpolarization (AHP) and discharge variability (Powers and Binder 2000). The experiments were carried out in accord with the animal-welfare guidelines in place at The University of Washington School of Medicine. Anesthesia was induced with an intraperitoneal injection of pentobarbitone sodium (40 mg/kg) and maintained at a deep level throughout the surgical and experimental procedures by supplementary intravenous doses (1–4 mg/kg). Following a conventional laminectomy from L1 to S1, and dissection of either the left sciatic nerve at the hip or the nerves to the left medial gastrocnemius and lateral gastrocnemius-soleus muscles, the animals were mounted in a rigid spinal cord recording frame, paralysed with gallamine triethiodide, and mechanically respired. Subsequently, the depth of anesthesia was adjusted to maintain the mean blood pressure (monitored with a cannula in the carotid artery) below 120 mmHg and to minimize anesthesia was also checked by testing for withdrawal reflexes during periods of recovery from paralysis.

Potassium sulfate- or potassium chloride-filled microelectrodes were driven into the spinal cord to penetrate motoneurons, which were identified by antidromic activation from muscle or mixed nerves. Only motoneurons with stable resting potentials greater than −60 mV and action potentials with positive overshoots were studied. At the conclusion of the experiments, the animals were killed with a lethal dose of pentobarbitone.

Experimental protocol

On successful impalement of a motoneuron, we first recorded a series of antidromic spikes, followed by a series of spikes directly elicited by 1-ms suprathreshold injected current pulses. Input resistance and rheobase were then measured as described previously (cf. Powers and Binder 1995; Zengel et al. 1985). We also measured the slope of the steady-state frequency-current relation and also to determine the degree of common input. Our results may be useful in the interpretation of studies of motor-unit synchrony in man where inferences on shared synaptic input have been drawn from the analysis of cross-correlation histograms (e.g., Bremner et al. 1991a). A preliminary account of some of these results has been presented (Powers and Binder 1999).

Data analysis

The computer files containing the membrane potential responses were analyzed off-line. The responses to the initial set of stimuli were used to determine motoneuron input resistance and rheobase (Powers and Binder 2000). The responses of the motoneuron to the series of 1-s suprathreshold current steps were used to determine the slope of its steady-state frequency-current relation and also to determine the minimum steady discharge rate in the absence of noise. The average voltage response to the 1-ms, −10-nA hyperpolarizing current pulses was used to calculate the passive impulse response of the motoneuron. After subtracting the background membrane potential, the result was multiplied by −1 and a double exponential fit (curve-fitting routine of Igor Pro; WaveMetrics, Lake Oswego, OR) was obtained to the voltage trajectory following the offset of the current pulse. The passive impulse response was obtained by normalizing the amplitude of each exponential component to that expected for a 1-nA pulse with a width corresponding to our sampling interval of 0.1 ms (cf. D’Aguanno et al. 1986). The membrane noise produced by the injected noise waveforms was estimated by convolving the injected current waveform with the passive impulse response of the motoneuron (Powers and Binder 2000). Following the onset of the long injected current step, but prior to the onset of the injected noise component, we measured the background synaptic noise in the motoneuron. In many cases, the background synaptic noise was negligible, as evidenced by the fact that the variance of the signal was roughly the same as that measured after withdrawing the electrode from the cell. However, in other cases, the variance of the background synaptic noise was an appreciable fraction of the estimated membrane variance produced by the noisy injected current waveform. For this reason, the percentage of simulated “common” input between any pair of neurons was determined from the mean firing rate obtained over the last 0.5 s of a series of 1-s suprathreshold current steps were used to determine the slope of the steady-state frequency-current relation and also to determine the minimum steady discharge rate in the absence of noise.
of trials was calculated on the basis of the total membrane noise variance.

We determined the power spectrum and autocorrelation function for each epoch of noise using standard routines in a commercial software package (Igor Pro; WaveMetrics). The power spectra were compiled from 1,024 point segments and a Hanning window, with the plots normalized by the value at 20 Hz. The autocorrelation function was compiled by summing the products of the values of the noise waveform at different time lags and normalizing the result by the peak value.

When the injected noise component was added to the current step, the motoneuron responded with a series of discharges. After the membrane potential records were corrected for electrode capacitance artifacts (Poliaikov et al. 1996), the time of occurrence of each spike was determined from the point at which the spike first crossed a specified threshold level in the positive-going direction.

To simulate a typical motor unit synchrony study, pairs of spike trains produced by the same motoneuron on repeated trials or those produced by two different motoneurons were treated as if they were recorded simultaneously. Cross-correlation histograms were compiled between pairs of spike trains using a 0.5-ms bin width and time lags ±100 ms. The histograms were based on from 1,774 to 16,013 reference events derived from several 26-s epochs of repetitive discharge. Stationarity of firing rate across epochs was assessed by comparing the mean interspike intervals in each epoch of repetitive firing. Epochs were combined as long as the coefficient of variation of the mean interval across different epochs was <0.2. The average coefficient of variation for different sets of epochs of repetitive firing included in a histogram was 0.094 ± 0.044 (SD); range 0.21–0.187. Cumulative summations (CUSUMs) (Ellaway 1978) were calculated for each histogram by subtracting the mean baseline bin count (i.e., lag times more than ±40 ms) from each bin and then integrating the remainder from −100 ms to +100 ms. The width and area of the histogram peak were determined by examining the CUSUM over lags from −10 to +10 ms. The area of the peak was defined as the difference between the maximum and minimum values of the CUSUM over this range and the width as the difference between the times of the minimum and maximum values. Two different measurements or indices of synchrony were then calculated from the peak area of the histogram. The first, \( E \), is equal to \( \left[ A - (\mu * B_p)/R \right] \), where \( A \) is the number of added spikes in the peak, \( \mu \) is average number of spikes per bin in the histogram, \( B_p \) is the number of bins in the correlogram peak, and \( R \) is the number of reference events used to compile the histogram (Datta and Stephens 1990). The second index of synchrony, \( C \), is equal to \( \left( A - (\mu * B_p) \right)/T \), where \( T \) is the duration of the spike train used to compile the histogram (Nordström et al. 1992).

### Neuron model and simulations

We used a simple threshold-crossing model of a motoneuron to investigate how variations in mean discharge rate and spike threshold might affect the relation between common input and synchrony simulated in our experiments. The model was a single compartment neuron with a postspike potassium conductance that decayed exponentially. The rate of change of the membrane’s membrane potential (relative to the resting potential) was described by the following equation: \( \frac{dV}{dt} = \left( 1/C \right) * \left( I_{inj} - gL(V - V_m) - gK(V - V_K) \right) \), where \( I_{inj} \) is the injected current, \( C \) is the neuron capacitance (4 nF), \( g_L \) is the leak conductance (0.5 \( \mu S \)), \( g_K \) is the potassium conductance and \( V_K \) is the potassium equilibrium potential (15 mV below rest). These values yielded a neuron whose passive membrane properties were comparable to a low-threshold (type S or FR) cat spinal motoneuron (i.e., input resistance of 2 \( \Omega \), time constant of 8 ms) (reviewed in Binder et al. 1996). The model produced a spike when the voltage exceeded 15 mV above rest with a 5-ms “refractory period” between spikes. Each spike elicited an exponentially-decaying potassium conductance with a peak value of 0.5 \( \mu S \) and a decay time constant of 20 ms. These parameters yielded an AHP with a peak amplitude of 4.7 mV and a duration of ~120 ms.

The neuron model was excited with the same filtered noise waveforms used in our experiments. The differential equation describing the membrane potential was solved using the exponential integration scheme described by MacGregor (1987), with an integration time step of 0.1 ms. The mean level of the current was set at 8 nA, which when combined with the superimposed noise produced a mean firing rate of 14.5 imp/s. Subsequently, one of two different sources of variability was introduced into the simulations: variations in spike threshold or variations in mean firing rate. Moment-to-moment variations in spike threshold were produced at each time step by adding a random value to the threshold level that was drawn from a Gaussian distribution with a standard deviation of 0.1, 0.2, or 0.5 mV. Trial-to-trial variations in firing rate were induced by adding a random variable to the mean current level that was drawn from a Gaussian distribution with a standard deviation of 0.1, 0.2, or 0.5 nA.

### RESULTS

The following analyses are based on intracellular recordings from 14 cat lumbar motoneurons. The AHP durations of these motoneurons ranged from 61 to 239 ms [mean = 96 ± 44 (SD) ms]. The mean input resistance of our motoneuron sample was 1.5 ± 0.4 (SD) \( \Omega \) (range 0.7–2.1), and the mean rheobase was 8.5 ± 4.7 nA (range 1.9–16.6 nA). The rheobase values are lower and the input resistance values are higher than those that we and others have previously reported (e.g., Binder et al. 1998; Zengel et al. 1985), indicating that our sample was biased toward low-threshold motoneurons.

The voltage noise produced by the injected current waveforms could be estimated by convolving the injected noise current waveforms with the estimate of the passive impulse response of the motoneuron (see METHODS). In most cases, the variance of the background synaptic noise was <10% of the variance of the voltage fluctuation produced by the injected current noise. However, in a few cells, the background synaptic noise was appreciable, allowing a comparison between the characteristics of real synaptic noise and our simulated synaptic noise. Figure 1 compares the characteristics of simulated and actual synaptic noise in one such cell. Segments of the estimated membrane fluctuations produced by the filtered and unfiltered injected current noise waveforms are shown in the left and middle panels of A. Fig. 1A, right, shows the voltage fluctuations produced by summing together eight recorded segments of background synaptic noise.

Figure 1 B–D, compares the characteristics of actual and simulated synaptic noise in more detail. Figure 1B shows the normalized amplitude distributions for the three different noise records. The simulated voltage noise records (solid thin and thick lines) both exhibit a Gaussian amplitude distribution, as expected from the fact that the amplitude distributions of the injected current noise waveforms were Gaussian. The summed background synaptic noise also exhibits a Gaussian amplitude distribution, as expected on theoretical grounds (cf. Svirskis and Rinzell 2000) and also reported for synaptic noise recorded in motoneurons (Calvin and Stevens 1968) and other cells (e.g., Stern et al. 1997).

In contrast, the temporal structure of the simulated voltage noise did not exactly match that of the actual synaptic noise. Figure 1 C and D, shows the normalized autocorrelograms and power spectra for the simulated filtered voltage noise (thick solid trace), the unfiltered noise (thin solid trace), and the
**FIG. 1.** Characteristics of simulated and real synaptic noise. 

A: examples (100 ms) of the voltage noise produced by filtered injected current noise (*left*, bold trace), unfiltered injected current noise (*middle*), and summing 8 records of background synaptic noise (*right*, dotted trace). In each trace, the mean value has been subtracted to emphasize the variance. Eight records of real synaptic noise were summed for display purposes because the variance of the real synaptic noise was much lower than that of the simulated noise. See text for details.

B: normalized amplitude histograms of the 3 types of noise. C: normalized autocorrelation functions of the 3 types of noise. D: normalized power spectra of the 3 types of noise. Bold lines in B–D represent simulated, filtered noise, thin lines represent simulated, unfiltered noise, and broken lines represent actual noise recorded in the motoneuron.
actual synaptic noise (dotted trace). The actual synaptic noise exhibited a somewhat larger correlation time (Fig. 1C) and a steeper frequency fall-off (Fig. 1D) than either of the simulated noise waveforms.

Figure 2 shows examples of the effects of the noisy injected current waveforms on motoneuron discharge. The top traces show portions of the injected current waveforms applied at different times to the same motoneuron: those on the left were identical, whereas those on the right had only one-third of their variance in common. The middle traces show the corresponding portions of the spike trains, and the bottom traces are markers indicating the times of spike occurrence. When the injected current input was identical, five of the seven spikes occurred at the same time within their respective spike trains (left), whereas when the two injected current waveforms shared only one-third of their variance, only three of the seven spikes occurred at the same time on successive trials.

As described in METHODS, each motoneuron was tested with a number of different injected current waveforms, each composed of three subcomponents. Thus a given pair of waveforms may have been completely independent or shared from one to three subcomponents. We treated a pair of trials of repetitive discharge as if they represented simultaneous recordings from a pair of motoneurons as is typically done in the human experiments. Cross-correlation histograms were then compiled between the discharge of motoneurons stimulated with noise waveforms with variable degrees of similarity. Figure 3A shows four cross-correlation histograms compiled from 629 s of discharge obtained in two different motoneurons under four different noise conditions: 100, 67, 33, and 0% similarity. (In
this case, the background synaptic noise was negligible; see METHODS.)

Figure 3B shows the relation between the percentage of simulated “common input” and the probability that the occurrence of a spike in one motoneuron is associated with a near-synchronous spike in the other (i.e., $E$; the number of added spikes in the peak with respect to the average bin count/the number of reference events used for the histogram) (Datta and Stephens 1990). This type of monotonic, nonlinear relationship was found in every case.

As shown in Fig. 4, the relationship between simulated synchrony and shared input held regardless of what type of injected current noise was used [i.e., filtered ($F$), unfiltered ($h$), or high-amplitude, unfiltered ($n$); see METHODS] or which index of synchrony ($E$ or CIS; see METHODS) was applied to the histograms. We found that there was little difference between the amount of simulated synchronous discharge in the spike trains of the same versus different motoneurons. Figure 5 compares the relation between the percentage of simulated common input and the two different measures of synchronization strength for histograms compiled between different trials in the same motoneuron ($F$) and in different motoneurons ($E$). This analysis was restricted to the subset of cases in which filtered noise was used and the level of background synaptic noise was very low (<3% of the membrane potential variance). The average strength of synchronization was not significantly different for within cell and between cell comparisons except at the highest level of common input ($E, t = 3.04, P < 0.01; \text{CIS}, t = 2.90, P < 0.05$).

In all cases, we found a high degree of variation in the value of the index and the amount of simulated shared input, which paradoxically increased as the amount of common input increased. Even when the input to a motoneuron was nearly identical (>90% common) on repeated trials, only ~25–45% of the spikes were synchronized.

Our finding that relatively low levels of synchronization occurred even when the two correlated spike trains were elicited by nearly identical injected current waveforms suggests that the simulated synaptic noise was not the only source of variation in spike timing. We used a simple one-compartment neuron model to determine the effects of two additional factors that might affect spike timing: variations in spike threshold and variations in mean firing rate (see METHODS). Figure 6, A and B, shows the effects of variations in spike threshold on the relation between the percentage of common input and two different measures of synchronization. These results were obtained from the responses of the model neuron to filtered noise waveforms. In the absence of any variation in spike threshold ($F$), the spike trains elicited in the model neuron by an identical input are nearly perfectly synchronized, as evidenced by an $E$ value approaching unity ($0.99$) and a CIS value about equal to the mean discharge rate (14.4 imp/s vs. a mean rate of 14.5 imp/s). The nonlinear relation between the percentage of simulated common input and the amount of synchrony observed in the

![FIG. 4](http://jn.physiology.org/)

**FIG. 4.** Relationship between 2 different measures of synchronization ($E$ in A and CIS in B) and the percentage of common input. The cross-correlation histograms were compiled by comparing several different epochs of discharge in the same motoneuron. $F$, trials in which filtered noise was used as the synchronizing input; $h$, those using unfiltered noise; $n$, those using high-amplitude, unfiltered noise.

![FIG. 5](http://jn.physiology.org/)

**FIG. 5.** Comparison of the relationship between 2 different measures of synchronization (A, $E$; and B, CIS) and the percentage of common input for within cell comparisons ($\bullet$) and between cell comparisons ($E$). Error bars indicate SD; $\ast$, the differences reached statistical significance at the $P < 0.05$ level. See text for further explanation.
Experimental data (cf. Figs. 3–5) is also apparent in the simulations using the model neuron. Adding a small amount of variation in the spike threshold (standard deviation of 0.1 mV) reduced the probability of synchronous spikes elicited by identical inputs from near 1 to 0.8. The largest amount of threshold variability used (standard deviation of 0.5 mV) reduced the probability of synchronous spikes in response to an identical input to 0.46. It is notable that even the largest amount of threshold variation we used in these simulations is comparable to that reported experimentally (cf. Calvin and Stevens 1968; Powers and Binder 1996). The effects of threshold variability on synchrony in the model neuron were much less apparent for 67% shared input, and were negligible for 33% shared input.

Slow variations in the resting potential during our prolonged intracellular recordings led to variations in the mean firing rates elicited by our noisy injected current waveforms, even when identical injected currents were applied to the same motoneuron. To reproduce similar variations in mean firing rate in the neuron model, we added random trial-to-trial variations in the mean level of injected current. The effects of changes in mean firing rate on the relation between common input and synchrony are shown in Fig. 6, C and D. The effects of varying firing rate by adding different amounts of variation to the level of injected current are qualitatively similar to those of spike threshold variations. As in the case of spike threshold variations (Fig. 6, A and B), variation in mean firing rate produced large decreases in synchrony for identical inputs and progressively less change at lower levels of shared input. For the model parameters used in these simulations, changing the standard deviation of the mean current level from 0 to 0.1, to 0.2, and to 0.5 nA produced standard deviations of mean firing rate across trials of 0, 0.4, 1.1, and 1.8 imp/s, respectively. These differences in mean firing rate are well within the range we observed in the present experimental data.

Analyses of human motor-unit recordings have also shown that both discharge variability and changes in motoneuron firing rate affect the size of the central peak in the cross-correlation histogram (Datta and Stephens 1990; Nordstrom et al. 1992), and similar findings have been reported for both alpha and gamma motoneurons in the cat (Connell et al. 1986; Davey and Ellaway 1988). Thus these factors must be taken into account when drawing inferences about shared synaptic input from any “index of synchrony” derived from the histograms. In the present data, we found that the relationship between discharge synchrony and either the variability of the spike trains (geometric mean of the coefficient of variation of
the two spike trains) (Nordstrom et al. 1992) or the mean firing rates of the motoneurons (product of the mean interspike interval of the 2 spike trains) (Nordstrom et al. 1992) depended on which index of synchronization was used. Figure 7 shows the relationship between the strength of synchrony and discharge rate (A and B) or discharge variability (C and D) for trials in which the amount of shared input was >90%. Figure 7A shows that the E index was not correlated with the product of the mean interspike intervals of the pairs of motoneuron spike trains (r = −0.249, n.s.), whereas the CIS index (Nordstrom et al. 1992) showed a strong inverse correlation (Fig. 7B, r = −0.814; P < 0.01). Figure 7C shows that the E index of synchrony (Datta and Stephens 1990) increased significantly as a function of discharge variability (r = 0.663; P < 0.01), in agreement with the human data (Nordstrom et al. 1992). However, the CIS index of synchrony did not show a significant dependence on discharge variability (Fig. 6D, r = −0.08, n.s.).

**DISCUSSION**

A common technique for assessing neuronal synchrony has been to compile cross-correlation histograms between the spike trains of concurrently active neurons (e.g., Moore et al. 1970; Nirenberg et al. 2001; Smith and Fetz 1989). A short-duration central peak in the cross-correlation histogram is taken as evidence of synchronized discharge, and the size of this corregogram peak is thought to vary with the proportion of input that is shared by a pair of neurons (Datta and Stephens 1990; Kirkwood and Sears 1978). The aim of this study was to determine whether in fact the size of the central peak provides a reliable quantitative measure of shared input.

Our experiments were designed to minimize the uncertainties inherent in the typical synchronization study in which extracellular recordings are made from pairs of spike trains without any direct knowledge of the inputs to the neurons. We made intracellular recordings from cat spinal motoneurons, measured the background synaptic noise in the cells, and then injected additional currents into the cells through the microelectrode. To simulate a typical motor unit synchrony study, pairs of spike trains produced by the same motoneuron on repeated trials or those produced by two different motoneurons were treated as if they were recorded simultaneously. Cross-correlation histograms were then compiled between pairs of spike trains. We found that the central peak in the cross-correlation histogram increased with the amount of simulated “common” input. However, even when two spike trains were activated by simulated synaptic inputs that were nearly identical (>90% common elements), only ~25–45% of their spikes were synchronized.

We used a simple neuron model to explore how variations in neuron properties during repetitive discharge may lead to the low levels of synchronization we observed experimentally. We found that small variations in spike threshold and firing rate during repetitive discharge lead to large decreases in synchrony, particularly when neurons have a high degree of common input.

Although we have studied the behavior of spinal motoneurons in the anesthetized cat, our current injection protocols yield interspike interval distributions that are remarkably similar to those generated in the motor units of human hand muscles during sustained voluntary contractions (Powers and Binder 2000). Moreover, the size of the cross-correlation peaks we found in the present data are well within the range reported in studies of synchronization of human motoneurons (Datta and Stephens 1990; Nordstrom et al. 1992). Thus one can tentatively draw several important inferences from our data.
that may aid in the interpretation of measurements of motor unit synchrony in man.

Our results demonstrate that the sensitivity of the cross-correlation technique to detect shared synaptic input is quite limited. Although we did find clear cross-correlation peaks with only 33% common input, our histograms were typically compiled using 3,000–5,000 reference spikes, whereas in many human studies only 1,000 reference spikes may be available (e.g., Bremner et al. 1991b). Again, even when the input to motoneurons was nearly identical, our measurements of the central peak in the cross-correlation histograms suggest that there was relatively little short-term synchronization.

These findings are consistent with recent modeling work showing that when the percentage of common input to motor units falls below 30%, significant synchrony is unlikely to be detected by any index derived from the area of the peak in the cross-correlation histogram (Rosenberg, personal communication; see also Halliday 2000). Further, our own simulations accompanying the present experimental study show how small amounts of variance in motoneuron threshold and/or firing rate produce large changes in the cross-correlation histogram and the values of the synchronization indices derived from the histogram. For example, our finding that the size of the peak in the cross-correlation histogram can vary more than twofold for the same amount of shared input (cf. Figs. 4 and 5) was reproduced in our model neurons by adding a relatively small amount of variance to either the spike threshold or the driving current.

Although it has not been explicitly stated in prior studies of motor-unit synchronization (e.g., Bremner and Stephens 1990; Farmer et al. 1993b; Garnett and Stephens 1990; Nordstrom et al. 1992; Schmied et al. 1993; Stephens et al. 1999), the implicit assumption has been that the different indices of synchronization used are a linear function of the amount of shared synaptic input that a given pair of motoneurons receive. In the present results, however, we found that the relationship between two different synchronization indices and the amount of shared input was markedly nonlinear, both for individual pairs of spike trains (e.g., Fig. 2B) and for data pooled from many different pairs of spike trains (Fig. 3).

Both our experimental and modeling results suggest that synchronization indices derived from cross-correlation histograms have only limited value as quantitative measures of shared synaptic input. This is particularly true in the standard experimental protocol when comparisons are made of different pairs of motor units firing at different mean rates. On a more positive note, our results indicate that generating central peaks in a cross-correlation histogram equivalent to those observed in human motor unit data requires that \( \approx 50\% \) of the input be common to the motoneurons. This value is well within the range predicted from the human data using estimates of mean excitatory post synaptic potential (EPSP) size from the cat spinal cord and simple threshold-crossing motoneuron models (Datta and Stephens 1990; Nordstrom et al. 1992).

Our findings regarding the effects of background discharge rate and discharge variability on the amount of synchronization differ from those reported in motor units of human hand muscles (Nordstrom et al. 1992). For example, we found that the value of the synchrony index \( E \) showed no dependence on the product of the mean interspike intervals of the correlated spike trains, whereas Nordstrom et al. (1992) reported a positive dependence. This difference could reflect the relatively small range of discharge rates examined in the present study or alternatively could reflect the fact that the amount of common input to pairs of human motor units changes with contraction level.

There are at least three other factors that could affect the relation between the proportion of shared input and the degree of motoneuron synchrony during physiological activation of motoneurons: EPSP size, synchronization of the discharge of presynaptic fibers, and variations in conduction time from different branches of common presynaptic axons. The synchronizing noise used in the present study was designed to simulate the combined action of large numbers of small EPSPs. Comparison of the voltage noise produced by our noise waveforms with background synaptic noise recorded in the same cells (e.g., Fig. 1), suggests that noise with a Gaussian amplitude distribution is a reasonable approximation to actual synaptic noise at least in some preparations (see also Calvin and Stevens 1968; Stern et al. 1997). However, under more physiological conditions the voltage noise might be dominated by a small number of large EPSPs. Both simulation (Halliday 2000; Segundo et al. 1968) and experimental work (Türker and Powers 2000) indicate that common inputs composed of relatively few large EPSPs (either due to presynaptic synchronization or a large unitary EPSP size) are unusually effective in producing synchronized discharge. Thus the degree of synchrony observed in human studies could result from a smaller proportion of common input than is implied by our findings here.

Although a relatively small number of common input fibers could have a disproportionately effect on synchronization of motoneuron discharge, this scenario requires systematic differences between the properties (i.e., EPSP size and degree of synchrony) of inputs that are shared between a pair of motoneurons and those that are not. If both shared and nonshared inputs have similar properties, then each population of inputs should contribute to the total variance of membrane potential fluctuation in proportion to their numbers and our conclusions regarding the synchronizing effect of common inputs should be valid.

Finally, variations in the time at which common EPSPs arrive at different motoneurons could reduce their synchronizing effect. In our experiments, we simulated the simultaneous arrival of common EPSPs, without any variation in conduction delay from different branches of the presynaptic neurons. Thus it is possible that the largest peaks in the human data result from cases in which significantly more than 50% of the input is shared as suggested by Bremner and colleagues (1991a,b) because any variation in conduction delay from branches of common presynaptic axons would lead to broader and smaller peaks in the histograms.

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