Monosynaptic EPSPs in Primate Lumbar Motoneurons

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SUMMARY AND CONCLUSIONS

1. Homonymous and heteronymous monosynaptic composite excitatory postsynaptic potentials (EPSPs) were evaluated by intracellular recordings from 89 motoneurons innervating triceps surae ($n = 59$) and more distal ($n = 30$) muscles in 14 pentobarbital-anesthetized monkeys (*Macaca nemestrina*).

2. Homonymous EPSPs were found in all motoneurons tested. The mean values ± SD for maximum EPSP amplitude of triceps surae motoneurons were 2.5 ± 1.3, 1.8 ± 1.3 and 4.5 ± 2.0 mV for medial gastrocnemius, lateral gastrocnemius, and soleus motoneurons, respectively. Heteronymous EPSPs were almost always smaller than their corresponding homonymous EPSPs.

3. Triceps surae EPSP amplitude was larger in motoneurons with higher input resistance. However, this relationship was weak, suggesting that factors related to input resistance play a limited role in determining the magnitude of the EPSP.

4. The mean ratio ± SD of the amplitude of the EPSP elicited by combined stimulation of all triceps surae nerves to the amplitude of the algebraic sum of the three individual EPSPs was 0.95 ± 0.05. This ratio was greater in motoneurons with lower rheobase.

5. Some patterns of synaptic connectivity in the macaque are consistent with previously reported differences between primates and cat (e.g., heteronymous EPSPs elicited by medial gastrocnemius nerve stimulation in soleus motoneurons are small in macaque and other primates but large in cat). However, no overall pattern emerges from a comparison of the similarities and differences in EPSPs among species in which they have been studied (i.e., macaque, baboon, and cat). That is, there are no two species in which EPSP properties are consistently similar to each other, but different from those of the third species. This finding suggests that for each species the pattern of monosynaptic connections reflects adaptations unique to that species.

INTRODUCTION

Intracellular studies of peripheral monosynaptic inputs to spinal motoneurons in laboratory animals have provided insight into the organization of segmental motor systems and the mechanisms of neural transmission (Henneman and Mendell 1981; Mendell 1988). However, almost all of these studies are in the cat or in other nonprimate species, so that their relevance to human motoneuron function is uncertain. Only two studies have provided data on peripheral monosynaptic transmission to motoneurons from nonhuman primates (Clough et al. 1968; Hongo et al. 1984), and little information is available concerning the relationship between peripheral input to motoneurons and the intrinsic properties of those cells.

A previous report from this laboratory described the intrinsic properties of monkey triceps surae (TS) motoneurons (Carp 1992). The present report describes homonymous and heteronymous monosynaptic EPSPs evoked in these same spinal motoneurons. The results permit comparison of primate with nonprimate species and also serve as a

control group for other primate studies now underway in this laboratory (Carp et al. 1992, 1993; Wolpaw and Lee 1989). Portions of this work have been presented in abstract form (Carp et al. 1989).

METHODS

Animal preparation

The preparation has been described previously (Carp 1992), and the methodology is summarized below. Experiments were performed in 14 male pigtail macaques (*Macaca nemestrina*, 4.5–9.3 kg). All surgical and experimental procedures described below conformed to Department of Health, Education, and Welfare Publ. No. (National Institutes of Health) 85-23, "Guide for the Care and Use of Laboratory Animals," and had been reviewed and approved by the Institutional Animal Care and Use Committee of the Wadsworth Center. Anesthesia was induced with ketamine, and a single dose of atropine was administered at the time of induction. Anesthesia was then deepened and maintained with pentobarbital. Animals were intubated, and the brachial vein was cannulated. Heart rate, expired CO_2 and urine volume, specific gravity, and pH were monitored routinely. Deep surgical anesthesia was maintained throughout the experiment. The depth of anesthesia was verified regularly by the absence of response to vigorous palpebral or tracheal stimulation and by the lack of respiratory or cardiac response to surgery (Green 1979; Steffey 1983). At the end of the study, the anesthetized animal was euthanized with an overdose of intravenous pentobarbital.

Animals were supported in a rigid frame. After a L_1–L_6 dorsal laminectomy, the dura and dentate ligaments were cut and the L_5–L_7 spinal cord segments were raised ~4 mm above the vertebral column on a plastic platform. The TS muscle nerves [i.e., medial gastrocnemius (MG), lateral gastrocnemius (LG), and soleus (SOL)] and the tibial nerve distal to the TS nerves (DT)[1] were dissected free from surrounding tissue in both hindlimbs, cut and mounted on bipolar stimulating electrodes. The cord dorsum potential evoked by peripheral nerve stimulation was recorded with a monopolar electrode. Cut skin edges of the incisions in the back and legs were retracted to hold mineral oil pools in which temperature was maintained with heat lamps.

A bilateral pneumothorax was performed just before beginning the recording session, and the animal was subsequently ventilated with a respirator using room air. Neuromuscular blockade was established (intravenous gallamine) at this point, and deep surgical anesthesia was maintained thereafter by continuing the pentobarbital dosage schedule established before neuromuscular blockade and by monitoring heart rate and pupillary light reflex (Committee on Pain and Distress in Laboratory Animals 1992). On the few occasions when heart rate increased or a pupillary light reflex was elicited, the dose of pentobarbital was increased. Expired CO_2

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[1] The DT nerve bundle was cut distal to the departure of the TS nerves, at the point where it passed between the heads of the gastrocnemii. The muscles innervated by this nerve bundle were not identified but presumably included plantaris, flexor hallucis longus, flexor digitorum longus, tibialis posterior, and intrinsic foot muscles.

was maintained at or slightly below pre-pneumothorax levels by adjusting respiratory rate and volume.

Intracellular recording of electrophysiological properties

Over 18–24 hr, intracellular recordings from spinal motoneurons on both sides of the spinal cord were performed with glass micropipettes filled with 3 M K-acetate plus 0.01 M KCl, (DC resistance = 2–8 MΩ). Capacitance and electrode resistance compensation were performed by conventional methods (Purves 1981). Only data from motoneurons with antidromically or current-evoked (0.5-ms pulse duration) action potentials of ≥ 60 mV and with stable resting membrane potentials are presented here.

Composite excitatory postsynaptic potentials (EPSPs) were elicited in motoneurons by stimulation (0.05-ms square pulses at 0.5 Hz) of individual homonymous or heteronymous peripheral nerves, and in some cases, by simultaneous stimulation of all three TS nerves. Averages of 15–25 individual trials were recorded at several stimulus intensities. Intensity was varied (typically from 1.5 to 3.0 times the voltage producing a just-threshold response at the cord dorsum electrode) to insure that the maximum EPSP was recorded. EPSPs were quantified in terms of maximum amplitude, risetime (i.e., the time for the maximum EPSP to rise from 10 to 90% of its amplitude), halfwidth (i.e., the width of the maximum EPSP measured at 50% of its amplitude), intraspinal latency (i.e., time from onset of cord dorsum potential until EPSP onset), and maximum afferent conduction velocity [calculated from the latency to onset of the cord dorsum potential and the conduction distance (measured postmortem after exposing the nerves)].

In 7 of the 89 motoneurons described below, antidromic activation made determination of the maximum EPSP difficult. In these cases, the form of the EPSP was estimated using the "subtraction" method (Burke 1968; Hamm et al. 1983). Briefly, EPSPs were elicited during hyperpolarizing current pulses to block the initial segment-somatodendritic action potential, leaving only the electronically conducted axon spike. Responses to a just-threshold stimulus with and without electrotonically conducted axon spikes were averaged, and the latter was subtracted from the former. The resulting trace (i.e., the axon spike alone) was then subtracted from the responses to higher intensity stimuli (i.e., axon spike plus EPSP) to produce an estimate of the maximum EPSP in isolation. Maximum EPSP amplitude required stimulus intensities greater than that which evoked antidromic action potentials in only 2 of these 7 motoneurons. Thus the maximum EPSP was elicited at or below antidromic spike threshold in most motoneurons. Similar results have been reported in baboon (Hongo et al. 1984).

Measurements of other properties were obtained in many cells from which EPSPs were obtained. The methodology for determining these motoneuron properties has been described previously (Carp 1992) and is summarized here. Axonal conduction velocity was determined from the conduction distance and the latency of the antidromic action potential. Input resistance and membrane time constant were determined from averages of voltage responses to several different small amplitude hyperpolarizing current pulses. Input resistance was calculated as the ratio of the maximal membrane potential deflection during the current pulse to the current pulse amplitude. Time constant was estimated using a curve-peeling method similar to that described by Zengel et al. (1975). Rheobase was defined as the current required to elicit single action potentials 50% of the time by injection of 100-ms depolarizing pulses. The net depolarization from the resting potential to the voltage level at which an action potential was initiated (threshold depolarization) was calculated as the difference between the action potential amplitude elicited by a 0.5-ms current pulse and that elicited by the 100-ms current pulse (Gus-

tafsson and Pinter 1984). The absolute voltage level at which an action potential was initiated (threshold voltage) was calculated as the sum of the resting potential and the threshold depolarization. The duration of the after hyperpolarization (AHP) following an action potential elicited by 0.5-ms current pulses was defined as the time between the initial repolarization to the mean pre-spike resting potential and membrane potential depolarization to within two standard deviations of the mean pre-spike resting potential.

Intergroup differences were assessed by analysis of variance (ANOVA), and relationships between variables were evaluated by linear regression. In accord with the previous study (Carp 1992), P values < 0.01 were considered to indicate statistically significant differences.

RESULTS

Homonymous TS EPSPs and DT EPSPs

EPSPs were recorded from 89 motoneurons with action potentials ≥ 60 mV and stable resting potentials. The sample consisted of 59 TS motoneurons (16 MG, 26 LG, and 17 SOL) and 30 DT motoneurons. The upper part of Table 1 summarizes the characteristics of maximum homonymous EPSPs in TS and DT motoneurons. Stimulation of the homonymous TS nerve elicited EPSPs in every motoneuron tested. Homonymous EPSPs in SOL motoneurons were significantly larger than those in MG and LG motoneurons ($P < 0.01$ for ANOVA). These maximum responses were elicited with low-intensity stimulation (e.g., median stimulus intensity producing just-maximal EPSP amplitude was 2.1 times threshold for the cord dorsum potential for all nerves, and 2.0 times threshold for TS nerves only). There were no significant differences among the three TS muscles in risetime or halfwidth of homonymous TS EPSPs elicited by just-maximal stimuli, using either the raw values or those corrected for variation in membrane time constant between motoneurons (i.e., risetime/time constant and halfwidth/time constant).

While these EPSPs largely reflected monosynaptic excitatory input from large diameter fibers, polysynaptic inputs could have affected EPSP size and/or shape. Figure 1 shows examples of EPSPs elicited in two motoneurons. The upper traces of Fig. 1A show EPSPs elicited at stimulus intensities that were just submaximal (1.4 × T, indicating stimulus strength in multiples of the threshold intensity for eliciting the cord dorsum potential), just maximal (1.5 × T) and supramaximal (1.7 × T and 1.9 × T). Once the maximal EPSP was attained in this motoneuron, further increases in intensity, within a modest range, did not affect EPSP shape. The excitatory component of these potentials was followed by a low amplitude, long duration inhibitory phase (Fig. 1A, bottom traces). Increasing the stimulus intensity produced a slight increase in the amplitude of the inhibitory component but did not alter its time course.

The top traces of Fig. 1B show EPSPs elicited in a different motoneuron at stimulus intensities that were just maximal (1.8 × T) and supramaximal (1.9, 2.1, and 2.4 × T). The EPSP elicited at 1.9 × T was almost identical to that elicited at 1.8 × T. In contrast to the motoneuron in panel A, further increases in stimulus intensity in this motoneuron produced a slight decrease in EPSP amplitude and a more rapid decay of the falling phase of the EPSP towards

TABLE 1. *Homonymous TS and DT EPSP and motoneuron properties*

Property	MG	LG	SOL	DT
EPSP amplitude (mV)	2.5 ± 1.3	1.8 ± 1.3	4.5 ± 2.0	4.3 ± 2.5
EPSP risetime (ms)	0.7 ± 0.2	0.7 ± 0.3	0.8 ± 0.1	0.8 ± 0.3
EPSP halfwidth (ms)	3.4 ± 1.1	3.3 ± 0.8	3.8 ± 1.2	3.8 ± 1.1
EPSP risetime/time constant	0.16 ± 0.06	0.19 ± 0.08	0.18 ± 0.08	0.26 ± 0.16
EPSP halfwidth/time constant	0.78 ± 0.23	0.87 ± 0.25	0.85 ± 0.38	1.20 ± 0.65
EPSP latency (ms)	4.7 ± 0.6	4.7 ± 0.4	4.9 ± 0.6	4.9 ± 0.5
Intraspinal latency (ms)	1.0 ± 0.2	0.8 ± 0.2	0.8 ± 0.1	1.0 ± 0.4
Maximum afferent condition velocity (m/s)	92 ± 3	89 ± 4	90 ± 6	88 ± 4
Axonal conduction velocity (m/s)	74 ± 6	72 ± 5	68 ± 5	69 ± 5
AHP duration (ms)	75 ± 25	80 ± 23	92 ± 36	73 ± 24
Input resistance (MΩ)	0.9 ± 0.3	0.9 ± 0.3	1.1 ± 0.4	0.9 ± 0.3
Time constant (ms)	4.6 ± 1.6	4.0 ± 1.1	4.9 ± 1.3	3.6 ± 1.2
Rheobase (nA)	12 ± 6	14 ± 8	10 ± 6	15 ± 6
Resting potential (mV)	-66 ± 5	-67 ± 5	-64 ± 6	-69 ± 5
Threshold voltage (mV)	-55 ± 5	-55 ± 6	-56 ± 4	-57 ± 5
Threshold depolarization (mV)	12 ± 5	12 ± 4	10 ± 2	12 ± 4

Values are means $\pm$ SD. TS, triceps surae; DT, distal tibial nerve; EPSP, excitatory postsynaptic potentials; MG, medial gastrocnemius; LG, lateral gastrocnemius; SOL, soleus; AHP; afterhyperpolarization.

the resting potential. This latter effect was expressed in the data analysis as a decrease in EPSP halfwidth. The effect of increased stimulus intensity was also apparent in the late inhibitory component of these potentials (*bottom traces,* Fig. 1 *B*). Increase in stimulus intensity increased the magnitude of this inhibitory component and appeared to hasten its onset.

For homonymous EPSPs elicited in TS motoneurons by supramaximal stimuli up to 2 times the just-maximal stimulus, halfwidth decreased by $\sim 30\%$ for a two-fold increase in stimulus intensity ($r^2 = 0.21$, $P < 0.0001$ for regression of halfwidth on stimulus intensity with both variables normalized to their respective values determined for the just-maximal EPSP), while risetime did not vary with stimulus intensity ($P > 0.4$, $r^2 = 0.01$ for linear regression). With supramaximal stimuli, EPSP amplitude tended to vary inversely with stimulus intensity, but only decreased by $\sim 10\%$ for a two-fold increase above the just-maximal intensity ($0.01 < P < 0.02$, $r^2 = 0.05$ for linear regression). These data suggest that, while polysynaptic inhibitory inputs may have contaminated the falling phase and thus affected halfwidth measurements, amplitude and risetime of maximal composite EPSPs provided good estimates of EPSP size and shape.

In addition to having larger EPSPs, SOL motoneurons tended to have slower axonal conduction velocities, higher input resistances, higher rheobases, longer AHP durations, and longer time constants than MG or LG motoneurons. The results are summarized in the lower part of Table 1, and they are consistent with those described previously for the larger population of motoneurons from which these data are drawn (Carp 1992). These motoneuron properties were measured in 90–100% of the motoneurons from which EPSPs were recorded, except for threshold depolarization, threshold voltage, intraspinal latency, and maximum afferent conduction velocity, which were assessed in only 67% of the cells.

The extent to which EPSP size is determined by postsynaptic factors would be expected to be reflected in cell-by-cell comparisons of EPSP amplitude and motoneuron properties. Homonymous TS EPSP amplitude varies directly with input resistance (Fig. 2; $r^2 = 0.18$, $P < 0.01$ for linear regression). A significant linear relationship between log (homonymous EPSP amplitude) and log (input resistance) with a slope of 0.99 ($r^2 = 0.17$, $P < 0.01$) indicates that the relationship between EPSP size and input resistance is best described as linear. After accounting for differences in EPSP amplitude introduced by the muscle innervated by each motoneuron ($r^2 = 0.25$, $P < 0.001$; analysis of covariance), only a small portion of the variation in EPSP amplitude can be attributed uniquely to intercell differences in input resistance (i.e., the covariate; $r^2 = 0.06$, $P < 0.02$). This suggests that post-synaptic factors related to input resistance (e.g., motoneuron surface area, geometry, and specific resistivity) are weak determinants of EPSP size. No significant linear relationships were found between homonymous EPSP amplitude and any other motoneuron property.

Stimulation of the DT nerve elicited EPSPs in every DT motoneuron tested (i.e., "homonymous" DT EPSPs), which were comparable in size to homonymous SOL EPSPs. Their large size probably reflects the activation of a mixed population of homonymous and heteronymous tibial nerve afferents. The broad shape of DT EPSPs (as reflected in their risetime and halfwidth) was similar to that of homonymous SOL EPSPs. After correction for differences in time constant [i.e., (risetime/time constant) and (halfwidth/time constant)], EPSPs of DT motoneurons tended to be broader than those of any of the TS motoneurons. Thus the broad shape of DT EPSPs probably reflects pre-motoneuronal factors (e.g., temporal dispersion of afferent input) rather than postsynaptic factors related to membrane resistivity and/or capacitance.

Relationship between homonymous and heteronymous EPSPs

Table 2 summarizes the results for projection frequency and magnitude of heteronymous EPSPs. Stimulation of individual heteronymous nerves elicited short-latency EPSPs in 88 out of 94 TS afferent-TS motoneuron pairs tested, and 50 out of 51 TS motoneurons exhibited at least one
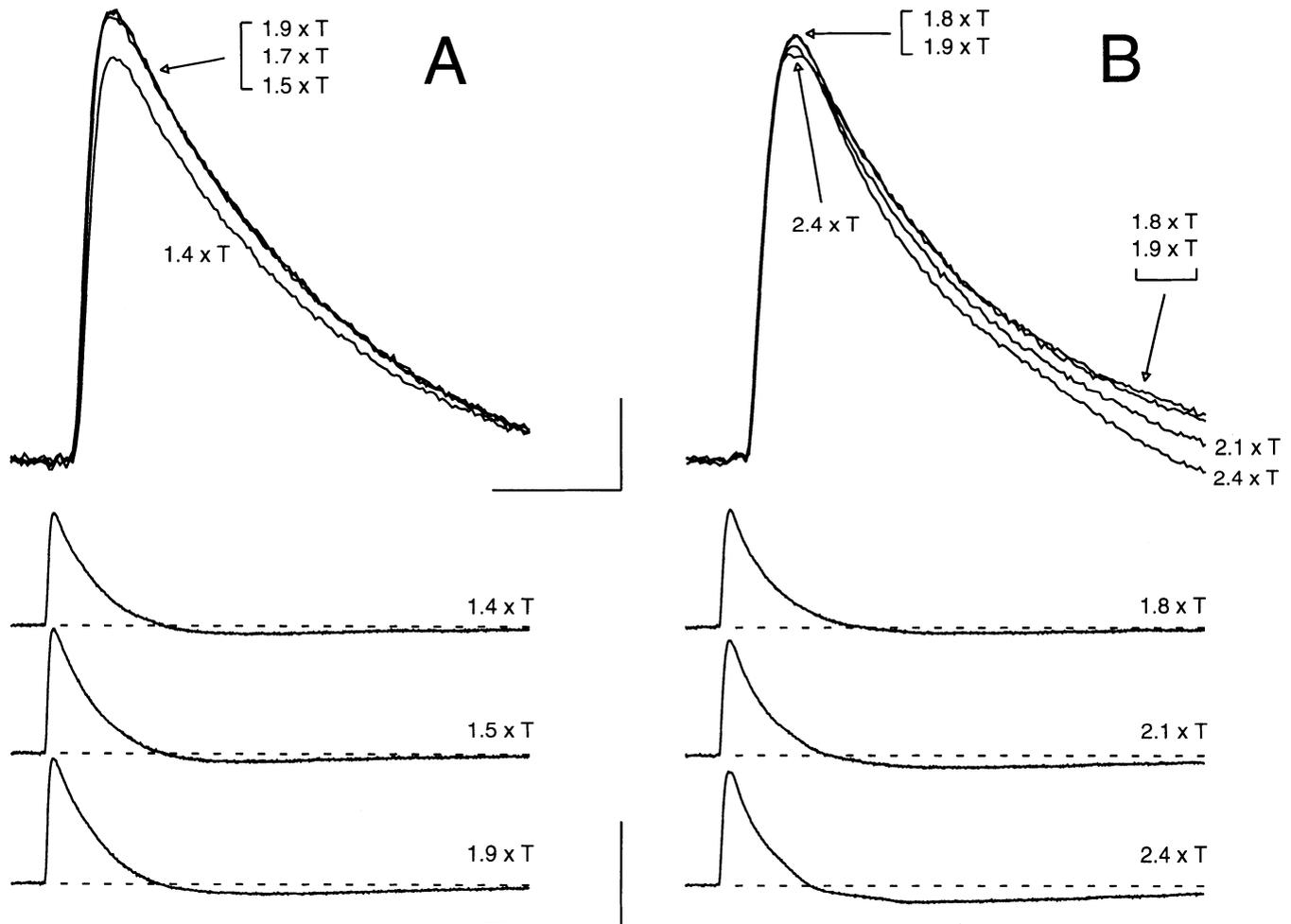
FIG. 1. Postsynaptic potentials in 2 different soleus motoneurons (*A* and *B*, with resting potentials of ~−68 and −62, respectively). All traces are averages of 15–25 individual trials elicited at the indicated stimulus intensity × T (i.e., stimulus intensity normalized to the threshold stimulus for the cord dorsum evoked potential). *Top*: a maximal excitatory component of the postsynaptic potential (EPSP) can readily be determined (just-maximal intensities were 1.5 and 1.8 × T in *A* and *B*, respectively; calibration: horizontal, 4 ms and vertical, 1 mV). In the motoneuron in *B*, supramaximal stimuli elicited an inhibitory response that was evident at the peak and during the falling phase of the EPSP and during the later long-duration inhibitory component of the postsynaptic potential. The latter phenomenon is seen most clearly in the *bottom panels*, in which individual traces selected from the ones in the *top panels* are shown separately on a more compressed time scale (calibration: horizontal, 20 ms; vertical, 4 mV).

heteronymous EPSP. For these motoneurons, heteronymous EPSPs were smaller on average than homonymous EPSPs, although in a few LG motoneurons, individual heteronymous EPSPs were larger than their corresponding homonymous EPSPs (see points above the dashed unity slope lines in Fig. 3*B*). While heteronymous EPSPs in SOL motoneurons tend to be smaller than those in gastrocnemius motoneurons, the difference among the heteronymous EPSP amplitudes in MG, LG, and SOL motoneurons (mean amplitude of pooled heteronymous EPSPs ± SD = 1.1 ± 1.0, 0.8 ± 0.6, and 0.5 ± 0.4 mV, respectively) did not attain statistical significance ($0.01 < P < 0.02$ for ANOVA).

Assuming that the spatial distribution and efficacy of heteronymous and homonymous afferents were comparable, homonymous and heteronymous EPSP amplitudes would be expected to co-vary on a cell-by-cell basis. Using all TS afferent-TS motoneuron pairs, there was only a weak relationship between heteronymous and homonymous EPSPs

($r^2 = 0.06$, $0.02 < P < 0.03$ for linear regression of heteronymous on homonymous amplitudes). For individual motoneuron pools, the only case in which a significant positive relationship was found between heteronymous and homonymous EPSP sizes was for EPSPs elicited in MG motoneurons by stimulation of SOL nerve (+ in Fig. 3*A*; $r^2 = 0.53$, $P < 0.01$). Weak relationships were seen for EPSPs elicited in MG motoneurons by LG nerve stimulation (▲ in Fig. 3*A*; $r^2 = 0.32$, $0.03 < P < 0.04$) and for EPSPs elicited by MG nerve stimulation in SOL motoneurons (○ in Fig. 3*C*; $r^2 = 0.54$, $0.02 < P < 0.03$).

Stimulation of DT afferents also elicited heteronymous EPSPs in the majority of TS motoneurons tested (i.e., DT stimulation elicited EPSPs in 32 out of 35 TS motoneurons tested). No significant linear relationships were found for TS motoneurons between heteronymous DT EPSP amplitude and homonymous TS EPSP amplitude. On the other hand, TS afferents projected more weakly to DT motoneurons than to other TS motoneurons. Heteronymous EPSPs
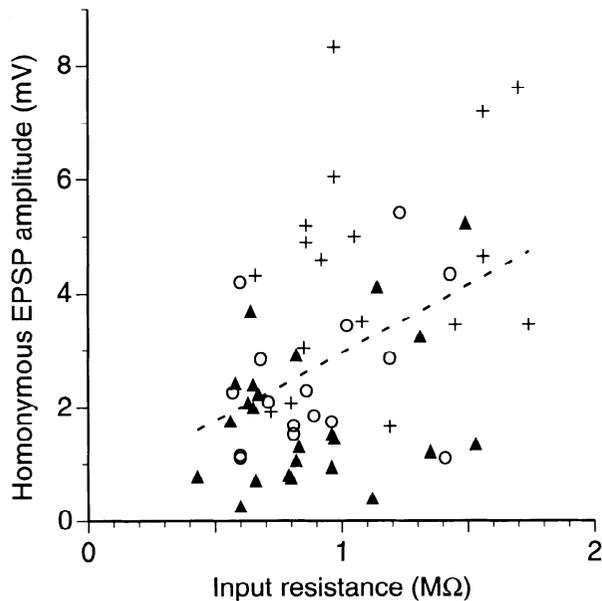
FIG. 2. Homonymous EPSP amplitude varies weakly with input resistance in medial gastrocnemius (o), lateral gastrocnemius (▲), and soleus (+) motoneurons. The dashed line shows the relationship predicted by linear regression of EPSP amplitude on R_N ($r^2 = 0.18, P < 0.01$).

were observed in only 27 out of 74 TS afferent-DT motoneuron pairs, and only 16 out of 26 DT motoneurons received at least one heteronymous EPSP.

The bottom part of Table 2 shows the relative magnitude of heteronymous EPSPs (i.e., the mean ratio of heteronymous EPSP amplitude to homonymous EPSP amplitude). For each pool of TS motoneurons, there were no significant differences in the relative amplitudes of EPSPs evoked by stimulation of any of the four different heteronymous afferent nerves ($P > 0.3$ for ANOVA).

If synaptic contacts formed by all afferents were similarly distributed across the somatodendritic axis of a given motoneuron, the shapes of homonymous and heteronymous EPSPs would be expected to be similar. In fact, the risetime and halfwidth of EPSPs elicited by just-maximal homonymous nerve stimulation did not differ from the corresponding values of EPSPs elicited by stimulation of heteronymous TS nerves.

Summation of TS EPSPs

In 14 TS motoneurons (3 MG, 8 LG, and 3 SOL), EPSPs were also recorded in response to stimulation of all 3 TS nerves simultaneously (mixed EPSP). In nine cases, the amplitude of the mixed TS EPSP was only slightly smaller (1–6%) than the amplitude of the algebraic sum of the three individual TS EPSPs (e.g., Fig. 4A). In four cases, it was 9–14% smaller (e.g., Fig. 4B), and in one case, it was 5% larger. The mean summation ratio (i.e., the ratio of the mixed TS EPSP to the summed TS EPSP) was 0.95 ± 0.05, which is similar to the ratio of 0.97 in cats [estimated from Fig. 2 of Burke (1967)]. There were no significant differences in the summation ratio among the individual TS motoneuron pools ($0.96 \pm 0.01, 0.95 \pm 0.06$, and 0.93 ± 0.07 for MG, LG, and SOL, respectively). In addition, the summation ratio did not vary with the resting potential of the motoneuron, the amplitude of the mixed EPSP or the difference between the homonymous and average heteronymous EPSP amplitude, risetime, or halfwidth. However, the summation ratio was negatively correlated with rheobase (Fig. 4C; $r^2 = 0.57, P < 0.01$ for linear regression).

DISCUSSION

Spinal segmental input to motoneurons has been studied primarily in cats (Henneman and Mendell 1981; Mendell 1988). The only nonhuman primate in which segmental transmission to motoneurons has been studied intracellularly is the baboon (Clough et al. 1968; Hongo et al. 1984). In the present study, composite EPSPs elicited by stimulation of homonymous and heteronymous peripheral nerves were studied in macaque TS and DT motoneurons. These EPSPs are likely to reflect largely the activation of monosynaptic inputs, since the EPSP latency varies little from trial to trial for a given motoneuron, and the intraspinal latency is brief. They are probably the result of activation of large diameter (primarily group Ia) afferents, since the maximum TS EPSP tends to occur at a low stimulus intensity, and since the conduction velocity of the fastest afferents involved in this response is consistent with that of group I afferents. Stimulation at intensities greater than that producing a just-maximal EPSP evoked inhibitory components that occurred near to or well after the time of

TABLE 2. *Heteronymous EPSP properties*

Property	Afferent	Motoneuron			
		MG	LG	SOL	DT
Projection frequency*	MG	16/16	20/22	6/9	5/23
	LG	14/14	25/25	13/13	10/26
	SOL	13/13	23/23	17/17	12/25
	DT	7/9	15/15	10/11	30/30
Mean EPSP amplitude (mV)	MG	2.5 ± 1.3	0.8 ± 0.7	0.3 ± 0.3	0.2 ± 0.5
	LG	1.1 ± 1.1	1.8 ± 1.3	0.6 ± 0.4	0.2 ± 0.6
	SOL	1.1 ± 0.9	0.9 ± 0.5	4.5 ± 2.0	0.2 ± 0.4
	DT	0.5 ± 0.5	0.9 ± 0.7	0.8 ± 0.4	4.3 ± 2.5
Mean ratio of heteronymous	MG		0.52 ± 0.40	0.07 ± 0.06	0.07 ± 0.16
to homonymous EPSP amplitude	LG	0.42 ± 0.29		0.19 ± 0.17	0.09 ± 0.17
	SOL	0.44 ± 0.23	0.63 ± 0.47		0.08 ± 0.13
	DT	0.23 ± 0.23	0.52 ± 0.47	0.22 ± 0.16	

Values are means ± SD. For abbreviations see Table 1. *Number of motoneurons with EPSPs > 0.1 mV/number of afferent-motoneuron pairs tested.
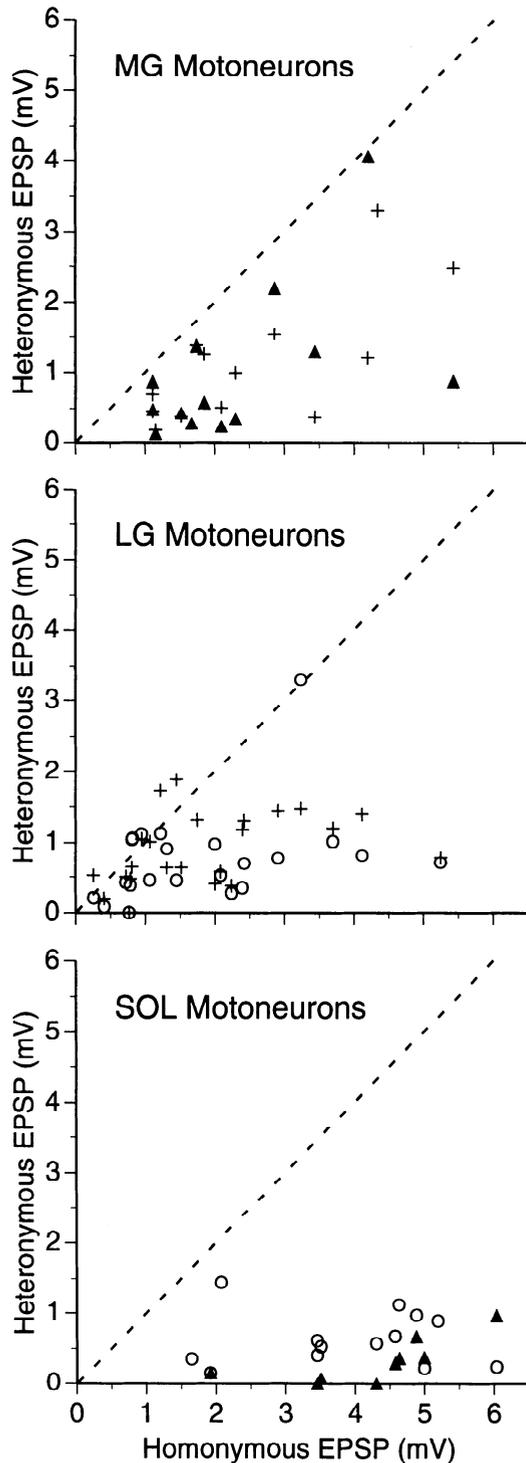
FIG. 3. Relationships between heteronymous EPSPs in medial gastrocnemius (MG), lateral gastrocnemius (LG), and soleus (SOL) motoneurons elicited by stimulation of MG (o), LG (▲), and SOL (+) muscle nerves. The dashed lines are unity slope lines, where heteronymous and homonymous EPSPs from a given motoneuron are the same size.

the peak of the EPSP (e.g., Fig. 1). While the sources of these effects were not specifically evaluated in this study, they probably comprised polysynaptic inhibition via group I and/or II afferents (Baldissera et al. 1981) and recurrent inhibition via antidromic activation of motoneuron axons (Eccles et al. 1954). Regardless of the source of this inhibi-

tion, it appeared to have minimal impact on amplitude and risetime of EPSPs elicited by just-maximal stimuli.

Monosynaptic TS EPSPs of macaque motoneurons are qualitatively similar in many ways to those of cat (Burke 1967, 1968) and baboon (Hongo et al. 1984) motoneurons. In all three species, homonymous EPSPs can be elicited in all TS motoneurons, EPSP shapes are similar, and heteronymous EPSPs are usually smaller than their corresponding homonymous EPSP. In addition, in both macaque and cat, homonymous EPSP amplitude is positively correlated with
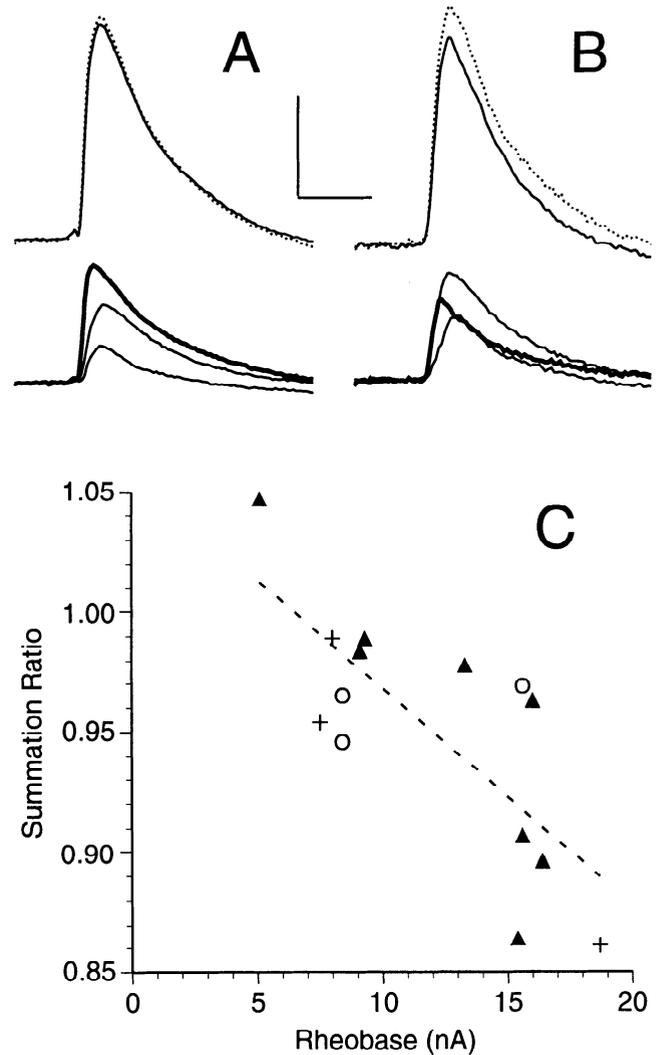

FIG. 4. Examples of spatial summation of EPSPs evoked by stimulation of MG, LG, and SOL nerves individually (bottom traces) or simultaneously (——, top traces) in a MG motoneuron (A) and a LG motoneuron (B). Bottom traces: homonymous EPSPs are shown by thick lines, and the heteronymous EPSPs are shown by thin lines (heteronymous EPSP amplitude from SOL greater than that from LG in A; heteronymous EPSP amplitude from MG greater than that from SOL in B). The dashed line in the top traces shows the algebraic sum of the 3 individual EPSPs shown below. Calibration: horizontal, 5 ms; vertical, 1.6 mV in A and 1 mV in B. (C) Rheobase of MG (o), LG (▲), and SOL (+) motoneurons varies inversely with summation ratio (i.e., the ratio of the amplitude of the EPSP elicited by simultaneous stimulation of MG, LG, and SOL nerves to the amplitude of the algebraic sum of the EPSPs elicited by stimulation of these nerves individually). The dashed line shows the relationship predicted by linear regression of the summation ratio on rheobase ($r^2 = 0.57$, $P < 0.01$).

TABLE 3. *Interspecies comparison of homonymous TS EPSP amplitude and ratios of mean heteronymous TS EPSP amplitude to mean heteronymous TS EPSP amplitude*

| Animal | Afferent | Motoneuron | | |
		MG	LG	SOL
Macaque*	MG	(2.7 mV)	0.41	0.08
	LG	0.43	(1.8 mV)	0.16
	SOL	0.44	0.48	(5.0 mV)
Baboon†	MG	(2.5 mV)	0.95	0.03
	LG	0.29	(1.5 mV)	0.22
	SOL	0.65	1.12	(5.7 mV)
Cat‡	MG	(7.1 mV)	1.00	0.41
	LG	0.17	(3.6 mV)	0.30
	SOL	0.24	0.62	(6.6 mV)

Numbers in parentheses are TS EPSP amplitudes. For abbreviations, see Table 1. *Present study; EPSP amplitudes adjusted for differences in resting potential from a nominal value of -70 mV according to the method of Hongo et al. (1984) to be directly comparable with their data. †Hongo et al. (1984). ‡Data of Eccles et al. (1957) as reported in Hongo et al. (1984).

input resistance and EPSPs evoked from different TS nerves sum in a nearly linear fashion. Human data, although limited and indirect, are consistent with the qualitative pattern described above of strong homonymous and weaker heteronymous EPSPs in TS motoneurons (Mao et al. 1984; Miles et al. 1989; Pierrot-Deseilligny et al. 1981). Estimates of EPSP risetimes in humans (Ashby and LaBelle 1977; Ashby and Zilm 1982; Miles et al. 1989) are longer than those reported here and in the other animal studies mentioned above. This difference could be due to a greater degree of temporal dispersion in afferent input as a result of the longer conduction distance in humans (Ashby and Zilm 1982) or to an overestimation of risetime due to the high background noise level in the human data (Mao et al. 1984).

Although TS EPSPs are qualitatively similar among the different species studied, several quantitative differences are apparent. Table 3 summarizes EPSP properties of the three TS motoneuron pools for macaque, baboon, and cat. In primates, SOL EPSPs are more than twice the size of pooled gastrocnemius EPSPs. This difference is less pronounced in the cat (e.g., SOL EPSPs are even smaller than MG EPSPs). The opposite pattern occurs with motoneuron properties, where the differences in the distributions of conduction velocity and input resistance between motoneurons innervating SOL and gastrocnemius muscles appear to be less pronounced in macaque than in cat (Carp 1992). This contrast suggests that postsynaptic factors related to these motoneuron properties (e.g., membrane resistivity and surface area) make only a modest contribution to determining EPSP size. This explanation is consistent with the finding that EPSP size depends only weakly on input resistance in macaques (Fig. 2) and in cats (Burke 1968).

Another difference between cat and the two nonhuman primate species is apparent in the comparison of heteronymous and homonymous EPSP amplitudes.[2] In macaque

and baboon, MG EPSPs in SOL motoneurons are relatively small compared with their homonymous EPSPs (ratios of mean heteronymous to mean homonymous EPSP amplitudes = 0.08 and 0.03, respectively), while SOL EPSPs in MG motoneurons are relatively large (ratios = 0.44 and 0.65, respectively). In cat, MG EPSPs in SOL motoneurons are relatively large (ratio = 0.41), and are larger than SOL EPSPs in MG motoneurons (ratio = 0.24). Because homonymous and heteronymous EPSPs are being compared in the same motoneuron, it is difficult to envision how this difference could result from an interspecies difference in intrinsic motoneuron properties. These interspecies differences probably reflect differences in presynaptic factors, such as synaptic density or distribution of synaptic input along the somatodendritic axis (Lev-Tov et al. 1983; Rall et al. 1967). A difference in distribution seems less likely, because homonymous EPSP risetimes and halfwidths of TS motoneurons are similar in macaque (present data) and cat (Burke 1968; Eccles et al. 1957). However, this inference can only be regarded as tentative, since interpretation of variations in the shape of composite EPSPs is limited by the confounding effects of temporal and spatial dispersion of afferent input (Walmsley and Stuklis 1989).

The differences in homonymous and heteronymous projections among species is potentially relevant to the evolution of locomotor patterns (Pierrot-Deseilligny et al. 1983; Vilensky 1989). SOL motoneurons in humans receive little or no excitatory heteronymous inputs from MG afferents (Bouaziz et al. 1975; Gritti and Schieppati 1989; Mao et al. 1984; Pierrot-Deseilligny et al. 1981). Thus the projection frequency of MG afferents to SOL motoneurons is greatest in cats, less in nonhuman primates, and least in humans. As noted above, the pattern of heteronymous inputs to SOL motoneurons in macaque is most similar to baboon. That this and other EPSP properties (see above) are shared by these two primate species are consistent with the marked similarity in footfall and electromyographic patterns during walking in baboon and macaque (Ishida et al. 1985; Kimura 1985). However, not all interspecies EPSP differences are consistent with a simple dichotomy between nonhuman primate and cat. The range of heteronymous relative to homonymous EPSP sizes is broad in cat and baboon and more limited in macaque. For example, in cat and baboon, MG nerve stimulation elicits heteronymous EPSPs in LG motoneurons that are about the same size as their homonymous EPSPs, while LG nerve stimulation elicits heteronymous EPSPs in MG motoneurons that are less than one-third of the size of their corresponding homonymous EPSPs. In contrast, in macaque, there is no difference in reciprocal heteronymous EPSPs between MG and LG motoneurons. Other patterns reflect differences between baboon and the other two species. For example, heteronymous SOL and LG EPSPs in MG motoneurons are of roughly equal size (relative to the homonymous EPSP) in

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[2] These data are presented in Table 3 as the ratio of the mean heteronymous to mean homonymous EPSP amplitudes, as opposed to the mean ratio of heteronymous to homonymous EPSP amplitudes, as in Table 2. In

addition, EPSP amplitudes have been adjusted for differences in EPSP size due to differences in driving potential by scaling the EPSP amplitude to the expected value for a nominal resting potential of -70 mV, assuming a reversal potential of 0 mV (Hongo et al. 1984). These steps have been taken to permit direct comparisons between the present data and those presented in Hongo et al. (1984) for baboon and cat.

both cat and macaque, while a more than two-fold difference is present in baboon. In sum, no consistent pattern of relationships in EPSP properties among these species (i.e., 1 species vs. the other 2) is apparent. Thus EPSP characteristics of each species probably reflect adaptations unique to that species.

On average, homonymous and heteronymous inputs to TS motoneurons summate in a nearly linear fashion. On a cell-by-cell basis, the magnitude of deviation from linearity of spatial summation of EPSPs varied inversely with rheobase, an index of motoneuron excitability by current injection. Highly linear spatial summation would be expected to enhance a motoneuron's ability to reach its voltage threshold for action-potential discharge. However, there is no clear reason to predict a priori that the degree of spatial summation would be causally related to a measurement of a motoneuron's current threshold for action-potential discharge. The co-variation of these phenomena probably reflects a joint dependence on some third factor relevant to motoneuron excitability and/or recruitment.

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