Crossed Reflexes of Cutaneous Origin

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ABSTRACT

PERL, EDWARD R. (State U. New York Coll. Med., Syracuse, N. Y.) Crossed reflexes of cutaneous origin. Am. J. Physiol. 188(3): 609-615. 1957.—Changes in excitability of spinal motorneurons produced by a volley of impulses in cutaneous nerves of the contralateral hindleg were studied in cats acutely made spinal or decerebrate. Motorneuron excitability was determined by measuring changes in electrical activity recorded from ventral roots or muscle nerves. Depending upon the size of fibers fired, at least two different effects were produced by synchronous impulses in crossed cutaneous nerves. When the cutaneous nerve activity was confined to the low threshold, rapidly conducting fibers, 14-6 μ in diameter, crossed knee and ankle flexor motorneurons were facilitated after a central latency of some 3 msec., and on occasion discharged. In several instances crossed extensor motorneurons were depressed during the course of flexor facilitation. When the cutaneous nerve activity involved the smaller (6-2 μ) myelinated fibers as well, prolonged inhibition of the crossed flexor motorneurons followed the initial facilitation and the crossed extensor motorneurons were facilitated, after a delay of 6-30 msec., for periods up to 300 msec.

Much of the recent work on the functional organization of the spinal cord has been devoted to the relation between activity of a specific sense organ or its afferent fiber and the subsequent change in ipsilateral motorneuron activity. Information of a similar type on the afferents capable of provoking the bilateral or crossed responses, known to occur in spinal animals, would make it possible to better understand the manner in which they and the ipsilateral reflexes are tied into integrated patterns. In preliminary experiments, undertaken with this objective in mind, it was noted that a single shock to a peripheral nerve containing cutaneous fibers evoked a discharge in contralateral ventral roots which was short in latency (5 msec.) and brief in duration (5-10 msec.). These features were in contrast to properties of the one well known crossed reflex of cutaneous origin, the crossed extensor response. The crossed extensor reflex is characteristically long in latency (20 msec. or more), slow to develop, and of long duration when evoked by single shocks or repetitive stimuli (1, 2). This paper presents an analysis of the short-latency crossed activity. Experiments were designed to determine the motorneurons contributing to the discharge, the afferent fibers evoking it, and the distinction of these afferent fibers from those responsible for crossed extension. The ventral root discharge itself was studied by recording the electrical activity from ventral roots or muscle nerves discharged in response to a volley of impulses in a contralateral nerve; however, a more useful tool proved to be the effects produced by an afferent volley in a contralateral nerve on the electrical signs of an ipsilateral reflex.

PROCEDURE

The majority of experiments were performed on cats acutely made spinal (transsection of the spinal cord at C1 and occlusion of the carotid and vertebral arteries) under ether anesthesia and maintained thereafter on artificial respiration with anesthesia discontinued. In some instances acute decerebrate animals were used.

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In all cases, 3–6 hours elapsed between the cessation of ether anesthesia and the observations.

Appropriate peripheral nerves and spinal roots supplying the hindleg were dissected out for recording or stimulation. All of the branches of the sciatic nerve were ordinarily cut and in many instances the femoral nerves and a number of ventral roots (L4, L5, S1, S2) were also divided. In the most responsive preparations even extensive denervations were insufficient to prevent reflex contractions of muscles of the hip or spine induced by strong stimulation of the peripheral nerves.

To reduce complication of the results by afferent stimulation produced by these contractions, a number of the animals were fully paralyzed by injections of gallamine triethiodide (Flaxedil), repeated as necessary. To reduce complication of the results by afferent stimulation produced by these contractions, a number of the animals were fully paralyzed by injections of gallamine triethiodide (Flaxedil), repeated as necessary. This drug, though noted to slightly depress both mono-synaptic and polysynaptic segmental reflexes in some animals, did not significantly change the pattern of crossed effects established prior to its injection or obtained after the most extensive denervations. The exposed nerves and spinal cord were covered with warm mineral oil, saturated with 92% O2 and 8% CO2. The rectal temperature of the preparations was maintained between 36° and 39.5°C by external heat. Recording and stimulating electrodes for nerves or roots were pairs of silver wires spaced from 0.5 to 1 cm. In a few instances potentials were recorded from the dorsal aspect of the spinal cord, between a silver wire placed at the entrance of the dorsal root under study and a clip on a nearby vertebral body or cut skin. The stimuli employed were 0.05–0.1 msec. pulses delivered over isolating transformers with the cathode centrally placed. Independent shocks could be delivered to two sites and the interval between them controlled over a wide range by delay circuits. Stimuli were ordinarily repeated once every 2 seconds. The recorded activity was amplified, displayed on an oscilloscope (bandpass of system 0.8 cps to 10,000 cps) and photographed.

At least 10 consecutive observations for a given set of conditions were photographed. In those experiments in which reflexes with an afferent source and efferent effect in one leg were conditioned by nerve stimuli applied to the contralateral leg, the usual method was to alternate a control (no contralateral stimulation) and a test situation. The test results were compared only with the bracketing controls. Mean values obtained from 10–50 such paired observations were then used to judge the effects produced.

RESULTS

Activity in Crossed Ventral Roots Following Nerve Stimulation. The type of discharge recorded from ventral roots following a single shock to a contralateral nerve is shown in figure 1. In excitable preparations (those that exhibited brisk reflexes during dissection) it was usually possible to record crossed ventral root activity following stimulation of either cutaneous or mixed nerves. The latency of the discharge, exclusive of conduction time to and from the spinal cord, varied from 3 to 5 msec., and the duration from 4 to 10 msec. It can be seen in figure 1 that the waveform was irregular and variable. Observations on this directly evoked activity also indicated that it could be elicited by stimulation of the lowest threshold fibers from a number of cutaneous nerves supplying widely different skin areas of the hindlimb (posterior femoral cutaneous, sural, superficial peroneal), but not from purely muscle nerves; i.e., those supplying the hamstring or gastrocnemius muscles.

A similar discharge could be evoked by stimulation of dorsal roots. As is illustrated in figure 2, a volley in one dorsal root gave rise to short-latency activity in the crossed ventral roots above and below as well as in the stimulated segment. By stimulating a contralateral cutaneous nerve or dorsal root and then sampling the reflex discharge produced in a number of muscle nerves, it was possible to demonstrate that this crossed discharge in ventral root fibers was distributed to hindlimb muscles subserving physiological flexion (flexion of the knee, dorsiflexion of the ankle). The responses obtained in such an experiment are depicted in figure 3. Stimulation of the dorsal roots of segments lumbar 6, 7 or sacral I evoked a discharge in the nerves supplying the semitendinosus (ST), the long head of the biceps femoris (BF), and the tibialis anterior (TA) muscles and the remainder of the deep peroneal nerve (DP). No such discharge was present in the nerves to extensor muscles: the nerves to the two heads of the gastrocnemius (MG and LG), the remainder of the tibial nerve (T) or to the middle branch of the femoral (F) supplying the quadriceps. In a few instances afferent volleys in cutaneous nerves produced...
by strong shocks were found to evoke activity in contralateral hindleg extensors as well, but both the latency (15-30 msec.) and duration of the responses were considerably longer than for the discharge in nerves to flexor muscles.

**Effects of Cutaneous Nerve Stimulation on Contralateral Reflexes.** Discharge of motorneurons in response to a stimulus can only give evidence of excitatory processes which reach the threshold level and inhibitory or subthreshold excitatory effects may be hidden (3, 4). At the onset of this study it was found that the short-latency crossed activity in a ventral root could be made to coincide in time with a monosynaptic reflex evoked from an extensor muscle nerve (gastrocnemius) without a marked change in the size of the monosynaptic reflex discharge. Under the conditions of the present experiments the motorneurons forming a monosynaptic reflex are known to be those supplying the muscle from which the afferent leg originates (5). Therefore the absence of marked interaction between the two forms of ventral root discharge suggested that the motorneurons contributing to the crossed discharge and those whose activity formed the monosynaptic discharge to the extensor muscle were excited independently. As might be expected, the findings were different when the monosynaptic reflex was evoked from a flexor muscle nerve. By conditioning the reflex discharge destined for a flexor muscle with a stimulus to a contralateral cutaneous nerve it was possible to ascertain the time course of the excitatory effect and also to demonstrate a later inhibition of the type associated with the crossed extensor reflex (1, 2).

Figure 4 exemplifies the resultant change in the size of a flexor monosynaptic reflex (semitendinosus) when preceded at various intervals by two different volleys in a contralateral cutaneous nerve (posterior femoral cutaneous), volleys which in themselves did not evoke appreciable crossed ventral root activity. The open circles represent the amplitude of flexor monosynaptic responses when conditioned by a stimulus to the contralateral cutaneous nerve sufficient to excite most of the lower threshold, more rapidly conducting fibers. A monitor of the volley, the dorsal cord potential recorded from the side of the cutaneous nerve, is shown in the upper right corner of figure 4. This volley facilitated the crossed flexor motorneurons for some 10 msec.; the effect began after 3 msec.
INTERVAL BETWEEN STIMULI (msec)
Fig. 4. Effects of volleys in the left posterior femoral cutaneous nerve on the size of a monosynaptic reflex evoked from the right semitendinosus nerve and recorded from the right sacral-1 ventral root. Interval between the stimuli applied to the conditioning cutaneous and crossed muscle nerve is indicated on the abscissa. In this and figs. 5, 7 and 8: weak conditioning stimulus—open circles, strong conditioning stimulus—filled circles. Dorsal cord potentials (left sacral-1) evoked by each of the two conditioning stimuli (left posterior femoral cutaneous nerve) are shown in the upper right. Spinal cat; rectal temperature—38°C (exp. SP-31).

Fig. 5. Effect of volleys in the right tibial nerve on the size (area) of the polysynaptic reflex discharge evoked from the left peroneal nerve and recorded from the left semitendinosus nerve. Reflex responses evoked in the right peroneal nerve by each of the two conditioning stimuli (right tibial nerve) are shown in the upper right. Decerebrate cat, rectal temperature—36°C (exp. SP-9).

and reached a peak 5 msec. later. The facilitation corresponds quite well in time with the crossed discharge described above. Following the facilitatory effect a depression of questionable significance can be seen. The depression (or inhibition) became more evident without a significant increase of the facilitatory effect (fig. 4, solid circles), when the shock to the cutaneous nerve was increased so as to activate more of the higher threshold fibers. A number of experiments showed that facilitation of crossed flexors was elicited by a volley containing the most rapidly conducting fibers of cutaneous nerves and that a period of inhibition lasting up to several hundred milliseconds followed if the stimulus evoked appreciable activity in fibers conducting between 40 and 100 m/sec. In contrast, when the conditioning stimuli were applied to muscle nerves generalized crossed flexor facilitation could not be demonstrated.

McCouch, Snape and Stetwurt (8) pointed out that the pattern of crossed responses evoked by hindleg skin stimulation in acute spinal animals changed, during recovery from spinal shock, from a bilateral flexor reaction to ipsilateral flexion and contralateral extension. To ascertain whether the crossed flexor activity just described was a peculiar phenomenon associated with spinal shock, some of the experiments were repeated on decerebrate preparations. Figure 5 summarizes an experiment on a decerebrate animal which showed that the effects on flexor motorneurons described above could be reproduced using a polysynaptic reflex discharge for the test. A flexor reflex (polysynaptic), evoked by stimulation of the common peroneal nerve and recorded from the muscle nerve of the ipsilateral semitendinosus, was conditioned by stimulating the contralateral tibial nerve. The conditioning tibial nerve volley was monitored by recording from the peroneal nerve of the same side (fig. 5, upper right corner). A weak stimulus to the tibial nerve (open circles), only sufficient to evoke a short-latency reflex in the companion peroneal nerve, resulted in a facilitation of the crossed flexor reflex similar to that seen in figure 4. A stronger stimulus to the tibial nerve (open circles) only sufficed to evoke a short-latency reflex in the companion peroneal nerve, resulted in a facilitation of the crossed flexor reflex similar to that seen in figure 4. A stronger stimulus (+SP-9) to the tibial nerve (open circles) did not cause a marked change in the facilitatory effect but did result in a subsequent depression of a marked degree. The tibial nerve volley which produced the pattern of facilitation and subsequent depression evoked a larger and more prolonged discharge in the monitoring (ipsilateral) peroneal nerve than the weaker volley, corresponding to the type of response associated with activity in both large and small myelinated fibers (5). It is reasonable to con-
clude from these results: a) that certain of lower threshold, more rapidly conducting and therefore larger myelinated fibers of cutaneous nerves are responsible for a short lasting facilitatory effect on the contralateral flexor motorneurons; b) that a prolonged inhibition of crossed flexors is related to activity in smaller myelinated fibers; and c) that these findings are not dependent upon spinal shock.

Volleys in cutaneous nerves could be shown to provoke two general types of effects on contralateral extensor monosynaptic reflexes with sufficient regularity to allow analysis. When the conditioning volley was limited to fibers conducting above 40 m/sec., the effect on the reflex destined for an extensor in the crossed leg was small. As has been mentioned, the short-latency crossed ventral root activity evoked by such a volley and the extensor monosynaptic reflex could frequently be made to coincide with no great change evident in the size of the monosynaptic discharge. On the other hand, when the effects on the monosynaptic reflex, particularly that evoked from the triceps surae, were carefully checked at stimulus intervals which would result in facilitation of flexor motorneurons (5-15 msec.), a slight inhibition of the extensor reflex was found in several experiments. When the contralateral conditioning volley also included some smaller fibers the inhibition was followed by facilitation. An experiment illustrating the relation of these two effects for gastrocnemius motorneurons is shown in figure 6. Figures 7 and 8 give two more examples of the crossed extensor facilitation evoked by volleys in cutaneous nerves containing smaller myelinated elements (filled circles). In both instances a weaker stimulus, sufficient to activate fibers conducting above 40 m/sec. but few smaller fibers (open circles), produced little or no extensor facilitation compared with that found when more of the small fibers were stimulated. The stronger stimulus caused an increase in extensor motorneuron excitability reaching a peak between 20 and 30 msec. after the contralateral shock (figs. 7 and 8) as contrasted to 8 msec. (fig. 4) for the flexor facilitation produced by the larger afferent fibers. As was the case for the flexor inhibition, the facilitation of knee and ankle extensors by a single volley in myelinated cutaneous afferents lasted for surprisingly long periods of time: 70–300 msec. The time relations of this crossed extensor facilitation are comparable to those described by Matthes and Ruch (2) for myographic evidence of crossed extension evoked by single shocks in chronic spinal cats, giving support to the conclusion that the facilitation was associated with the crossed extensor reflex. When the powerful extensor facilitation produced by a single volley in a contralateral cutaneous nerve is considered in light of the difficulty of
Fig. 8. Effect of volleys in the left sural nerve on the size of a monosynaptic reflex evoked by stimulation of the right dorsal root, lumbar-6, and recorded from the right quadriceps nerve. Reflex discharges evoked in the left sacral-1 ventral root by each of the two conditioning stimuli (left sural nerve) are shown in the upper right (note: stimulus to the sural nerve was delivered before the beginning of the oscilloscope trace used to record the left ventral root activity). Spinal cat, paralyzed by Flaxedil; rectal temperature—36°C (exp. SP-21).

directly recording an actual discharge in whole extensor muscle nerves (confirming the early observations of Forbes and Cattell, 9) it suggests: a) that many motoneurons were subliminally excited, and b) that those motoneurons which actually were fired, discharged in an asynchronous manner.

**DISCUSSION**

In the experiments described above, it was possible to relate afferent fiber diameter to contralateral reflex activity by examining the effects of a single afferent volley on crossed motoneurons. A similar relation for the ipsilateral limb is well known and allows comparison of the results for prediction of bilateral reflex connections. Unfortunately extension of the analysis to the long spinal reflexes is not possible, because data are available only for the foreleg to hindleg pathway (4).

Lloyd (5) demonstrated that a volley in the large cutaneous fibers of a hindleg nerve evokes a generalized facilitation and discharge of motoneurons supplying the knee and ankle flexors of the same leg. The present study indicates that impulses in some of the same group of fibers, those between 14 and 6 µ in diameter, also facilitate flexor motoneurons of the opposite leg with approximately the same latency. A bilateral facilitatory connection to flexor motoneurons has been indicated by other studies. Dusser de Barenne and Koskoff (10, 11) reported a bilateral hindleg ‘flexor rigidity’ in spinal cats which was dependent upon both cutaneous and proprioceptive afferents. There is a notable difference, however, between the elements contributing to the flexor posture described by these authors and those which are concerned with the generalized flexor facilitation are reported here. Cutaneous afferents augmenting ‘flexor rigidity’ were said to arise from the ventral aspects of the thigh (10), while crossed flexor facilitation was produced in the current study by volleys initiated in cutaneous nerves of the dorsal surface of the limb. In the study by McCouch et al. (8) electrical stimulation of hindlimb cutaneous afferents in spinal cats initially evoked bilateral flexion of the hindlegs. A variable time thereafter, the response changed to ipsilateral flexion and crossed extension. If one assumes that the internuncial paths mediating crossed flexion and crossed extension are affected to different degrees by spinal transection, the present findings may offer an explanation for the change in the crossed reflex pattern noted by these workers. The stimuli employed may have excited the equivalent of both large and small afferent fibers with the effects produced by the former and then the latter dominating the contralateral motor pathways. Moreover, this latter suggestion may be used to help account for the relatively long latency of the crossed extensor reflex (1, 2). A stimulus eliciting crossed extension would be likely to activate elements capable of facilitating crossed flexors and inhibiting crossed extensors, delaying the rise of excitability in the extensor motoneurons.

It has been observed that excitation of the smaller myelinated fibers of cutaneous nerve (6 - 24 µ) in addition to the larger ones evokes a more prolonged discharge to ipsilateral flexors (9). This type of flexor motoneuron activity has been correlated with withdrawal of the leg (12). However, Hagbarth (13) has shown that the ipsilateral reflex evoked by small cutaneous afferents may be more complex, since in his studies the muscle underlying the skin area stimulated was facilitated. Localization could not be demonstrated for the crossed extensor facilitation described in the present report.
Thus, while activity in small cutaneous afferent fibers may have variable results in one hindleg, the crossed effect is likely to be extension.

A further consideration in evaluating the reflex effects described is the modality of cutaneous sense represented by volleys in various sized fibers. Without knowing the modality concerned, the relation between activity in the large myelinated fibers to bilateral flexor facilitation and inhibition of antigravity muscles is difficult to understand. There is considerable evidence that forms of touch and pressure sense are carried by large myelinated afferents of cutaneous nerve (14, 15). From this it might be concluded that the bilateral flexor effect is not protective in function. However, it has recently been reported (15) that certain large cutaneous fibers of the cat could be discharged only by ‘noxious’ stimulation and this observation would make it possible to consider that the large fiber connections have a protective significance. Correlation of modality, fiber size and crossed extension is less difficult. The role of some small myelinated fibers in the transmission of pain or noxious sense is well established (14, 15), and until further data are available, it may be assumed that the fibers mediating a painful sense facilitate crossed hindleg extensors. Therefore, facilitation of the contralateral hindlimb extensors by activity in small myelinated fibers of cutaneous nerves can be regarded as part of a protective reflex response in which one hindleg is removed from a noxious stimulus while the contralateral limb extends to support the body weight (17).

Finally, it is perhaps worthwhile to reemphasize a point Lloyd and McIntyre (4) made on reciprocal effects following nerve stimulation. Reciprocal innervation, in the Sherringtonian sense, demands that activity in the same afferents produce opposite results in opposing muscle groups (17). The crossed effects described in this paper did have opposite results on motorneurons supplying antagonistic muscles, but no direct evidence can be given that activity of one afferent fiber could produce the reciprocal responses.

REFERENCES