Electrophysiology of the Fetal Spinal Cord

II. *Interaction among peripheral inputs and recurrent inhibition*

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ABSTRACT Interactions of peripheral inputs to the motoneuron of the kitten fetus as young as 3 weeks prenatal were studied by reflex discharge from the ventral root as well as by recording from single motoneurons. Facilitation was found between two synergists in fetuses 1 to 2 weeks before birth. Intracellular recording showed that the facilitation could be explained by summation of excitatory postsynaptic potentials. Inhibition was found between antagonists in the fetuses 2 to 3 weeks before birth and was accompanied by inhibitory postsynaptic potentials. Recurrent inhibition was very powerful in the fetal spinal cord as shown by large motoneuron hyperpolarization by antidromic stimulation. Cells presumed to be "Renshaw cells" and which responded to both ortho- and antidromic stimulation with repetitive firing were shown in the 2 weeks prenatal fetus. These results lead to the conclusion that there is considerable effective synaptic connection of afferent collaterals already established by the later stage of intrauterine life and that this may be achieved independently of external stimuli.

INTRODUCTION

Malcolm (1953 and 1955) was the first to record the ventral root (VR) reflex in the neonatal kitten and to observe interaction of various peripheral inputs. In his series of papers, Skoglund (1960 *a*, *b*, *c*) concluded that: (*a*) inhibition is present in the newborn kitten and (*b*) facilitation appears considerably later than inhibition. His conclusions were partly supported by Arutyunyan (1961) and Wilson (1962).

No attempt has been made to study changes in synaptic organization

during prenatal development although this would offer important clues to the understanding of the processes of maturation of the central nervous system (CNS). In this paper the interaction of different afferent inputs in the kitten fetus was studied by observation of the VR discharge and by the recording of synaptic potentials from single motoneurons.

Antidromic stimulation of motoneurons gave a hyperpolarizing post-synaptic potential (R-IPSP). Recordings were also made from cells which responded with repetitive firing to both ortho- and antidromic stimulation. The latter were identified as the "Renshaw cells" (J. C. Eccles *et al.*, 1954; Frank and Fuortes, 1956 *a*; J. C. Eccles *et al.*, 1961 *b*) which receive their excitation from motoneuron axon collaterals and which inhibit directly the same or other motoneurons. It was concluded that there is a Renshaw feedback loop in the fetal spinal cord (Renshaw, 1946).

TECHNIQUE

As already described in a preceding paper (Naka, 1964) four nerves—two gastrocnemius nerves (GSs), tibial (TIB), and common peroneal (PER)—were dissected for peripheral stimulation. Facilitation was sought between two ipsilateral GSs and inhibition among different combinations of nerves. It was our experience that good dissection of the peripheral nerves and VRs was essential. Such a dissection could not be performed before 45 days' gestation (on a fetus of less than 30 gm). The technique for intracellular recording is described in a previous paper (Naka, 1964).

RESULTS

I. *Facilitation in the Kitten Fetus*

In Fig. 1, which is from a fetus of 57 ± 2 days' gestation, one shock was delivered to the medial gastrocnemius (GSM, conditioning) and another shock to the lateral gastrocnemius nerve (GSL, test) while activity was recorded from a VR. In A the interval between these two shocks was so adjusted that the maximal response was obtained. It can be seen from A through D that, as the interval between the test shock and conditioning shock was increased, the amplitude of the test response decreased (while the response from the conditioning shock remained unchanged). As the response shown in A was far larger than could be accounted for by summation of the two control responses (E and F), the augmentation of the reflex must be due to facilitation between two GSs. The possibility of stimulus escape was eliminated by comparing responses to shocks of different amplitudes.

To compare the time course of facilitation with that of an EPSP, an EPSP from a GS motoneuron was recorded from a fetus at term and its amplitude graphically normalized to match the peak of fifteen superimposed reflex responses (Fig. 2) taken at different conditioning-test intervals. There is fairly good agreement between the EPSP and the general profile of the re-

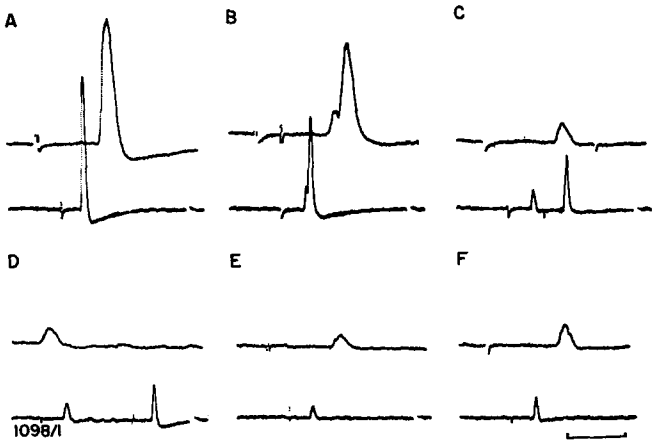

FIGURE 1. Facilitation of VR discharge from two GSs in a fetus of 57 ± 2 days' gestation. In A through D shocks of 20 volts (nominal) were delivered one each to GSL and GSM at increasing intervals. In A, shocks were spaced to get the maximal response, and were almost simultaneous. E and F are controls from shocks of the same intensity to GSL(E) and GSM(F). In all figures (except Fig. 2) upper trace is a fast sweep, and lower trace is a slow sweep taken simultaneously. In this figure and in Fig. 4 both traces are capacitatively coupled. In all other figures upper trace is capacitatively coupled and lower trace is direct coupled. Unless otherwise mentioned, horizontal bar is 10 msec. for upper and 30 msec. for lower trace in this and following records.

flex responses. This seems to indicate that the facilitation observed was due to summation of EPSPs as in the case of the adult cat (J. C. Eccles, 1953, 1957). This conclusion presumably implies that dorsal root (DR) fibers from muscle receptors had already made functional connection with the motoneurons of synergist muscles.

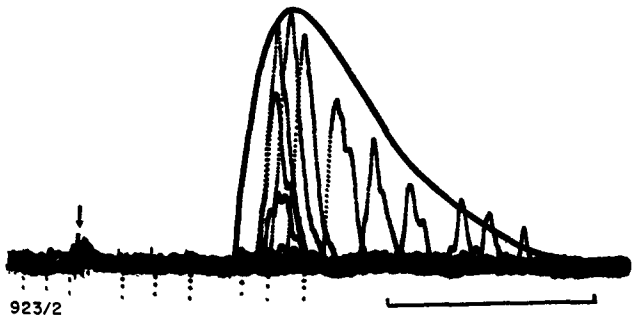

FIGURE 2. Comparison between EPSP and facilitation of the VR discharge in the same fetus at term. About fifteen traces of VR discharge obtained with varying intervals between conditioning (to GSM) and test shock (to GSL) were superimposed to get time course of facilitation. Arrow shows the artifact of conditioning shock to GSM. Traces were taken at one per sec. EPSP graphically normalized to match the height of the maximal VR response. Horizontal bar is 10 msec.

Results from the study of the VR reflex can be confirmed by intracellular recording from a motoneuron. Records in Fig. 3 obtained from a fetus[1] of 59 ± 1 days' gestation illustrate the summation of synaptic potential. It may be concluded that this cell shows a convergence of excitatory fibers from the two GSs. It is interesting that the EPSP from GSL in Fig. 3C showed much faster return to the base line than the EPSP from the same nerve in Fig. 3B. It is also worthy of note here that these EPSPs were followed by a long lasting phase of hyperpolarization which is more prominent in younger fetuses (Fig. 12, Naka, 1964).

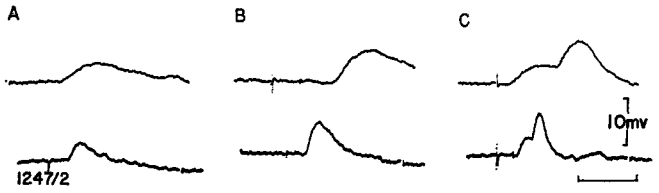

FIGURE 3. Summation of EPSPs in a fetus[1] of 59 ± 1 days' gestation. Stimuli were delivered to GSM (A) and to GSL (B), each giving rise to an EPSP. In C, two shocks were given, one to GSM and the other to GSL and summation of two EPSPs was obtained

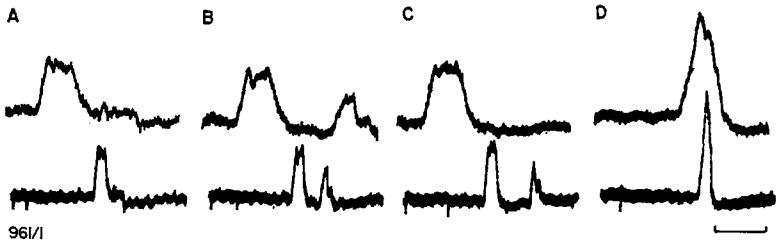

FIGURE 4. Inhibition between PER and TIB in a fetus of 48 ± 2 days' gestation. Conditioning shock to PER which gave rise to the first reflex discharge was followed by a test shock to TIB at increasing intervals (A through C). The test response from TIB increased in amplitude as the interval increased. D is a control response from test shock to TIB alone.

II. *Inhibition in the Kitten Fetus*

Inhibition between TIB and GS, PER and GS, or TIB and PER was observed as routine whenever reflex discharges were recorded from stimulation of these afferents, indicating the existence of powerful inhibitory interaction in the spinal cord of the kitten fetus. Inhibition between TIB and PER could be shown even in a fetus of 48 ± 2 days' gestation (Fig. 4). In this record TIB served as a conditioning and PER as a test nerve and the interval between the two shocks was increased from A through C. In A, in which the test shock followed the conditioning shock at an interval of 5 msec., the reflex

[1] The records in Figs. 3, 5, and 6 were all obtained from the same cell.

from PER was almost completely inhibited. A test shock given 20 msec. after the conditioning shock gave rise to a reflex discharge of about 50 per cent of the control in D.

In the spinal cord of the adult cat inhibition can be divided into two types, (*a*) inhibition due to a conductance change leading to hyperpolarization (J. C. Eccles, 1953, 1957) and (*b*) remote or presynaptic inhibition involving different processes (Frank and Fuortes, 1957; Frank, 1959; J. C. Eccles *et al.*, 1961 *c*). Recently Eccles and Willis (1963) reported that the prolonged depression of monosynaptic reflexes in the kitten found by Malcolm (1955) and

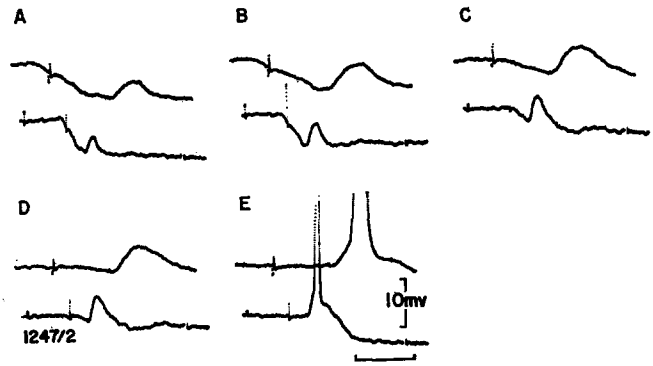

FIGURE 5. Interaction of EPSP from GSL and IPSP from TIB in a fetus[1] of 59 ± 1 days' gestation. Intensity of the shock to GSL which gave rise to EPSP was kept unchanged while the stimulus to TIB which gave rise to IPSP was progressively decreased from A through E. Note smaller EPSP with faster decay at the bottom of IPSP. In E, the EPSP produced a spike potential. Amplitude of spike potential was about 40 mv.

Skoglund (1960 *b*) is a form of presynaptic inhibition due in part to an interaction of impulses from a large DR reflex. Evidence was obtained in the present study to suggest that some of the inhibition seen was due to the transient hyperpolarization of the motoneuron membrane, or IPSP, as described in the case of the adult cell.

One example of inhibitory action of transient hyperpolarization (Fig. 5) was obtained from a fetus[1] of 59 ± 1 days' gestation. In this record shocks were delivered to GSL which gave rise to an EPSP and to TIB which gave rise to an IPSP. The intensity of the shock to GSL was kept constant while the intensity of the shock to TIB was decreased from A through E. As seen from the records the amplitude of the IPSP from TIB decreased with decrease of shock intensity while the amplitude of the EPSP from GSL steadily increased. In E, the IPSP from TIB decreased to such an extent that it could not keep the cell from firing a spike potential. These observations indicate that in the fetal motoneuron, as in the adult, inhibition may be due to a transient conductance change leading to a hyperpolarization. As might be expected the

EPSP falling at the peak of IPSP had smaller amplitude as well as a faster decay.

III. *Interaction among Several Inputs*

So far the description has been confined to interactions between two afferent inputs. However, with intracellular electrodes it was possible to see the effects of several afferent inputs on a motoneuron using postsynaptic potentials as an indication.

One example of convergence of several afferents on a single motoneuron

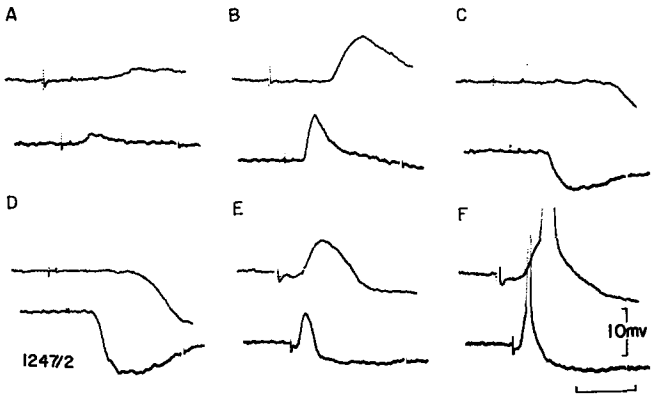

FIGURE 6. Interaction of several peripheral inputs in a fetus[1] of 59 ± 1 days' gestation. A and B were EPSP by GSM and GSL, respectively, and C and D were IPSP by PER and TIB, respectively. E and F were EPSP and spike potential by DR stimulation. Amplitude of spike potential was about 40 mv.

is shown in Fig. 6 which was obtained from a fetus[1] of 59 ± 1 days' gestation. The EPSP from GSM was only a few millivolts (A) while GSL gave rise to an EPSP of about 10 mv (B). In this cell the EPSP from GSL produced a spike potential of more than 40 mv (not shown). PER and TIB gave rise to powerful IPSPs of 7 mv in C and 13 mv in D. E was from DR stimulation and the EPSP showed much faster return to the base line than the EPSP in A or B, probably the result of monosynaptic activation. It was not uncommon for the EPSP due to DR stimulation to have a faster decay which eventually turned into large and long lasting hyperpolarization in the fetus 1 to 2 weeks prenatal. Two reasons can be suggested for this: First, the DR stimulation resulted in a more synchronized activation of the motoneuron, and second, the DR stimulation included inhibitory pathways.

Similar convergence of several peripheral inputs could be shown in a fetus of 52 ± 1 days' gestation, as is shown in Fig. 7. A shock to two combined GSs yielded an EPSP of about 7 mv (A). Though the rise time of the EPSP was very slow (about 10 msec.) the smooth rising and falling phases suggest

that the EPSP might have been activated monosynaptically. TIB (B) and PER (C) gave rise to rather large IPSPs of 5 to 10 mv. In D and E a shock was given to the VR which resulted in a recurrent inhibitory postsynaptic potential (R-IPSP) and a spike potential. The hump on the base of the falling phase of the spike potential indicates the start of the R-IPSP.

IV. *Renshaw Cell Activity*

Spike potentials from a Renshaw cell which responded to both anti- and orthodromic stimulation were reported by J. C. Eccles *et al.* (1954), J. C. Eccles *et al.* (1961 *b*), and Frank and Fuortes (1956 *a*). Frank and Fuortes

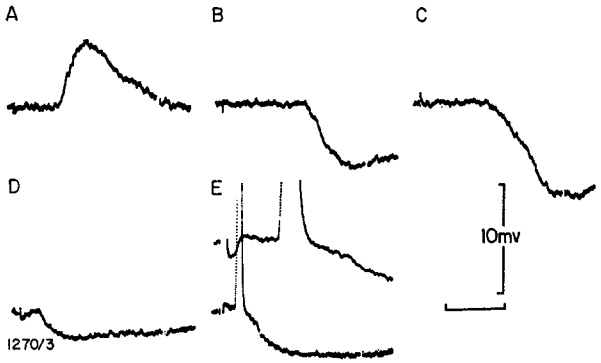

FIGURE 7. Interactions of several peripheral inputs in a fetus of 52 ± 1 days' gestation. A is an EPSP by GS. B and C are IPSPs by TIB and PER. D and E are R-IPSP and spike potential by antidromic shock. Horizontal bar is 30 msec. except for upper trace of E for which it is 10 msec.

first demonstrated direct connection between DR and Renshaw cells. In the present experiment a cell which could be fired repetitively by a single shock delivered to the DR and VR was classified as a Renshaw cell. Fast positive-negative spikes of less than 30 mv were usually recorded from cells in the vicinity of the motoneuron pool. The Renshaw cells were difficult to penetrate but no marked change in the firing pattern was observed even when the position of the electrode was slightly changed. The response thus obtained was quite stable for a considerable period of time.

In Fig. 8, which was from a fetus of 52 ± 1 days' gestation, a single shock was given once per second either to the VR or to the DR. Stimulation delivered to the VR (A through D) invariably evoked firing of the cell with practically no change in the firing pattern. However, the shock delivered to the DR (E through H) gave rise to quite a different pattern of response. The record in E obtained by the first of a train of repetitive stimuli gave rise to a train of nine spikes. Subsequent stimuli yielded fewer spikes: two in F and one in G and H.

As is apparent from the left column of Fig. 8, the Renshaw cell could follow stimulation at this frequency and the decrease in the frequency of firing by repetitive DR stimulation could be attributed to failure in activation of motoneurons by the orthodromic volleys. The marked decrease in the amplitude of the spike during repetitive firing by orthodromic shock seems to be due to intense depolarization of the cell.

In this paper it already has been shown that the fetal motoneuron receives various afferent inputs and it is also conceivable that an immature Renshaw cell receives inputs from several different afferents. One example of such con-

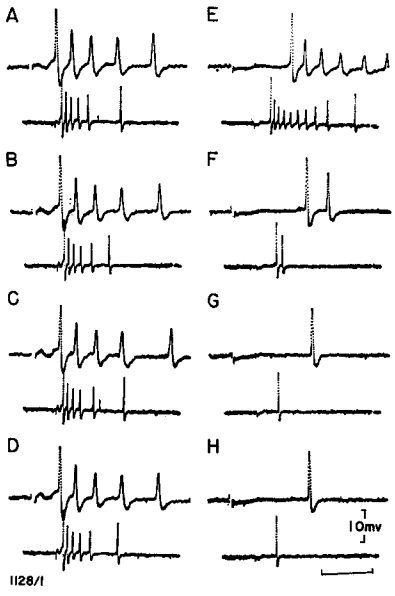

FIGURE 8. Response from a Renshaw cell in a fetus of 52 ± 1 days' gestation. In A through D shocks were delivered once per second to the VR while in E through H, shocks were delivered at the same frequency to the DR. Records were taken successively once per second.

vergence is shown in Fig. 9. This record was taken from a fetus of 59 ± 1 days' gestation. Shocks were delivered to four nerves: TIB, PER, and both GSs; all gave VR reflexes. This cell was seen to be a Renshaw cell by activation through VR shock (Fig. 9F) and it responded also to DR stimulation. It is clear from this record that at least two afferents, one from GSM and the other from GSL, could fire the Renshaw cell, probably through excitation of motoneurons. This cell was in the same region as the cell of Fig. 3. In that record it was shown that the motoneuron received afferent collaterals from both GSM and GSL. As the Renshaw cell is thought to receive excitatory inputs from several motoneurons, this finding seems reasonable. It is interesting to note that the spikes in this figure are of two types: large spikes of about 10 mv and smaller ones of about 5 mv. Furthermore, the large spike had a hump on its rising phase at an amplitude corresponding to the height of the small spikes. The second spike in D, which falls between the large and small

spikes in amplitude, showed a conspicuous hump on its rising phase. This suggests that the spikes from the Renshaw cell were composed of two components similar to the ones found in the immature motoneuron (Naka, 1964).

In a fetus of 44 ± 2 days' gestation similar cells were found which responded repetitively to a single shock to the whole cord. Increase in the intensity of stimulation was accompanied by an increase in the number of spikes fired. During repetitive firing the amplitude of the spike potential decreased and a hump appeared on the rising phase of the spike potential.

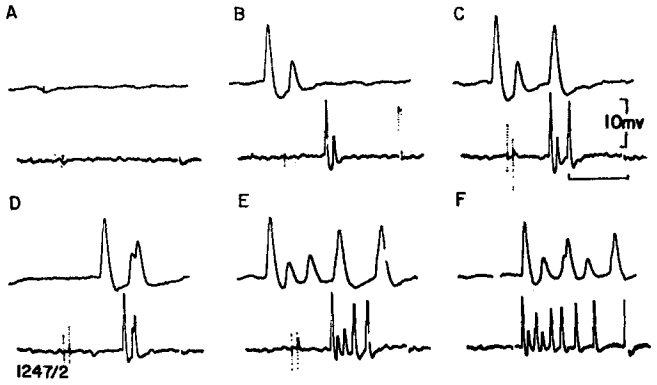

FIGURE 9. Activation of Renshaw cell from several peripheral inputs in a fetus of 59 ± 1 days' gestation. A from TIB (PER also gave no spike); B from one and C from two shocks to GSL. D from two shocks to GSM. E from two shocks, one to GSL and the other to GSM. F, by antidromic shock.

Though there was no conclusive evidence, the organization of the train of spikes suggests that these responses were recorded from a Renshaw cell.

V. *Antidromic Hyperpolarization of Fetal Motoneuron*

In the adult motoneuron, an antidromic shock which was subthreshold for initiation of a spike potential often produced a transient conductance change which resulted in a hyperpolarization, R-IPSP (J. C. Eccles *et al.*, 1954; J. C. Eccles *et al.*, 1961 *a*). This IPSP was shown to be instrumental in producing the antidromic inhibition first described by Renshaw (1941, 1946). In the fetal motoneuron it was possible to record hyperpolarization by an antidromic shock as early as 3 weeks prenatal. However, there are several factors which made interpretation of the results difficult: (*a*) Penetration of a cell usually resulted in damage or depression of the resting potential, especially in the fetus of less than 50 days' gestation. (The hyperpolarization due to antidromic shock was surprisingly resistant to deterioration of a cell and far outlasted the spike potential.) (*b*) Decrease of resting potential of less than 5 mv had a great effect on the amplitude of the hyperpolarization

produced by antidromic stimulation. This amount of change in the resting potential was usually difficult to distinguish from irregular shifts in DC recording level. These factors tend to augment the hyperpolarizing reaction and obscure whether the large amplitude of transient hyperpolarization was due to powerful recurrent inhibitory reaction or was partly due to deterioration of a cell.

Records shown in Fig. 10 obtained from a fetus of 59 ± 2 days' gestation

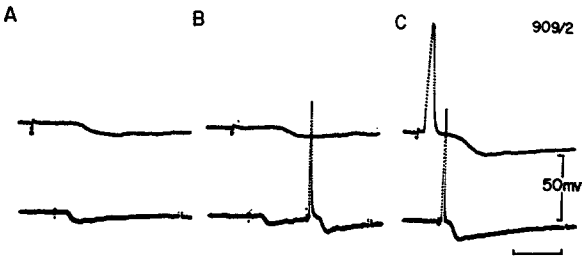

FIGURE 10. R-IPSP in a fetus of 59 ± 2 days' gestation. Shocks delivered to the VR gave rise to different degrees of R-IPSP. (See text for details.)

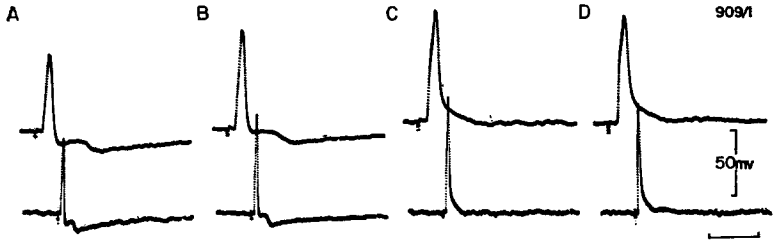

FIGURE 11. Effects on the afterpotential and R-IPSP of passing current through the electrode in a fetus of 59 ± 2 days' gestation. Current was depolarizing in A and hyperpolarizing in C and D. In B no current was passed. R-IPSP started about 5 msec. after termination of the spike potential in A and B.

illustrate the long lasting effect of antidromic inhibition which has already been noted in the kitten by several authors (Skoglund, 1960 *a*; Wilson, 1962). In A a shock to the VR which was subthreshold for antidromic invasion of the cell produced an R-IPSP. In B another shock which was strong enough to fire the cell antidromically followed 30 msec. after the first shock. In C one shock gave rise to both an antidromic spike and an R-IPSP which appeared about 5 msec. after termination of the spike potential. The R-IPSP was 10 mv in amplitude and it took about 60 msec. to return to the base line. In some cells, R-IPSP could inhibit antidromic invasion of the motoneuron from a shock delivered 50 to 60 msec. later. This illustrates powerful and long lasting recurrent inhibition in the fetal spinal cord.

In Fig. 11 which was from a fetus of 59 ± 2 days' gestation the effect of

the change in the membrane potential on IPSP was observed by passing current through the electrode by the method of Frank and Fuortes (1956 *b*). When depolarizing current passed through the electrode (A) the spike potential decreased in amplitude. This was followed by an immediate afterhyperpolarization of about 5 mv which was probably a transient return of the membrane potential toward the original resting level without current. The R-IPSP followed the afterhyperpolarization of the spike potential. Though the amplitude of the IPSP was smaller than the one in B the over-all amplitude of the hyperpolarization was greatly increased from 9 mv in B to 13 mv in A by the decrease in the membrane potential. With hyperpolarizing current (C and D) the spike potential increased in amplitude and the hump due to the "A-B" transfer appeared at a higher level relative to the new

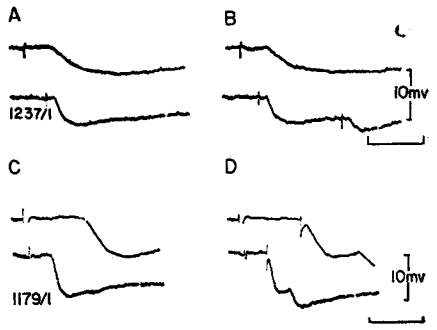

FIGURE 12. Comparison of R-IPSPs from fetuses within a week of term (A and B) and 44 ± 2 days' gestation (C and D). In A and C one shock, and in B and D two shocks were delivered to the VR.

base line. The R-IPSP disappeared in C and, though it is not clear in the figure, eventually reversed its polarity in D.

In Fig. 12, IPSPs from a fetus within a week of term and another fetus of 44 ± 2 days' gestation are compared. No marked difference could be found in the R-IPSPs from the fetuses though their gestation ages differed by about 2 weeks. R-IPSPs from both fetuses showed nearly the same slope and rise time. Though these records were selected, it was generally observed that the R-IPSP did not undergo any marked change during the late stage of gestation while, as shown in a previous paper (Naka, 1964), the EPSP increases remarkably during the late prenatal period.

DISCUSSION

I. *Excitation and Inhibition in the Fetal Spinal Cord*

In the adult spinal cord facilitation and inhibition among peripheral inputs have been thoroughly analyzed with intracellular electrodes and it is now well established that they are the result of interactions among EPSPs and IPSPs produced by various afferents (J. C. Eccles, 1953, 1957). Though the number of peripheral nerves dissected was limited to four and recordings

were unfavorable for precise measurements, results described above have revealed that essentially the same postsynaptic mechanisms are responsible for facilitation and inhibition among peripheral inputs in the fetus 3 weeks prenatal.

There is no reason why this conclusion cannot be extended to still younger fetuses in which it was shown behaviorally that there is interaction of reflexes. This requires a considerable amount of interconnection of afferent fibers to produce the various synaptic potentials.

According to the hypothesis of J. C. Eccles (1953, 1957) postsynaptic inhibition is mediated by a special interneuron in the case of orthodromic inhibition (J. C. Eccles *et al.*, 1956; J. C. Eccles *et al.*, 1960) and by the Renshaw cell in the case of antidromic inhibition (J. C. Eccles *et al.*, 1954). Though there is no direct evidence, it is quite possible that the Renshaw cell forms a feedback loop to produce antidromic or recurrent inhibition, in the fetal spinal cord as in the adult.

Generally speaking, results obtained in the present experiments could not resolve which of two processes, excitation or inhibition, appears first or which is more powerful in the fetal spinal cord. Within the scope of these results, *i.e.* as early as 3 weeks prenatal, no difference was found between the two reactions except that often the inhibitory response was larger in amplitude and was more stable. However, hyperpolarizations (HAP, IPSP, and R-IPSP) were augmented in deteriorating cells. Further study is needed to reach definite conclusions on this question.

II. *Comparison with Results Obtained from Neonatal Kittens*

Malcolm (1953 and 1955) who was the first to report on the reflex in the kitten found no inhibition at birth and he was supported by Arutyunyan (1961) who recorded "polysynaptic inhibition" in a 3 day old kitten and direct inhibition in a 4 day old kitten. Skoglund (1960 *a*), on the other hand, showed inhibition at birth as did Wilson (1962). R. M. Eccles *et al.* (1963) demonstrated that 3 weeks postnatal, motoneurons of kittens had properties and connections similar to those in adult cats. It should be noted, however, that there are considerable variations in the gestation periods of the cat which may range from 58 through 71 days (Scott *et al.*, 1957). It should also be taken into account that even fetuses or kittens from the same litter can show variation in their maturity as already described by Skoglund (1960 *b*). These authors did agree that facilitation developed later than inhibition and that it appeared 1 to 2 weeks postnatal (Malcolm, 1955; Skoglund, 1960 *a*). From this observation, Skoglund concluded that there was a postnatal development of the DR collaterals. There is fairly good agreement between the results obtained by Skoglund (1960 *a*) and Wilson (1962) and the results obtained in the present experiments on the presence of inhibition in the

immature spinal cord. However, the above-mentioned authors who recorded VR discharge from the kitten could not find any facilitation until 1 to 2 weeks postnatal. This is somewhat different from our conclusion that facilitation could be obtained in the young fetus with the VR discharge as well as by recording synaptic potentials from single cells. While there is no reason to doubt that pre- or postnatal development of the DR collaterals occurs, we conclude that a considerable amount of connection between the muscle and possibly cutaneous afferents (in the case of TIB or PER) and the motoneuron is already established at a fairly early stage of intrauterine life, including facilitatory, inhibitory, and recurrent inhibitory collaterals.

III. *Correlation with Results from Behavioral and Histological Studies*

Brown (1914–15) was the first to observe inhibition as well as the ipsilateral flexion reflex in a kitten fetus of 8 to 9 cm (which may correspond to a fetus of about 50 days' gestation). From these observations he concluded that the mechanisms for coordination develop during intrauterine life. In the hind leg of the kitten fetus, Coronios (1933) showed that extensor and flexor reflexes appeared at 28 to 29 days' gestation and ankle or knee flexion appeared at 38 days' gestation. Electrophysiological observations indicate that movements observed by behavioral studies were due to functional coordination of the nervous system produced by the same synaptic mechanisms as in adult cats.

Histological studies by Windle (1934) showed that appearance of the reflex could be closely correlated with formation of synaptic connections which could be either monosynaptic or polysynaptic. It is very interesting that a polysynaptic reflex arc appeared at the same time as the monosynaptic ones in view of the possibility that the inhibitory pathway may require a special interneuron. Presence of the R-IPSP also requires another interneuron, the Renshaw cell. Windle's (1934) observations suggest that there is no reason to suppose that the inhibitory reaction should appear later than the excitatory one simply because the former pathway may require an interneuron.

Windle (1940) observed that the normal fetus *in utero* was relatively quiescent and, in the cat, there was little spontaneous motor discharge because of the absence of afferent impulses. If this is the case, the functional development of the motoneuron and its connections with various afferent branches must be accomplished independently of external stimuli. Though it is certainly true that refinement of the various reflexes takes place after the animal is exposed to external stimuli, the fundamental mechanisms or interconnections of collaterals for coordination of nervous functions seem to develop during intrauterine life without extensive external stimulation.

IV. *General Conclusions*

Though the information obtained is only a fraction of what is needed to form a complete picture of prenatal development of the spinal cord, the following tentative conclusions can be drawn from this series of experiments:

1. No essential difference appears in the basic properties of the motoneuron or of synaptic potentials in the spinal cord of the adult and fetal cat.

2. Postsynaptically, interaction among peripheral inputs can be explained by interaction of PSPs as shown in the adult cat.

3. By the time intrauterine life is two-thirds completed some of the connections between afferents and the motoneuron are established including inhibitory and recurrent inhibitory pathways which may require an interneuron.

4. As far as these pathways are concerned the development during the rest of the pre- and postnatal periods produces a speeding up or increase in efficiency of synaptic transmission as well as an increase in the conduction velocity of axons (Hursh, 1939; Skoglund, 1960 *c*). This could be the result of further proliferation of the afferents and/or an increase in the efficiency of transmitter release. Myelination of axons would contribute to an increase in the conduction velocity and probably to a more synchronized afferent volley.

5. Our observation that as far as simple reflexes are concerned no difference could be found between the fetus and adult seems to support Windle's theory (1940) on the genesis of reflex behavior that "more complex reactions are formed by progressive neuronal integration of the less complicated activities."

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