FINAL REPORT
COO-1475-5

MASTER

RECEIVED BY DTIC OCT 9 1969

ATOMIC ENERGY COMMISSION GRANT

NO. AT (11-1) 1475

TECHNICAL PROGRESS REPORT

TITLE: The Effect of Ionizing Radiation on Recurrent Inhibition of
the Spinal Cord.

PRINCIPAL INVESTIGATOR: Charles D. Barnes, Ph.D., Associate Professor of
Neurophysiology, Indiana University, Bloomington,
Indiana, 47401

LEGAL NOTICE

This report was prepared as an account of Government sponsored work. Neither the United States, nor the Commission, nor any person acting on behalf of the Commission:

A. Makes any warranty or representation, expressed or implied, with respect to the accuracy, completeness, or usefulness of the information contained in this report, or that the use of any information, apparatus, method, or process disclosed in this report may not infringe privately owned rights; or

B. Assumes any liabilities with respect to the use of, or for damages resulting from the use of any information, apparatus, method, or process disclosed in this report.

As used in the above, "person acting on behalf of the Commission" includes any employee or contractor of the Commission, or employee of such contractor, to the extent that such employee or contractor of the Commission, or employee of such contractor prepares, disseminates, or provides access to, any information pursuant to his employment or contract with the Commission, or his employment with such contractor.

DISTRIBUTION OF THIS DOCUMENT IS UNLIMITED

DISCLAIMER

This report was prepared as an account of work sponsored by an agency of the United States Government. Neither the United States Government nor any agency Thereof, nor any of their employees, makes any warranty, express or implied, or assumes any legal liability or responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product, process, or service by trade name, trademark, manufacturer, or otherwise does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government or any agency thereof. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government or any agency thereof.

DISCLAIMER

Portions of this document may be illegible in electronic image products. Images are produced from the best available original document.

It has been observed that fetal tissues pass through a stage of development during which they are particularly vulnerable to the effects of ionizing radiation (Hicks, 1958). Two kinds of cells appear to be radiosensitive in the developing nervous system: those entering the prophase of mitosis and primitive differentiating cells (Hicks, et.al., 1962). The understanding of the effects of X-irradiation on the differentiation of neurons is made difficult by an absence of knowledge concerning that which constitutes a direct effect or by inference the contribution of this effect to the formation of any of the definitive abnormalities observed. Many of the sequelae may be secondary to the primary effect on the mitotic apparatus (Ledebinsky, et. al., 1961) of ependymal cells which in turn cause not only the death of many elements but also sterilization of those which survive, with the further result that the development of certain neural tissue is effectively halted. Berry, in 1963, emphasized an apparent differential effect of radiation on the thalamus and cortex. Inasmuch, as the thalamus in each irradiated group of animals remained relatively unharmed histologically, he contends that the normal projections from this structure to the cortex may be maintained. The EEG of prenatally irradiated rats has been demonstrated to be smaller in amplitude than those of normal animals and exhibited an abnormal amount of fast, spiked activity which occurred in bursts (Berry, et. al., 1963). Specific evoked responses were demonstrated to be longer in latency and have a lower amplitude in x-irradiated animals than in normal animals, and these changes become more pronounced the earlier in fetal life the x-irradiation is applied (Berry, 1964). A proposed possible explanation for these results is that an abnormal synaptic arrangement

within the specific projection system from the thalamus to the cortex has been developed in the irradiated animal. The first stage of the research, herein reported, addressed itself to the question: What effects do sublethal doses of radiation have on the developing central nervous system with respect to functional units.

A group of experiments were performed to assess the effect of ionizing radiation presented to newborn cats on their nervous system function at young adulthood. The radiation used was x-rays delivered by a G.E. Maxitron at 250 Kvp, 25 ma, with a filtration of 0.5 mm Cu and 1 mm Al for a total whole-body dose of either 100 or 150 R. Exposure was made on the first day of birth. After exposure to radiation, the animals were kept a minimum of five months before experimental procedures were performed.

Investigations on the monosynaptic reflex and various forms of inhibition and facilitation of this reflex were performed. The advantages of the spinal cord study were felt to outweigh the poverty of radiation research done in this area since decerebrate preparations could be used thus eliminating the need for anesthetic agents. The spinal cord studies have the advantage of utilizing a fairly well understood physiologic system, inasmuch as effects can first be looked at, at the simplest possible reflex connection, the monosynaptic reflex. Also, direct facilitation, direct inhibition, presynaptic inhibition, and recurrent inhibition are all separate systems reflecting on the monosynaptic reflex.

However, a detailed comparison of the various reflex elements in the spinal cord in these irradiated animals does not reveal any significant functional difference from non-irradiated control animals. One of the handicaps turned out to be the radiosensitivity of young kittens. The fatality with more than 150 R made such doses impractical.

Since changes in the monosynaptic reflex could be seen in acute animals with doses in this range, systems projecting influence to the spinal cord were investigated. The effects of brainstem stimulation on lumbar monosynaptic reflexes and its subsequent response to acute radiation exposure was investigated in a number of the chronic irradiated animals. The results of these investigations indicated that the sensitive site producing functional changes may be in the brainstem or cerebellum.

A number of investigations have emphasized the relative radiosensitivity of the cortex in mature and immature animals. Little attention has been focused however on the functional changes in the cortex subsequent to irradiation. An outstanding exception is the work of Shofer et. al., (1964) on the immature cerebellar cortex. This study reported that the functional consequences of destruction of the external granular layer and changes in the development of Purkinje cell dendrites and superficial axodendritic synaptic pathways due to radiation are increased excitability and complexity of afferent evoked responses.

The Purkinje cells, which are inhibitory in nature, have two main distributions, the vast majority ending in the cerebellar nuclei and the second group ending in the lateral vestibular nucleus of Deiters. The inhibitory effect of these latter fibers on Deiters cells has been demonstrated by Ito and Yoshida (1966).

Histological studies of the cerebellar cortex of the mature animal postirradiation have tended to show different phenomena from that of the immature one. Pyknosis of 1% of the granular cells after 4.2 kr and almost complete granular cell pyknosis following 9 kr was demonstrated in the rabbit with little evidence of morphological changes in Purkinje cells (Gerstner and Kent, 1957). While Schummelfeder in 1962 described changes in some

granular cells after an x-irradiation dose of 3kr in the rat along with scattered small Purkinje cell destruction. This single isolated cellular destruction increased with increasing radiation. Since the state of activity of the granular cell directly affects the Purkinje cell output to the brain stem, the brain stem would register changes in the granular cell in its interaction with spinal reflexes.

In the mammal there are four main long descending pathways into the lumbar spinal cord from higher centers: the pyramidal tract, rubrospinal tract, lateral vestibulospinal tract, and the reticulospinal system. Of the four the nuclei of origin remain for three in the precollicular decerebrate preparation; and, of these, two are closely associated with the cerebellar nuclei.

The most recent work of Courville and Brodal (1966) shows that rubrocerebellar fibers end in the nucleus interpositus. This is as one would expect for feedback control from the red nucleus to act on the nucleus interpositus because most cerebellorubral fibers in the cat arise in this nucleus. It is well established that the pathway that connects the interposate nucleus to the magnocellular part of the red nucleus is purely excitatory and that it maintains a permanent state of facilitation in the red nucleus (Tsukahara, 1965). The inhibition and the delayed excitation that appear in the rubral response to direct or reflex stimulation of the cerebellar cortex are the result of reduced or of increased activity in this interposate-rubral tract as modulated by the Purkinje cells. In turn, the projection from the red nucleus via the rubrospinal tract is predominantly disynaptic facilitation to flexors and inhibition to extensors (Hongo et. al., 1969a) with a more complex distribution to spinal reflex interneurons (Hongo et. al., 1969b).

A similar feedback mechanism can be seen in the lateral vestibular nucleus with vestibulo-cerebellar projection to and fastigio-vestibular fibers from the fastigial nucleus of the cerebellum (Brodal, Pompeiano, and Walberg, 1962). The vestibulo-spinal tract has been demonstrated to end monosynaptically on extensor motoneurons (Lund and Pompeiano, 1968) and have a disynaptic inhibitory influence on flexors (Grillner, et.al., 1968).

The remaining long brainstem-spinal cord tract, the reticulo-spinal, has been demonstrated to have the converse effects of the vestibulo-spinal, that is monosynaptic flexor facilitation and polysynaptic extensor inhibition (Engberg, et. al., 1968). There is ample evidence of connections from not only the cerebellar nuclei to the reticular formation, but both the red and Deiters nuclei as well.

The basic questions asked in this study have been the following:
Are changes detected at low radiation dosages in spinal cord reflex pathways and is the cerebellum, working through the long descending pathways, in any way responsible for the observed changes.

Cats, under ether anesthesia, were decerebrated at the midcollicular level. By means of a lumbar laminectomy, L5-L7 dorsal and ventral roots were exposed. In one group of animals a laminectomy was also done at T13 to expose the cord for cutting at the termination of the study. In this group of animals dorsal and ventral L7 were used for the monosynaptic reflex and dorsal L6, for conditioning. In another series of animals, the femoral nerves, the sciatic and hamstring nerves on the contralateral side, and the hamstring nerve on the ipsilateral side were cut. In these animals the lateral and medial gastrocnemius-soleus nerves were used to study extensor and the common peroneal nerve to study flexor reflexes. The tibial and sural nerves were cut. The cats were flaxedilized and artificially respired.

As stated above, in one series of animals L6 was used to condition an L7 testing reflex. In the other series, a conditioning stimulus of 200/sec. for 100 msec. was delivered to the vicinity of Deiter's nucleus. In cerebellectomized animals, the cerebellum was removed by a craniotomy of the occipital bone, excision of the dura over the fourth ventricle and lifting the posterior tip of the cerebellum so that the peduncles could be cut under visual inspection. A Koph stereotaxic unit and concentric microelectrode produced by In Vivo Metric Systems were used for stimulation. In these brain stem conditioned animals, either the peripheral nerves were stimulated and recordings were made from L7 ventral root, or L7 dorsal was stimulated and recordings were taken from the peripheral nerves. In two animals the cord was cut at the start of the experiment to serve as controls.

Radiation was delivered by a GE Maxitron Two-Fifty at the rate of 100 R/min. with 250 Kvp and 25 ma through a 0.5 mm Cu, 1 mm Al filter. Depending on the particular experiment, the radiation was delivered to either the brain stem, cervical, thoracic, or lumbar cord. In the first series of experiments a cylindrical collimator was used to cut the spread of radiation via scatter, the area radiated was therefore of a rectangular shape approximately 10 mm by 15 mm. This necessitated that brain stem radiation involved some cord exposure as well as peripheral nonnervous tissue. The apparatus was therefore further modified by the insertion of a piece of lead with a hole in the form of an ellipse, 4 X 6 mm, to allow specific brain stem exposure.

The radiation was delivered in different dosage packets as the accumulated dosage of radiation increased. A typical schedule would be 200, 200, 400, 400, 400, 400, 500, 500, 1000, 1000, 5000, 5000 rads per packet with continued 5000 rad doses until the experiment was terminated. Between each

delivery an interval of about 15 minutes was necessary for data gathering.

The form of the records was a histogram. The testing stimulus was ramped across the conditioning stimulus so that it could be studied in a nonconditioned state, at the time of conditioning, and at various time intervals following conditioning. This method has been described by Smith and Barnes in 1968.

Early Radiation Changes

Radiation changes were detected consistently with the lowest radiation dosage of 200 R. (See Fig. 1). The most characteristic feature of radiation

Fig. 1: Effect of acute radiation on the brainstem conditioned lumbar spinal cord extensor and flexor monosynaptic reflex. The upper histogram is the extensor monosynaptic reflex from gastrocnemius-soleus; the lower, the flexor monosynaptic reflex from common peroneal. The bar indicates a 100 msec. tetanus of 200/sec. to the region of Deiters' nucleus.

A: Preradiation control.

B: After an accumulated dose of 200 R to the brainstem.

changes were their unpredictability, making attempts at classification of responses according to the type of radiation or stimulus fairly impossible. However, some general statements seem to be possible as concerns early changes. The beginning unconditioned reflex, as well as the long latency response,

appears always to be affected with the direction of the effect, that is towards facilitation or inhibition, the same for both flexors and extensors. However, it is not true that the unconditioned response will be affected by radiation in the same direction as the longer latency response.

Another general tendency is that responses at the time of conditioning appear to be opposite for flexors and extensors with flexors more generally showing increased facilitation and extensors, increased inhibition.

Findings as Radiation Dose Increased

The most obvious feature of the effect of increasing radiation dosages were that trends toward inhibition or facilitation with radiation did not continue and that whether or not further dosage was likely to produce inhibition or facilitation was not predictable. Figure 2 illustrates a tendency towards increased inhibition at 400 R which with more radiation tends toward facilitation.

However, there was a consistent finding that increased radiation leads to inhibition of the unconditioned monosynaptic even if the early effect of radiation was facilitation. Another observation in two or three animals that were taken to high radiation dosages was that 15000-20000 R led to a nearly identical flexor and extensor pattern of facilitation followed by inhibition with no long latency responses to radiation. (See Fig. 3b). At the highest level studied in each animal before termination of the experiment oscillations of the type seen in figure 3c were observed. They occurred immediately after the pattern seen in figure 3b.

Cerebellar Effects

The effect of the removal of the cerebellum on the histogram patterns of the animal prior to radiation showed a lack of the long latency facilitation or inhibition that was seen in noncerebellectomized animals. These animals

Fig. 2: Effect of acute radiation on brainstem conditioned flexor monosynaptic reflex. The monosynaptic reflex from common peroneal conditioned by a 100 msec. tetanus of 200/sec to Deiters nucleus as indicated by the bar.

A: Preradiation control.

B: After an accumulated dose of 400 R to the brainstem.

C: After an accumulated dose at 800 R to the brainstem.

Fig. 3: Effect of high acute dose of radiation to brainstem and cerebellum on brainstem conditioned spinal cord reflexes. In each record the upper histogram is the gastrocnemius-soleus monosynaptic reflex. Each record is 500 msec. long with a 100 msec. conditioning tetanus of 200/sec. to Deiters nucleus indicated by the bar.

A: Preradiation control.

B: After accumulated dose of 20000 R to the brain stem.

C: After accumulated dose of 25000 R to the brain stem.

showed a pattern that lasted only slightly longer than the time of conditioning. (See fig. 4a.) As radiation was given these animals showed some effects but the basic pattern of the original histogram changed very little if at all. (See fig. 4.) At present a method to statistically evaluate this lack of pattern change, that is visually evident to independent observers, has not been found; but three separate animals have demonstrated minimal changes to radiation doses that were increased to 10000 rads in one animal. Individual histogram patterns for the cerebellectomized versus noncerebellectomized animals at the time of conditioning have not showed significant differences.

Discussion of the Early Effects of Radiation

The use of histogram records of a ramped monosynaptic reflex across a time constant conditioning pulse has allowed demonstration of the early effects of radiation which appear as pattern changes in the histograms. Such pattern changes have been evident at the lowest radiation doses whether the conditioning was by a spinal nerve, an antagonistic peripheral nerve, or brain stem stimulation. The effect of low radiation dosages supports the findings reported in Lebedinskiy and Nakhil'nitskaya's review in 1963.

The Unconditioned Stimulus and Radiation. In a given nondecerebellate cat the unconditioned reflex in both flexors and extensors has been found to be consistently affected by radiation. Likewise the reflex always is moved in the same direction; that is, towards inhibition or facilitation. This suggests that one or more tonically active systems are directly affected by radiation or indirectly through the effect of radiation on some other impinging system. Consequently this impinging system affects that system which directly influences spinal motoneurons. A system has been described that descends from the brain stem to the spinal cord that facilitates both flexors and extensors. This system was first described by Hongo and

Fig. 4: Effect of cerebellectomy on subsequent radiation induced changes of brainstem conditioning of spinal cord reflexes. In each record the upper trace is the monosynaptic reflex from common peroneal; the lower, the monosynaptic reflex of gastrocnemius-soleus. Each histogram is 500 msec. long with a 100 msec. conditioning tetanus of 200/sec. to Deiters indicated by the bar.

- A. Preradiation control.
- B. After 2000 R accumulated dose to the brainstem.
- C. After 5000 R accumulated dose to the brainstem.

Takówska (1967) and is known as the medullary reticular tract. Another tract from medullary centers described by Jankowska, Lund, Lundberg and Pompeiano (1968) disynaptically inhibits both flexors and extensors.

It is possible that one or both of these systems is activated by radiation and in any one cat the resultant change in the unconditioned stimulus is due to the balance between them prior to radiation and the new balance at each radiation level. However, it has also been found in these experiments that the decerebellectomized animal is appearing to show no changes in the unconditioned stimulus. The cerebellum is known to send collaterals to the reticular formation through the Brachium Conjunctivum Descendens Ventralis as described by Ito and Yoshida (1966). And as previously mentioned, the Purkinje cells are known to be affected early by radiation. Thus another possibility is that the descending systems are indirectly affected following the direct effect of the cerebellar nuclei on them. As in the case of a direct effect, the balance would again be determined by the relative strength of the cerebellar activation of either system prior to and following radiation.

A further possibility is that there is only one system directly or indirectly affected which is perhaps facilitated as radiation begins and inhibited as radiation is continued.

From the studies of Barnes (1967), it might be postulated that the effect on the unconditioned reflex is due to the state of activation of the substantia gelatinosa and the level of presynaptic inhibition. If this be true, then the lack of effect in the decerebellectomized animal might suggest a strong influence of the cerebellum on the mechanism of presynaptic inhibition.

The Short Latency Effects of Conditioning as Influenced by Radiation. Extensors and flexors were always affected differently by brain stem conditioning in control animals. This is not surprising since the conditioning was in the

vicinity of Deiters nucleus which gives rise to the vestibulospinal tract shown by Lund (1968) to facilitate extensors and inhibit flexors. Also, patterns were not the same in every cat which again can be related to the near vicinity of the medial vestibular nucleus which contributes to the mlf which has been shown by Grillner, Hongo, and Lund (1968) to have the opposite effect on spinal motoneurons. Thus the placement of the electrode in any one cat would determine the balance between the two systems at the spinal motoneuron and consequently the histogram pattern obtained.

The cats with intact cerebellums showed immediate effects of radiation on this part of the record. It appeared that the early effects of radiation were an inhibition of extensors and facilitation of flexors. However, this trend did not necessarily continue and often instead reversed itself.

In cats without cerebellums this part of the record reveals no significant changes to independent observers viewing the histogram patterns. Again a strong tonically active influence by the cerebellum bouth through direct monosynaptic connections of Purkinje cells and through the fastigial nucleus on to Deiters nucleus, as well as fastigial connections to the medial vestibular nucleus, has been noted by Ito and Yoshida (1966). Thus again it is possible that the effects of radiation are indirectly mediated via the vestibulospinal or mlf consequent to a direct effect on the cerebellar Purkinje Cells.

Long Latency Responses to Conditioning as Influenced by Radiation. In the noncerebellectomized animals the effects of brain stem conditioning continue for 100 to 300 msec. post conditioning. This late response to conditioning is always influenced by radiation and again flexors and extensors are affected in the same way. ~~However, it is not necessarily true that the direction of effect will be the same as in the nonconditioned stimulus.~~ However, in the decerebellates, there is no apparent post conditioning response and no effect

of radiation in this time period.

The cerebellum has been shown to have reciprocal relations with the brain stem vestibular nuclei and red nucleus. The fastigii connection to Deiters has been mentioned, but also should be noted the reciprocal connection to fastigii and the reciprocal connections between interpositus and the red nucleus which were discussed in the introduction. It is possible that through these and perhaps other connections a reverberating circuit or a long latency circuit is activated that causes this effect. Thus radiation affecting the cerebellum could again be the reason for the pattern changes observed.

Large Dosage Effects of Radiation Discussion

The pattern seen in figure 3 and the oscillations at the next higher dose appear to be a repeatable phenomenon due to the radiation. This evening out of pattern has begun to occur as early as 15000 R in one animal and as late as 20000 R in another. Perhaps it relates to the phenomenon observed by Lee, Helgason and Snider (1955). They describe a complete flattening of the cerebellar evoked response at 10000 R. The oscillations seem to be synchronized as to flexor and extensor and perhaps are the neurological representation of the clonic muscular seizures that have been described by Gerstner, Pickering, and Dugi in 1955.

Concluding Remarks

The results of this work, plus those histological studies of cerebellar effect due to radiation previously referred to, force one to consider the possibility that much of the early effect of radiation on the brain stem-cord interactions is due to its effect on the cerebellar Purkinje cells.

~~Furthermore if this radiosensitivity is further verified it will provide~~
a powerful tool for studying cerebellar-brainstem-cord interactions. But

also the radiosensitivity of this neuronal group could lead to an assay for drugs that hope to chemically protect cells from radiation damage. Also, it may be possible to mechanically protect this group and also similar isolated groups during radiation therapy.

These findings stress further the question of what kinds of cells are radiosensitive; for if only some are, then only those need to be considered in medical therapy dosages.

BIBLIOGRAPHY

1. Barnes, C.D. (1957) Rad. Res. 32: 347.
2. Berry, M. (1964) EEG Clin. Neurophysiol. 16: 622.
3. _____, B.G. Clendinnen and J.T. Eayrs (1963) EEG Clin. Neurophysiol. 15:91.
4. Brodal, A., O. Pompeiano, and F. Walberg. (1962) The Vestibular Nuclei and their Connections. Anatomy and Functional Correlations. Oliver and Boyd, Edinburgh.
5. Courville, J. and A. Brodal (1966) J. Comp. Neurol. 126: 471.
6. Engberg, I., A. Lundberg, and R. Ryall (1968) J. Physiol. 194: 201.
7. Gerstner, H. and S. Kent (1957) Rad. Res. 6: 626.
8. Gerstner, H., J. Pickering, and A. Dugi (1955) Rad. Res. 2:219.
9. Grillner, S., T. Hongo, and S. Lund (1968) Brain Res. 10: 259.
10. _____, Brain Res. 10: 477.
11. Hicks, S.P. (1958) Physiol. Rev. 38: 337.
12. _____, C. D'Amato and D. Jeffes (1962) Effects of Ionizing Radiation on the Nervous System. Vienna, IAEA.
13. Hongo T. and E. Jankowska (1967) Exp. Brain Res. 3:117.
14. _____, and A. Lundberg (1969a) Exp. Brain Res. 7:344.
15. _____, (1969b) Exp. Brain Res. 7:365.
16. Ito, M. and M. Yoshida (1966) Exp. Brain Res. 2: 330.
17. Jankowska, E., S. Lund, A. Lundberg, and O. Pompeiano (1968) Arch. Ital. Biol. 106: 124.
18. Lebedinskiy, A., V. Mastryukova, and A. Strzhovsky (1961) The Initial Effects of Ionizing Radiation on Cells (R.J.C. Harris, ed.) Academic Press, New York.
19. Lebedinskiy, A. and Z. Nakkil'nitshaya (1963) Effects of Ionizing Radiation on the Nervous System, Elsevier Publishing Company, New York.
20. Lee, J., S. Helgason, and R. Snider (1955) Rad. Res. 3: 267.

21. Lund, S. and O. Pompeiano (1968) Acta Physiol Scand. 73: 1
22. Schummelfeder, N. (1962) Response of the Nervous System to Ionizing Radiation (Haley, T. and R. Snider, eds) Academic Press, New York.
23. Shofer, R., Pappas, G. and Purpura, D. (1964) Response of the Nervous System to Ionizing Radiation (Haley, T. and R. Snider, Eds.) Little Brown, Boston.
24. Smith, J. and C.D. Barnes (1968) J. of Appl. Physiol., 24:272.
25. _____, (1969) J. of Appl. Physiol. 26: 221.
26. Tsukahara, N. Toyama, K., and K. Kosaka (1965) Experientia 21: 544.

of radiation in this time period.

The cerebellum has been shown to have reciprocal relations with the brain stem vestibular nuclei and red nucleus. The fastigii connection to Deiters has been mentioned, but also should be noted the reciprocal connection to fastigii and the reciprocal connections between interpositus and the red nucleus which were discussed in the introduction. It is possible that through these and perhaps other connections a reverberating circuit or a long latency circuit is activated that causes this effect. Thus radiation affecting the cerebellum could again be the reason for the pattern changes observed.

Large Dosage Effects of Radiation Discussion

The pattern seen in figure 3 and the oscillations at the next higher dose appear to be a repeatable phenomenon due to the radiation. This evening out of pattern has begun to occur as early as 15000 R in one animal and as late as 20000 R in another. Perhaps it relates to the phenomenon observed by Lee, Helgason and Snider (1955). They describe a complete flattening of the cerebellar evoked response at 10000 R. The oscillations seem to be synchronized as to flexor and extensor and perhaps are the neurological representation of the clonic muscular seizures that have been described by Gerstner, Pickering, and Dugi in 1955.

Concluding Remarks

The results of this work, plus those histological studies of cerebellar effect due to radiation previously referred to, force one to consider the possibility that much of the early effect of radiation on the brain stem-cord interactions is due to its effect on the cerebellar Purkinje cells.

Furthermore if this radiosensitivity is further verified it will provide a powerful tool for studying cerebellar-brainstem-cord interactions. But

also the radiosensitivity of this neuronal group could lead to an assay for drugs that hope to chemically protect cells from radiation damage. Also, it may be possible to mechanically protect this group and also similar isolated groups during radiation therapy.

These findings stress further the question of what kinds of cells are radiosensitive; for if only some are, then only those need to be considered in medical therapy dosages.