Hyperesthesia from Spinal and Root Lesions

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Hyperesthesia is a poorly understood phenomenon. Following peripheral nerve lesions a zone of persistent hyperesthesia relates to the presence of poorly differentiated sensation (pressure, cold) without the damping effect of more specific receptors. The mechanism for this suppressor effect is thought to be in the substantia gelatinosa of the spinal cord segments (Melzack and Wall). Following transverse lesion of spinal cord a zone of hyperesthesia at the sensory level was described by earlier writers, but is usually seen only with intramedullary pathology. Similarly, the most intense hyperesthesias following root lesion are those associated with an intrinsic lesion (herpes). Experiments with cord and root lesions on the monkey provide some explanation for dissociation of sensation from intrinsic lesions in these situations, but leave an unexplained paradox.

The classical delineation of the segmental dermatomes by Sherrington followed the method of residual sensation, whereby the root to be studied was isolated by section of the three roots above and the three below. The neighboring roots were sectioned intradurally. We have performed this operation in 18 monkeys and have, in general, confirmed the sensory pattern in thoracic and lumbar segments. The sensory response from the isolated nerve root begins to appear only on the third to eleventh day after operation, and at first is easily fatigued. The full extent of the dermatome is developed by the end of the second week after operation and does not change thereafter. The threshold of sensory response remains higher than normal, and pin scratch is usually the only effective stimulus. Any local reflex served by the isolated root (costal or abdominal reflex in the case of thoracic roots, knee jerk or ankle jerk for lumbosacral roots) is elicited with difficulty, is minimal in degree, and is easily fatigued.

If the root isolation is made by section of the neighboring roots distal to their ganglion (section of both motor and sensory roots) the outcome is different. In this case, the residual root sensation is usually apparent by the first or second day after operation and has reached its maximum area at the end of the first week. The area is more than approximately twice the size of that produced by intradural section of neighboring roots. The area of total sensory loss is less, so that the sensory borders of the next roots above and below the zone of root section have also expanded. In addition, sensation surrounding the zone of sensory loss on all sides is excessive at all border zones. The animal protests and scratches repeatedly in a poorly directed manner. Any local reflex served by the isolated root becomes very facile in the second week and is usually more brisk than on the opposite side.

In relation to isolation of 5th lumbar segment this change is most striking. Following section of lumbar dorsal roots 2, 3 and 4, and lumbar 6, 7 and sacral roots 1 beyond the ganglia, the only complete sensory loss in two monkeys was in the sacral zone, with a narrow strip down the back of the leg to the ankle. There was hyperesthesia to pin scratch and to application of ice cubes on the lateral and medial borders of the thigh. After subsequent section of the same roots intradurally in three monkeys there was the expected zone of sensory loss at the groin, and a broader area of sacral loss. The area supplied by lumbar 5 had greatly shrunk, and was then comparable to that found in other animals when the same roots had been sectioned intradurally at the first operation. All signs of hypersensitivity had disappeared, and only the center of the dermatome approached normal response to pin scratch.

Part of the explanation of this difference between root section proximal and distal to the ganglia is provided by recurrent sensory fibers in dorsal nerve roots. Recurrent sensory fibers in ventral roots, ending in the meninges were demonstrated by Claude Bernard and others. Small bundles of recurrent sensory fibers in dorsal nerve roots leave the root filaments as they enter the meninges and run up or down to make exit with the filaments of the next dorsal root above or below. These are small myelinated fibers of 1.5 to 3 micra in diameter. They are evidently part of a diffusely distributed system serving poorly differentiated sensation. Having their cell of origin in one ganglion they are distributed through other roots. They seldom course more than one root away from their origin, except in the high cervical region. Such small sensory fibers are intact after section of nerve roots distal to their ganglia, and some must be distributed with the neighboring intact roots. Their numbers would seem to be small in proportion to the large differences in area and degree of sensation we have described.

We next encountered another aspect of the same problem in relation to transection of spinal cord, for the sensory level was found to differ according to whether the cord was sectioned with its pial covering, or was sectioned inside intact pia. Section of the meninges with the spinal cord leaves a sensory level that corresponds to the lower border of the dermatome next above the section. There is the same mild hyperesthesia with brisk local reflex that was found with isolation of the same root by section of neighboring roots distal to ganglion.

If the cord is sectioned completely within its pial covering (performed by introducing a needle, sharpened on one side and blunt at the tip, through an avascular area of pia) the result is different. The sensory level is lower (e.g., 4 to 8 mm lower for section between D8 and D9 roots), and a wide zone of intense hyperesthesia (extending from the costal margin up to the nipple level in the case of D8-D9 section) with very facile local costal reflex appears on the first day after operation and persists for many weeks. By the end of the second week, vigorous protest and reflex are obtained not only by

pinprick but also by blunt stimulation in this area, and occasionally even by brush stroke. In the second week reflexes below the lesion become very brisk, expecially an abdominal reflex. In a small zone a few millimeters on either side of the sensory level both costal and abdominal reflexes can be obtained with ease. Subsequent section of the pia at the level of cord section three or more weeks after the initial intrapial transection results only in loss of this zone of overlapping reflex effects. The low sensory level is raised only a few millimeters if at all.

It was therefore apparent that though small nerve fibers looping from one nerve root to another in the meninges could account for some overlap of reflex effects from above and below a transection, the precocious recovery of sensation over a wide cutaneous distribution, its overactivity in terms of hyperesthesia and local reflexes require some further explanation. The excellent reflex recovery below anatomically proven transverse lesion, even up to the segment involved, indicates that intrapial transection preserves the nutrition of the isolated segments much better than does total section of meninges. The full potential of the segments bordering the actual transection is developed only if the blood vessels of the pia are preserved. The sensory function of the nerve roots next to the lesion then present a dissociation between protopathic and discriminative qualities of sensation that is comparable to those in skin bordering the sensory loss following nerve lesions at the periphery.

The real problem presented by these observations is the depression of the full sensory potential of a nerve root isolated from its neighbors by intradural section, or by complete transection of the cord. In the former, the input to the substantia gelatinosa must be impaired by selective loss of some of the diffuse fiber system. In the latter case, the mechanism of the substantia gelatinosa must be impaired by poor blood supply at a critical period in the development of spinal shock. These effects suggest that a certain density of background activity of the diffuse sensory system is necessary for effective sensory function, and conversely too intense diffuse sensory input results in hyperesthesia. In support of this concept we found that a subconvulsive dose of strychnine converted the dermatome area of a residual root isolated by intradural section to even larger extent than that of the same root isolated by section peripheral to ganglia.

It has been confirmed in three such animals that for some hours the dermatome then becomes comparable to that following intrameningeal cord section. Thus, relatively small differences in diffuse sensory input from surrounding areas make enormous and lasting changes in transmission of differentiated sensation by the substantia gelatinosa.

DISCUSSION

VERNON MOUNTCASTLE (*Baltimore, Md.*): These experiments of Drs. Denny-Brown and Kirk provide very strong evidence that recurrent nerve fibers leave the dorsal root of

origin to course peripherally in each adjacent dorsal root. The results are important from the anatomical, particularly the developmental point of view as well as for understanding the reflexology of the spinal cord. For me, their greatest interest lies in the fact that they present another example of what one might call a denervation hyperesthesia, that is, an alteration in sensation which results when peripheral structures are deprived of their large myelinated innervation but retain at least a portion of their innervation by small myelinated fibers and perhaps of unmyelinated fibers as well. The result is a hyperpathia objectively experienced and reported in humans and a heightened reflex excitability objectively demonstrable in experimental animals. This is particularly true for those reflexes that are nociceptive in nature.

The same results appear in more or less identical form whether the differential denervation follows a peripheral lesion, as in the case of the experiments reported, or whether it is central as in the classic syndrome which follows pathological or neurosurgical lesions of the somatic afferent pathways at the mesodiencephalic junction. The resulting hyperpathias and reflex hypersensitivities appear to differ only in distribution and degree, all having certain qualitative features in common.

Findings such as those reported here pose important problems for understanding functional interrelations of the several ascending systems that serve the several varieties of somatic sensibilities. It appears certain that afferent input in the larger delta and beta fibers which is mechanoreceptive in nature under normal circumstances, exerts a suppression of the sensory experience and of the reflex action elicited by input in the small delta and unmyelinated fibers.

Both sensory experiences and reflex action occur in distressing exaggeration when peripheral tissues have access to the central nervous system only by the smaller fibers. The major question which we face from this point of view then—and indeed one which has remained unsolved since the time of Head—is: What is the mechanism of this regulatory interaction?

Some questions of fact need answers before a successful conceptualization is possible. Firstly, does the regulatory interaction occur only at the segmental level of dorsal root entry? This seems to me to be altogether unlikely for severe hyperpathias of central origin commonly follow more cephalad lesions of the afferent pathways, up to the level of the primary sensory cortex itself. Nevertheless, there is now acceptable electrophysiological evidence that afferent input in large fibers does, indeed, influence in a regulatory fashion the transfer of activity in small fibers through the complex synaptic transfer region of the dorsal horn into the anterolateral system.

Secondly, is there a feed-forward regulatory interaction, for example, at the diencephalic level, where the ascending components of the somatic system (divergent at dorsal root entry) reconverge to a certain extent? There can be no doubt that a lesion of either the lemniscal system or the neospinothalamic system which spares the paleospinothalamic and spinoreticulothalamic components may lead to a severe hyperpathia of central origin. But, we cannot at once conclude that this is due to regulatory interaction at the thalamic level, for such a lesion may also interfere with a third possible mechanism; that is, a reflected descending control taking origin in the cerebral cortex and influencing afferent transmission at every level from that of the dorsal horn to the thalamus. Indeed, it is these systems to which Dr. MacLean referred in his discussion this morning.

The answers to these questions from the physiological point of view still elude us, although the anatomical pathways have now become clear. Meanwhile, the further documentation of instances in which large fiber denervation leads to hyperesthesia and hyperreflexia is of great value. And, particularly important is the fact that such a result has been demonstrated by Drs. Denny-Brown and Kirk to occur in experimental animals such as the monkey in which it should now be possible to apply the paraphernalia of electrophysiology in an attempt to elucidate the mechanism.

DR. DENNY-BROWN (*closing discussion*): Dr. Mountcastle has himself shown that

sensory interaction must occur at many levels. The pattern of the dermatome as revealed by a coarse stimulus such as pinprick appears to be an objective index with which to explore such interaction. Since the density of innervation is greatest in the center of the area of segmental innervation and least at its edge, change in efficiency of transmission leads to expansion or contraction of the effective field. The effect of cord section in enlarging the effective dermatome of the roots immediately above and below the section indicates that some mechanism in each segment normally suppresses, in some degree, transmission in its neighbors. The release is associated with over-activity, hyperesthesia, that is powerful enough to overcome the converse shrinkage that results in one root from section of its neighboring roots.

If enough neighboring roots are sectioned, the dermatome of an isolated root becomes reduced to vanishing point. This effect, which indicates that a surround of diffuse sensation is necessary for punctate highly differentiated sensation to be effective, appears to us to be most important. It implies that punctate sensation cannot exist alone but is a polarization of an undifferentiated sensory or reflexogenous field. The defect can be reversed, in large degree, by strychnine or by section of cord immediately below the segment concerned. In the state of reduced effectiveness residual sensation is extremely vulnerable to fatigue. Continued stimulation in one area, for example, can cause the response of other parts of the dermatome to disappear for many hours. This effect is comparable to that of nerve stimulation in relieving some states of pain as described by Dr. Sweet earlier today.

It seems therefore that ideas of sensory function at the first synapse require some review.