SENSITIZATION OF THE SPINAL CORD OF THE CAT TO PAIN-INDUCING STIMULI*

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Sensitization of a functional unit of the central nervous system by partial injury or destruction is well known. Cannon and Haimovici in 1939 reported that motoneurones could be sensitized by partial “denervation.” Cannon and Rosenblueth described the sensitization of both cholinergic and adrenergic elements in the autonomic system following injury to its neurones. Cannon then postulated a “law of denervation” for the efferent systems which required sensitization as the result of partial destruction. Drake and Stavraky then carried this concept into the afferent systems and showed that deafferentation caused systems to react more quickly and more intensely than did normal units. In their chronic cats, injection of either cholinergic drugs, camphor or metrazol produced convulsions which appeared earlier and more intensely in deafferented limbs than elsewhere.

Clinically, lowered threshold and increased sensitivity may result from direct sensitization of cells within a system. Injury to dorsal root ganglia is thought to cause pain in this way and trauma can so sensitize the cells of the cerebral cortex that epilepsy results from minor stimulation. Such cortical sensitization may follow destructive lesions and scar formation. It may be relieved in man by the removal of the scars. Chronic experimental epilepsy, produced by the application of alumina cream to the cerebral cortex in monkeys, must be the result of similar processes.

When peripheral nerves are damaged sensitization of the sensory system which mediates pain may result in hyperalgesia or causalgia. These painful states are most often unrelieved by the removal of the original source of the disorder at the site of initial injury. It has therefore been assumed that the initial injury has in some fashion sensitized the central nervous system. The concept of the neuron pool which effectively perpetuates the afferent input has been developed here.

The presence of hyperalgesia in cats as the result of injection of alumina cream into the spinal subarachnoid space may be considered as an example of chronic sensitization of an afferent complex within the central nervous system. It has been reported in detail elsewhere. The present paper is the result of subsequent investigations and will deal with the nature of this sensitization. A brief review of the development of the hyperalgesia as previously reported is here necessary.

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Nature of the Hyperalgesia. In the cats described in the previous papers hyperalgesia developed according to a fixed pattern which was similar in each animal. Following the injection of the colloidal substance into the dorsal spinal subarachnoid space, segmental skin areas became greatly sensitized to any form of cutaneous stimulus. Light touch or pin-prick, which produced only mild responses if applied to normal skin areas, caused extreme reactions of displeasure in the affected regions. Blowing on the hair, a slight touch, or even the tension caused by the animal’s moving would produce withdrawal, crying-out and, sometimes, resistance. The animals became sedentary and dirty, since they could not clean the hypersensitized fur. But their non-affected regions were clean and they remained friendly and sought petting in the normal areas. A causalgia-like syndrome was thus defined.

Rate of Development. Following injection, the hypersensitivity to touch and pain first appeared, in some animals, on the 5th postoperative day. In others, symptoms were not noted until the 3rd week. The amount of substance injected was thought to have direct relation to the rate of development, although no quantitative experiments were carried out. Following the onset, the hyperalgesia usually became intensified over a period of several weeks. Once fully established it was permanent for as long as 3 years.

Extent of Hyperalgesia. The hyperirritability to sensory stimuli appeared first just below or at the level of the injection. It then spread bilaterally during a period of about 2 weeks, becoming equally intense through all levels below the site of the injection and for one or two segments above it. This occurred whether the injection was made low in the lumbar region or high in the cervical; thus a varying amount of skin area might be involved, increasing as the injections were made higher in the cord. It was thought that this must indicate a local action of the substance at the level of injection rather than action over a long distance of cord, for, in the latter instance, the diffusion should be equal in either direction from the site of injection. No actual determination of the diffusion of aluminum ions has been made, however.

METHOD

The details of the injection of alumina cream have have been given previously, as have the method of examination and the clinical status of the animals.\(^7\),\(^8\) In the present study as in the previous ones the colloidal alumina cream has been made for us by Dr. Lenore Kopeloff according to her original method.\(^10\) In the present study the substance was injected into the cervical, rather than lumbar region; either into the subarachnoid space (3 cats) or directly into the lateral column of the cord of one side (5 cats). Findings have been compared with those of the earlier series.

DATA

The findings in all 8 cats are consistent although different secondary procedures often altered the course of the disorder. The following brief