Chapter 10

Anatomy and Physiology of Head Pain

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A large body of indirect evidence supports the idea that some types of headaches, including migraine, are caused by activity in nociceptive afferents that innervate the cranial meninges, particularly the dura mater encephali and large intracerebral blood vessels (133,146). This idea was initially based on the classical intraoperative experiments by Ray and Wolff (149), followed by supplementary studies of other investigators, who demonstrated that pain, but not other sensations, can be evoked by electrical, mechanical, thermal, or chemical stimulation of dural blood vessels and sinuses or large intracerebral arteries (26). Importantly, the painful sensations were referred to the trigeminal dermatomes where typically headaches are localized (144). These early studies formed the basis of many anatomic and physiologic examinations that were made with regard to the pathophysiology of headaches.

MENINGEAL REPRESENTATION IN THE TRIGEMINAL GANGLION

Cranial nerve V, arising from the trigeminal ganglion, also referred to as the semilunar or Gasserian ganglion, conveys sensory information from the orofacial region, including intracranial structures, to the central nervous system. Mayberg et al. (123) and Steiger and Meakin (163) traced meningeal afferents by applying horseradish peroxidase (HRP) to pial and dural structures in the cat. Afferents around the medial meningeal artery projected predominantly to the ophthalmic division (V1) of the ipsilateral trigeminal ganglion, but to a minor extent also to the maxillary (V2) and mandibular (V3) divisions (123). The basal dura mater in the middle cranial fossa was represented mainly in V3 (163). The finding that all three divisions of the trigeminal nerve, although not equally, contribute to the innervation of the meninges is in accordance with old anatomic observations in primates (126). Retrograde labeling of nerve fibers around basal intracranial arteries, from which head pain can be provoked in humans (149), was found not only in the trigeminal ganglion but also in the first and second spinal ganglia in the rat (9). Because of the limited experimental access to intracerebral arteries, most of the morphologic and nearly all functional studies have focused on the innervation of the cranial dura mater and dural venous sinuses.

INNERVATION OF THE CRANIAL DURA MATER AND INTRACEREBRAL BLOOD VESSELS

The dura mater encephali is richly innervated by afferent nerve fibers, most of which originate in the ipsilateral trigeminal ganglion, and by sympathetic fibers predominantly arising from the ipsilateral superior cervical ganglion (52,100,178). In addition, a comparatively sparse parasympathetic innervation was described (5,52). The innervation of intracerebral (pial) blood vessels is similarly organized (67,173), but with more parasympathetic fibers that originate mainly from the internal carotid and sphenopalatine ganglia (172). Several studies described neuropeptide immunoreactive nerve fibers in the dura mater (99,183) and around cerebral (pial) blood vessels in different species including man (50,117,177). Meningeal nerve fibers immunoreactive for substance P (SP), neurokinin A, and calcitonin gene–related peptide (CGRP) are thought to belong to the afferent (sensory) system, and nerve fibers immunopositive for neuropeptide Y are most likely of sympathetic and those immunoreactive for vasoactive intestinal polypeptide of parasympathetic origin. Light and electron microscopic studies of the rat dura mater have shown that the peptidergic (sensory) nerve fibers form a dense network both around blood vessels as well as in nonvascular regions (99,132,171) (Fig. 10-1).

CGRP-immunoreactive nerve fibers and trigeminal ganglion cells innervating the meninges are much more abundant than SP-immunoreactive afferents (178), suggesting an enrichment of CGRP in trigeminal fibers that supply