Med. J. Malaysia Vol. XXXII No. 2, December, 1977

Pathway for pain – some anatomical and clinical considerations

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Introduction

PAIN has been aptly described by Sherrington as the "psychical adjunct of an imperative protective reflex". Associated with it is a strong emotional component, and a "built-in" unpleasant affect. This paper attempts to analyse the anatomical pathway involved in pain sensation, and some common clinical applications of this basic knowledge.

Receptors for pain

The end-organs for pain are free, naked, or unencapsulated nerve-endings found in almost every tissue of the body. These endings are believed to be concerned in the perception of other modalities of sensation, like temperature, also. It is pertinent to note that both pain and temperature have protective functions; giving warning of real or potential injury, and hence are known as nociceptive (noceo; to injure) senses. They are phylogenetically old sensory modalities, and share a common pathway in the central nervous system.

Fibers transmitting pain impulses

White and Sweet (1965) showed that transmission to the central nervous system occurs through two fibre systems. The first are small, Type A fibres, with a thin myelin sheath; an average diameter of 2–5 microns; and conduction velocities of around 12–30 metres/second. These fibres conduct "fast-pain" which is first perceived, and is sharp and localised. The second type of fibres are Type C fibres. These are unmyelinated, with an average diameter of 0.4–1.2 microns, and conduction velocities of around 0.5–2 metres/second. Impulses travelling along these fibres produce "slow-pain" which is diffuse, disagreeable, and of a dull and acting character.

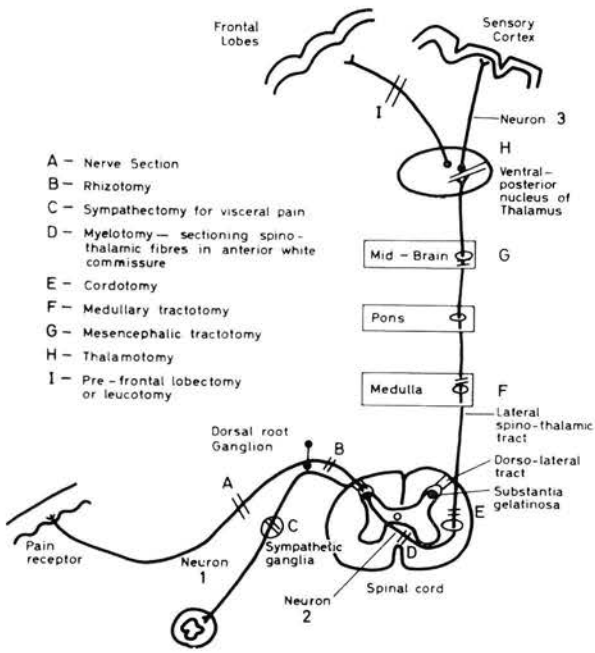
Pathway for the body

(a) *First order neurons*

The first order neurons of the Type A and C fibres have their cell bodies in the dorsal (posterior) root ganglion. The neurons are pseudo-unipolar, of moderate size, with their peripheral processes (Type A and C fibres) bringing in pain formation, and their central processes entering the spinal cord. The central processes enter the dorso-lateral fasciculus (zone of Lissauer) where they give rise to ascending and descending branches which travel for one or two spinal segments only. Finally, they end in the substantia gelatinosa of Rolandi, which is mainly made up of Type II Golgi neurons. The axons of the Type II Golgi neurons are confined to this nucleus, or may ascend in the dorso-lateral fasciculus, connecting adjacent regions of the substantia gelatinosa.

(b) *Second order neurons*

The second order neurons are located in the nucleus proprius or the chief sensory nucleus of the dorsal (posterior) horn of the spinal cord. Pearson (1952) found that most of the Type C fibres relay their impulses through the Golgi Type II neurons, of the substantia gelatinosa, to cells of the nucleus proprius. Type A fibres bypass the substantia gelatinosa and end directly on neyrons of the nucleus proprius. The axons of cells of the nucleus proprius (tract cells) cross the mid-line of the spinal-cord, passing through the anterior white and grey com-



Pathway for pain for the Body and some anatomical sites for surgical relief of pain.

missure, and then turn upwards in the antero-lateral funiculus of the opposite side. The tract thus formed is the lateral spino-thalamic tract (for pain and temperature), and as this tract ascends up the spinal cord, there is some spatial and temporal organisation within it. Information from the sacral and lower limb areas lies dorso-laterally, and from the cervical region and upper-limb ventro-medially, with the lumbar and thoracic areas in an intermediate position.

The lateral spino-thalamic tract ascends in the medulla, in a position near its lateral surface (Monakow's area), lying between the inferior olivary nucleus and the nucleus of the spinal tract of the trigeminal nerve. Proceeding upwards in the dorsal pons, its position is again ventro-lateral. In the mid-brain, the tract lies close to the tegmentum, and eventually it terminates in the ventral-posterior-lateral (VPL) nucleus of the thalamus.

Some fibres of the lateral spino-thalamic tract cross in the posterior commisure to end in the contralateral VPL nucleus of the thalamus. Thus, there is bilateral representation of pain at the thalamic level (Bowsher, 1957). Only a small percentage of fibres in the lateral spino-thalamic tract reach the thalamic relay stations, and a large number stop at lower levels in the reticular formation of the medulla, pons, and mid-brain, and are called spino-reticular and spino-tectal fibres.

(c) *Third order neurons*

The cell bodies of these neurons lie in the ventral-posterior-lateral nucleus of the thalamus. In this nucleus, the lower limb and sacral areas are again represented dorso-laterally, and the upper limb and cervical regions ventro-medially. This thalamic nucleus has connections with other thalamic nuclei, but its main projection is to area 3 of the sensory cortex which is located in the post-central gyrus. Area 3 lies in the posterior wall of the central (Rolandic) sulcus. Some authors consider cortical representation as very minor and less significant than thalamic representation. It is certain that crude appreciation of pain can occur at the thalamic level, but cortical analysis is necessary for more meaningful and discriminative interpretation, like locating the precise source of the pain, its severity and quality. In the post-central gyrus, the contra-lateral half of the body-form or homunculus is represented in an inverted form. The sequence is the head, neck, upper-limb, and trunk, followed by representation of the leg, foot, and ano-genital areas on the medial surface of the hemisphere. The cortical areas for some parts of the body, like the hand, is unusually large, providing for maximum sensory discrimination.

Some recent concepts

The spino-thalamic tract contains fibres proceeding to the thalamus, and also has spino-reticular and spino-tectal fibres ending in the reticular formation of the brain stem. This long-fibre system can thus be sub-divided into the polysynaptic system and the paucisynaptic system. The polysynaptic system is a phylogenetically old pathway and concists of chains of short neurons ending in the reticular formation and the thalamus. The paucisynaptic system is a more recent evolutionary development and consists of three orders of neurons having their cell bodies in the dorsal root ganglia, nucleus proprius, and the sensory nuclei of the thalamus, respectively. If the paucisynaptic system is interrupted, pain impulses can still be transmitted by switching onto the polysynaptic system.

In addition, a short system has been described, though anatomical demarcation of this system is scanty. It probably consists of short relays at a spinal level.

Some spino-thalamic fibres end in other thalamic nuclei as well, such as the mid-line nuclei and the reticular nuclei, and constitute the diffuse projection system of the thalamus. The polysynaptic pathway which ends in the reticular formation also contributes to this diffuse projection system of the thalamus. This entire complex is referred to as the spino-

reticulo-thalamic system, and has the property of transmitting diffuse, poorly-localised pain that persists for a long time even after the stimulus is removed. This concept has been accepted by workers dealing with the treatment of pain by stereo-tactic surgery.

Pathway for the head

The peripheral fibres are found in the branches of the ophthalmic, maxillary, and mandibular divisions of the trigeminal nerve. A small part of pain sensation from the head (Fig. 2) is carried through the facial, glosso-pharyngeal, and vagus nerves from the tongue, pharynx, oesophagus, larynx, external auditory meatus, middle-ear cavity and Eustachian tube. The cell-bodies of the first order neurons lie in the trigeminal ganglion, and the sensory ganglia of the facial, glossopharyngeal, and vagus nerves. The central processes from all these ganglia enter the pons and medulla, and then run caudally. These descending fibres constitute the spinal tract of the trigeminal nerve. The fibres terminate in the nucleus of the spinal tract of the trigeminal nerve (nucleus caudalis) which lies in the lateral medulla and the upper three cervical segments of the spinal cord. The second order neurons have their cell-bodies in this nucleus, and their axons cross the mid-line and run upwards in the trigemino-thalamic tract (trigeminal lemniscus). This tract terminates in the most medial part of the ventral-posterior nucleus of the nucleus, which has been variously labelled as the ventral-posterior-medial (VPM) nucleus, the arcuate or the semilunar nucleus. Third order neurons from this thalamic nucleus relay via the internal capsule to the area for the head in area 3 of the sensory cortex.

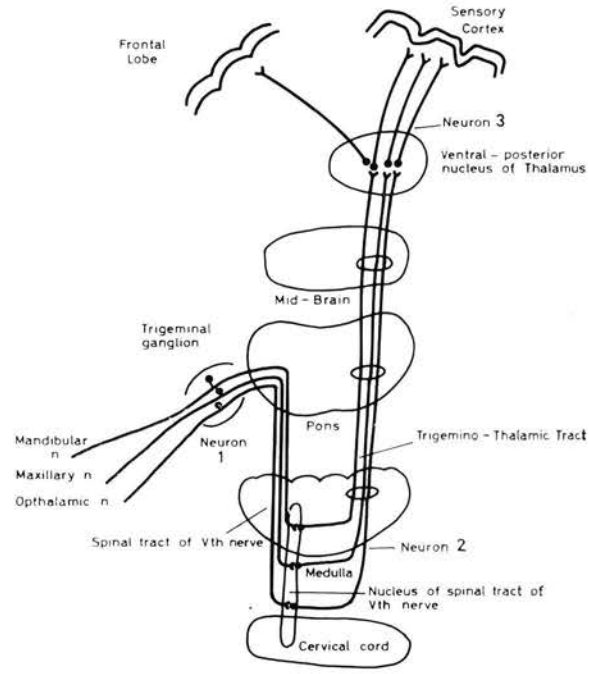
The trigemino-thalamic tract is now believed to have a bilateral distribution ending in the VPM nucleus and also in the diffuse thalamic system. A polysynaptic pathway has also been described with a bilateral projection to the reticular formation of the brain-stem and the diffuse thalamic system.

Pathway for visceral pain

The pain-receptors lie in the walls of hollow viscera. The afferents travel through sympathetic and parasympathetic nerves, and pass through the sympathetic chain before entering the dorsal roots. They travel the same path as somatic sensation. The cortical area for visceral pain are intermixed with somatic areas.

Stimuli causing pain

A wide variety of stimuli can cause pain receptors to be activated. Electrical, thermal, mechanical, and chemical agents are believed to cause the liberation of a chemical agent, possibly a kinin, which then



Pathway for pain for the Head

stimulates the free nerve endings. Histamine probably acts by causing local release of kinins. Muscle pain, e.g. in angina pectoris and intermittent claudication, is believed to arise from local ischemia caused by pathological obliterative changes in blood vessels supplying the area concerned. The chemical agent released in response to ischemia was identified as "Lewis P substance", which is probably again a kinin. Deep pain, arising from ligaments or bone, is poorly localised, has a nauseating effect, and is associated with spasm of overlying skeletal muscles. The resultant ischemia from this spasm causesthe release of chemicals which stimulate pain-receptors in muscle. It is accompanied by autonomic changes, like sweating and a fall of blood pressure.

Visceral pain

It tends to be poorly localised and can be of a severe intensity, Other visceral afferents may be stimulated at the same time as pain-receptors, and associated phenomena like nausea and vomitting can thus be accounted for. In inflammatory conditions of viscera which involve the parietal peritoneum, there is reflex spasm or "guarding" of the overlying muscles of the anterior abdominal wall.

Referred pain

The classical examples are that of cardiac pain being referred to the inner aspect of the left arm, and diaphragmatic pain from irritation of the central

tendon of the diaphragm being referred to the tip of the right shoulder. Usually, the area where pain is referred to shares the same spinal segment for its sensory nerve supply as the area from where the pain originally arises. By convergence, the first order neurons from the two areas could synapse upon the same second order neuron in the nucleus proprius; and pain impulses coming in from the primary area may be interpreted as coming from the referred area.

Gate control theory of pain – after Melzack and Wall

It is believed that the rate of incoming impulses via the Type A and C fibres are controlled by the cells in the cerebro-spinal ganglia, and these cells can transmit only a certain number of impulses per unit time. The substantia gelatibosa acts as another "gate", and can be facilitated or inhibited by impulses reaching it along collaterals for other sensory modalities. Proprioceptive fibres, which travel in the dorsal columns, send collaterals to the substantia gelatinosa, and can cause inhibition of pain transmission. Thus, vigorous shaking of the hands, as after a burn, causes a volley of proprioceptive impulses to travel in the dorsal columns of the spinal cord, and their collaterals can cause inhibition of the substantia gelatinosa, thereby reducing the severity of pain.

The "gate" in the substantia gelatinosa is also under the influence of higher centres, and can be inhibited by impulses coming from the cerebral cortex. Such inhibitory influences from higher centres can explain why pain during combat and sport is not felt as intensely as under normal circumstances. The gate-control theory of pain has been used to explain the basis for acupuncture being successfully used for pain-relief. It is believed that a volley of impulses travelling to the spinal cord from rapid stimulation of acupuncture needles, inserted at appropriate points, wound tend to block impulses from a painful area because the hypothetical "gate" can only transmit a certain number of impulses per unit time.

Clinical considerations

1. Pain fibres can be stimulated by inflammatory lesions in peripheral nerves (peripheral neuritis) or in the dorsal roots (radiculitis). Pressure on the nerve root, as by a herniated intervertebral disc, causes stimulation of both pain and temperature fibres, thus explaining the pain and burning sensation in the area supplied by the affected nerve roots.
2. In syringomyelia, where there is progressive cavitation of the central canal of the spinal cord, the decusating pain and temperature fibres are progressively encroached upon. The disease process is usually limited to the cervical segments of the spinal cord, and there is loss of pain and temperature in the hands, arms, and shoulders on both sides producing "yoke-like.' anaesthesia. However, touch sensation is preserved because it partly travels, on the same side, through the dorsal white columns, and this phenomenon is referred to as dissociated anaesthesia.
3. Spinal hemisection causes loss of pain and temperature, below the level of the lesion, on the opposite side of the body, because of the crossing-over of the second-order neurons in the spinal cord.
4. In infarction of the brain-stem, produced by occlusion of the posterior inferior cerebellar artery, the lesion affects the lateral medullary area where the lateral spino-thalamic tract ascends and where the spinal tract of the trigeminal nerve descends. There is contralateral loss of pain and temperature in the body, and ipsi-lateral loss over the face. The resulting syndrome is known as Wallenberg's syndrome, and includes other features like bulbar palsy, and ipsilateral cerebellar signs.
5. The thalamic syndrome, produced by vascular lesions involving the sensory nuclei of the thalamus, causes exaggerated, perverted, and disagreeable responses to minor cutaneous stimulation.

Surgical relief of pain

An anatomical knowledge of the pain pathway enables one to understand clearly the various surgical procedures that have been devised for the relief of intractable pain. In Fig. 1, one can see that this interruption of the pain pathway can be done by peripheral section or avulsion of the nerve; dividing the dorsal nerve roots (rhizotomy) will also cause loss of touch and proprioception but will produce no motor deficits; or by sympathectomy for the relief of visceral or cardiac pain. In the spinal canal, the nerve roots can be blocked by extradural or subarachnoid injections of phenol or alcohol. In the spinal cord, medulla, or mid-brain, the lateral spinothalamic tract can be divided by the operations of cordotomy, medullary tractotomy or mesencephalic tractotomy respectively. These operations are usually reserved for intractable pain in the terminal cancer patient. The results are often disappointing, leading to the speculation that other pathways may be involved in pain transmission as well. Pre-frontal

leucotomy or lobectomy are designed to cut off the deep connections of the thalamus and sensory cortex with the frontal lobes. These patients often obtain considerable relief. Although they can still feel pain, it does not bother them. The operation serves to dissociate pain from its unpleasant or subject affect.

Other methods for relief of pain

The general practitioner must never forget the value of psychological support, social and environmental help, and the use of placebos in dealing with those patients affected by a painful malady. Some narcotic analgesics have a central action in lowering pain perception; whereas steroids, aspirin, and related drugs produce pain-relief by reducing inflammation. Aspirin is believed also to block peripheral chemoreceptors. Tranquilisers, sedatives, and antidepressants act by modifying the reaction to pain. Atropine probably relieves pain by causing relaxation of smooth muscle, and skeletal-muscle relaxants are effective because they relieve spasm. For trigeminal neuralgia, drugs like Tegretol and Dilantin are effective, but in resistant cases, injection of alcohol or phenol into the trigeminal ganglion or even surgical division of the affected nerve root may be considered. Deep x-ray therapy, chemotherapy, and endocrine therapy are usually reserved for bone-pain of endocrine-dependant metastases. Local anaesthetics act by blocking peripheral nerve endings and can be used to produce analgesia for minor operative procedures. Acupuncture and hypnosis are becoming more popular with general practitioners nowadays, thus increasing their armanterium in tackling the problem of pain which afflicts a very large percentage of their patient.

Conclusion

The clinical management of pain is a problem that continuously confronts the physician, but there are still wide gaps in our knowledge regarding the structure and physiology of pain receptors and the central pathways mediating this sensory modality. It is hoped that a sound knowledge of the anatomical pathway for pain, outlined earlier, will help the doctor understand some of the clinical phenomena produced when this pathway is interferred with by pathological processes, and also rationalise the many and varied methods available to produce relief of pain.

Acknowledgement

Grateful thanks to Mrs. S. P. Lee for her typing assistance.

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