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Visceral Nociception: Peripheral and Central Aspects of Visceral Nociceptive Systems

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Visceral nociception: peripheral and central aspects of visceral nociceptive systems

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Discomfort and pain are the sensations most commonly evoked from viscera. Most nociceptive signals that originate from visceral organs reach the central nervous system (c.n.s.) via afferent fibres in sympathetic nerves, whereas parasympathetic nerves contain mainly those visceral afferent fibres concerned with the non-sensory aspects of visceral afferent function. Noxious stimulation of viscera activates a variety of specific and non-specific receptors, the vast majority of which are connected to unmyelinated afferent fibres. Studies on the mechanisms of visceral sensation can thus provide information on the more general functions of unmyelinated afferent fibres. Specific visceral nociceptors have been found in the heart, lungs, testes and biliary system, whereas noxious stimulation of the gastro-intestinal tract appears to be detected mainly by non-specific visceral receptors that use an intensity-encoding mechanism.

Visceral nociceptive messages are conveyed to the spinal cord by relatively few visceral afferent fibres which activate many central neurons by extensive functional divergence through polysynaptic pathways. Impulses in visceral afferent fibres excite spinal cord neurons also driven by somatic inputs from the corresponding dermatome (viscero-somatic neurons). Noxious intensities of visceral stimulation are needed to activate viscero-somatic neurons, most of which can also be excited by noxious stimulation of their somatic receptive fields. The visceral input to some viscero-somatic neurons in the spinal cord can be mediated via long supraspinal loops. Pathways of projection of viscero-somatic neurons include the spino-reticular and spino-thalamic tracts. All these findings give experimental support to the 'convergence–projection' theory of referred visceral pain.

Visceral pain is the consequence of the diffuse activation of somato-sensory nociceptive systems in a manner that prevents accurate spatial discrimination or localization of the stimuli. Noxious stimulation of visceral receptors triggers general reactions of alertness and arousal and evokes unpleasant and poorly localized sensory experiences. This type of response may be a feature of sensory systems dominated by unmyelinated afferent inputs.

1. Introduction

The experience of pain in normal subjects is the consequence of injury, damage or potential damage of the skin, subcutaneous tissues or internal organs. As a normal sensory experience pain has a protective role and like all other sensations the feeling of pain results from the excitation of peripheral sensory detectors which activate the appropriate spinal cord pathways and their sensory nuclei within the central nervous system (c.n.s.). However, like all other forms of normal sensory experience, the final perception of pain will depend on the interactions and modulations of the sensory message that take place at all relay stations within the c.n.s. Thus, a normal individual can have different pain experiences under similar conditions of peripheral

noxious stimulation. Psychological, cultural, social and religious factors acting via c.n.s. interactive mechanisms, including those of endogenous anti-nociception, will eventually determine the pain response and behaviour of a normal subject. This type of pain sensation can be termed 'normal pain' and its neurophysiological analysis should follow an approach similar to that of normal vision or normal hearing.

In addition to the feeling of normal pain, unpleasant and aversive sensory experiences can be felt under abnormal or pathological circumstances. In these cases the experience of pain is not the result of the activation of a sensory nociceptive channel via peripheral nociceptors but the consequence of altered nervous function at central or peripheral level. Examples of 'abnormal pain' include the pain of trigeminal neuralgia triggered by light touch of the skin of the face or the pain of the thalamic syndrome that develops after lesions of some thalamic nuclei. Abnormal pain is conceptually a sensory experience similar to the visual or auditory sensations that can be evoked after damage to their respective sensory pathways and result in sensory hallucinations in the absence of peripheral stimuli.

There is a fundamental difference between normal and abnormal forms of pain sensation in that these two types of pain are mediated by quite different neural mechanisms. Normal pain is a sensory experience felt by all normal individuals and evoked by the physiological activation of anatomically intact nerve pathways. Abnormal pain is due to lesion or altered function of neural systems as a consequence of disease. Its presence indicates an abnormality in the functioning of the sensory systems responsible for the integration of nociceptive messages. Abnormal pains are only present in a minority of subjects and are always associated with lesion or disease of the neural sensory mechanism.

The distinction between normal and abnormal pain is particularly relevant in the field of visceral nociception. Normal visceral pain can occur under circumstances not necessarily associated with injury, whereas extensive damage to some viscera may not evoke painful sensations (see Cervero (1980, 1983*c*) for reviews). The protective role of normal visceral pain has been repeatedly questioned (Leriche 1939) as there seems to be little need for painful sensations associated with situations that cannot be improved by natural therapy. On the other hand, many forms of abnormal visceral pain can be evoked by lesions or disease of visceral sensory systems. Visceral pain associated with some forms of malignant growth is a good example of a manifestation of visceral pain due to damage or compression of the peripheral sensory system responsible for the normal transmission of visceral nociceptive messages.

The study of the altered function that leads to the perception of abnormal pain needs to be conducted within the context of the causal disease. Hence, it is likely that the physiopathology of trigeminal neuralgia will be very different from that of cancer pain or phantom limb pain. Attempts to unify all manifestations of pain under a single and common hypothetical mechanism are bound to be fruitless, if not misleading. In contrast, the neurophysiological analysis of normal pain follows the same experimental protocol than that of other forms of normal sensation and can provide some useful models of the peripheral and central mechanisms employed by the nervous system to signal nociceptive events.

In this article, visceral nociception and visceral pain will be dealt with only from the point of view of the neural mechanisms responsible for the integration of normal pain experiences. For the reasons given above, no attempt will be made to use this information in order to postulate hypothesis of abnormal pain mechanisms. All higher mammals have developed a sensory system associated with the signalling of visceral nociceptive events and responsible for

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the experience of visceral pain or for the production of pseudaffective reactions evoked by noxious events. A good deal of information is now available on the functioning of such system. In this paper the current state of knowledge of normal visceral nociception will be reviewed and comparisons will be established with nociceptive systems that mediate other forms of normal pain experience.

2. Visceral nociception and afferent C-fibre function

The sensory innervation of viscera is mediated by afferent fibres that join sympathetic and parasympathetic nerves. It has long been established that the majority of nociceptive signals that originate from visceral organs are conveyed to the c.n.s. by afferent fibres in sympathetic nerves (Schrager & Ivy 1928; Davis *et al.* 1929, 1932; Gernandt & Zotterman 1947; Stulrajter *et al.* 1978). Parasympathetic nerves, like the vagus nerve, appear to contain the afferent fibres responsible for the non-sensory aspects of visceral afferent function such as the maintenance of homeostasis (Schrager & Ivy 1928; Ruch 1947).

The distinction between sensory and afferent innervation of viscera has been previously discussed in some detail (Ruch 1947; Cervero 1983*c*) and highlights a fundamental difference between the mechanisms of cutaneous and visceral sensation. The innervation of the skin is both afferent and sensory since activation of cutaneous receptors always has the potential to evoke sensations. In the case of viscera, some organs have an exclusive afferent innervation (i.e. arterial baroreceptors) whose stimulation does not evoke sensations and some organs have both an afferent and a sensory supply.

Unmyelinated afferent fibres (C-fibres) constitute the largest group of afferent fibres in visceral nerves. A recent study of the fibre spectrum of the splanchnic nerve of the cat has shown a ratio of 10:1 in favour of unmyelinated afferent fibres with only a few hundred small myelinated fibres present in the nerve (Kuo *et al.* 1982). Similar disproportions of A and C afferent fibres have been described in other visceral nerves including the vagus nerve. Afferent C-fibres are also present in large numbers in somatic nerves, but in these nerve trunks they are accompanied by many thin and thick myelinated afferent fibres connected to a variety of cutaneous sensory receptors. The large proportion of afferent C-fibres in visceral nerves and the comparatively small numbers of myelinated fibres in these nerves are the features that make the analysis of visceral sensory systems a good model for the study of the more general sensory functions of afferent C-fibres.

Following Head's proposal (Rivers & Head 1908) that sensations could be separated into two groups: protopathic and epicritic, Ranson (1915) suggested that protopathic sensations were mediated by impulses in unmyelinated afferent fibres. This suggestion forms the basis for the close relationship established by some authors between impulses in afferent C-fibres and unpleasant or painful sensations. However, Head's definition of protopathic sensation included not only the experiences of pain and discomfort but, in addition, all those sensations characterized by radiation to parts other than those stimulated and by failure of the subject to localize accurately the point stimulated. In his argument for the correlation between protopathic sensation and impulses in afferent C-fibres, Ranson (1915) mentions the scarcity of myelinated afferent fibres in visceral nerves as supporting evidence for Head's suggestion that visceral stimulation gives rise to protopathic but not to epicritic sensations. It is quite clear that the type and quality of sensations evoked by visceral stimulation are different from those of the sensations evoked from the skin, particularly in respect to the lack of spatial localization

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and of accurate discrimination of stimulation intensities. It is therefore possible to establish a parallel, as Ranson (1915) had suggested, between the different forms of afferent innervation of the skin and of viscera and the different types of sensory experience evoked by cutaneous and by visceral stimulation. Epicritic cutaneous sensations would be mediated by impulses in myelinated afferent fibres and protopathic cutaneous and visceral sensations would be the consequence of the activation of receptors connected to afferent C-fibres. Visceral sensation can therefore be considered a typical example of a protopathic sensory experience with little contamination by epicritic components.

3. Visceral nociceptors

In a recent review article (Cervero 1983*c*) the concept of visceral nociceptor was discussed in some detail including the description of the different types of visceral receptor that could detect visceral nociceptive signals. Essentially, the argument is whether visceral noxious events are signalled in a similar way and by conceptually similar types of sensory receptor than noxious events in cutaneous and subcutaneous organs.

The skin, muscles, joints and other somatic structures are innervated by a category of sensory receptor that responds specifically to intensities of stimulation within the noxious range. These are the somatic nociceptors whose adequate forms of stimulation are injury and potential damage. A very important factor in the separation of nociceptors as an individual group is the fact that other non-nociceptive sensory receptors in the skin are unable to respond to noxious stimuli in a graded and stimulus related fashion. Such a general category of specific nociceptor has not been found in visceral organs.

Injury and potential damage may not always be visceral noxious stimuli as they do not evoke pain when applied to certain visceral organs. This complicates the analysis of the different types of visceral sensory receptor since the discrimination between noxious and innocuous forms of visceral stimulation is not always simple. Some of the most common forms of cutaneous noxious stimulation, such as heating, may not be visceral noxious stimuli at all. A visceral noxious stimulus should reproduce the circumstances in which a viscus is normally stimulated and should lead to the experience of pain or to the triggering of nociceptive reactions. When searching for visceral nociceptors the association to look for should be between the intensity and quality of the stimulus and the occurrence of nociceptive reactions. Visceral nociceptive afferents should not be able to respond to potential injury of the viscus that they innervate if such an injury does not normally evoke pain.

(*a*) *Specific visceral nociceptors*

Sensory receptors that may fulfil the role of visceral nociceptors have been described in several locations. Baker *et al.* (1980) have described a group of receptors in the heart connected mainly to unmyelinated afferent fibres and specifically sensitive to the chemicals released by the ischaemic myocardium. These receptors are activated only by those forms of stimulation associated with pseudaffective responses indicative of pain and are not excited by stimuli that do not evoke pain even if these stimuli are abnormal or outside the physiological range. In spite of this evidence, an alternative case can still be made for the notion that cardiac nociception is mediated by non-specific receptors using an intensity-encoding mechanism (Malliani & Lombardi 1982).

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In the lungs and respiratory tract, receptors have been found that may be responsible for the cough reflex and the responses to inhalation of irritant gases and aerosols (see Widdicombe (1974) for review). These lung irritant receptors have distinctive properties due to their intrapulmonary site and can be stimulated by pulmonary congestion, micro-embolism, anaphylaxis, atelectasis and pneumothorax. Their activation contributes to the unpleasant respiratory sensation of dyspnoea in various lung conditions, or to the sensation of burning pain that accompanies the inhalation of irritant chemicals. Other types of pulmonary receptor, such as the juxta-pulmonary-capillary receptor or 'J-receptor' have been implicated in the generation of pain in pulmonary oedema and lung embolism (Paintal 1973). Most of these pulmonary receptors are connected to afferent fibres that join the vagus nerve and are therefore part of a visceral nociceptive system mediated via a parasympathetic nerve.

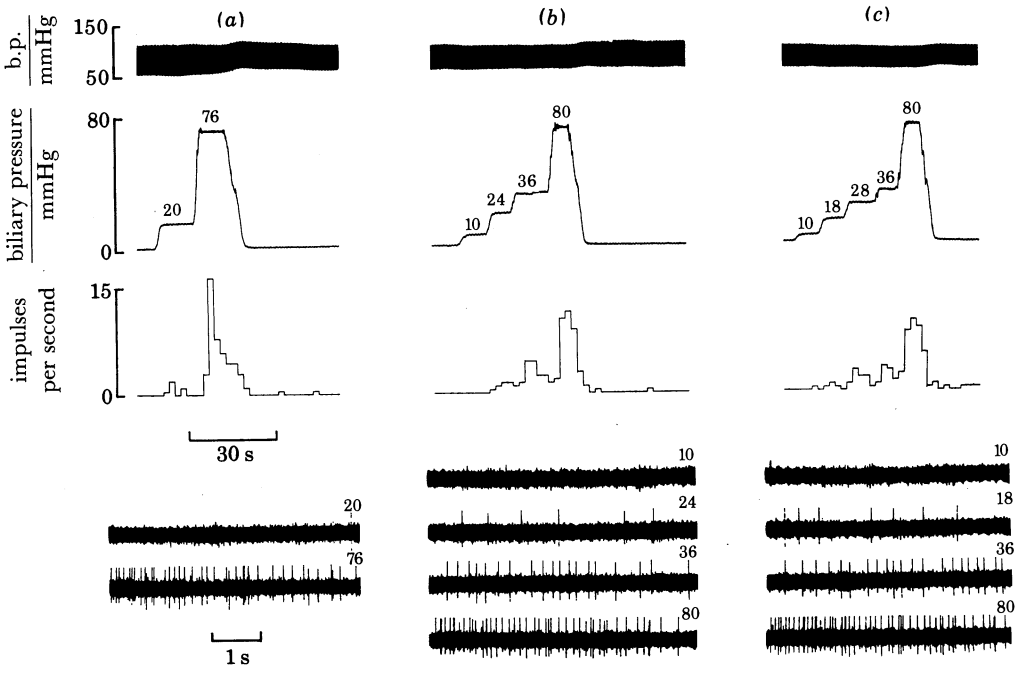

FIGURE 1. Visceral nociceptors in the biliary system of the ferret. Blood pressure (b.p.), biliary pressure (with numerical values), rate of firing of the afferent fibre and sample recordings for different biliary pressures are displayed for each unit (*a*), (*b*) and (*c*). Activity appears only at higher biliary pressures, which evoke transient increases in systemic blood pressure. (From Cervero (1982*a*).) (1 mmHg ≈ 133.3 Pa.)

Cervero (1982*a*) has described in the biliary system of the ferret a population of receptors whose threshold for activation coincides with the maximum physiological levels of biliary pressure and that give further and vigorous responses when biliary pressure reaches noxious levels (figure 1). The nociceptive nature of the level of stimulation was ascertained by pseudaffective reactions such as transient increases in blood pressure. This group of receptors could not be activated by levels of biliary pressure below the intensity necessary to evoke a nociceptive reflex and were therefore considered to be visceral nociceptors.

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(*b*) *Non-specific visceral receptors*

An alternative system by which noxious intensities of visceral stimulation can be encoded is the 'intensity' mechanism based on the 'summation hypothesis' of Goldscheider (1926). In this hypothesis, pain occurs when sensory receptors are excessively stimulated and not as a consequence of the activation of specific nociceptors. An intensity-encoding mechanism has been disproved in relation to somatic pain but some functional types of visceral receptor have been described whose responses are similar to those postulated by the intensity hypothesis.

Pain arising from the alimentary canal has been attributed to the activation of the 'in-series' tension receptors located in the muscular wall of hollow viscera. These receptors respond to passive distensions of the viscus, as well as to isometric contractions, impactions and constrictions (Iggo 1962; Leek 1977). In-series tension receptors respond to levels of mechanical stimulation well below the noxious threshold and raise their frequency of discharge as the stimulus intensity increases. Morrison (1977) described splanchnic afferent fibres whose receptive fields contain up to eight punctate mechanosensitive sites distributed along the superior mesenteric artery and along the vessels in the mesentery and in the walls of the viscera. These serosal receptors respond to light mechanical stimuli as well as to tension applied to the mesentery and visceral peritoneum, to smooth muscle contractions and to visceral distensions. Therefore, Morrison (1977) concluded that they must play a role in the mechanisms of abdominal pain.

Jänig and co-workers (Blumberg *et al.* 1983; Haupt *et al.* 1983) have recently reported the functional properties of a sample of visceral afferent fibres innervating the colon of the cat. These fibres were connected to mechanoreceptors in the colon whose distension thresholds were, in general, below the nociceptive level. Most of these receptors responded with an increased steady state discharge throughout the distension and reacted in a graded manner to higher intra-luminal pressures that reached nociceptive values. In addition, they responded to administration of bradykinin and KCl and to ischaemia of the colon. The authors concluded that these sensory units are involved in visceral nociception from the colon.

It is possible that both specific and non-specific visceral nociceptors act in parallel conveying information to the c.n.s. about noxious visceral events. On the other hand, it could be that the activation of specific visceral nociceptors results in more restricted and clear-cut forms of visceral pain, whereas the vague and dull forms of abdominal discomfort are due to general stimulation of non-specific gut receptors. The precise functional role of specific and non-specific visceral nociceptors remains to be determined.

4. Visceral afferent input to the spinal cord

Visceral nociceptive signals reach the spinal cord by way of a small number of sympathetic nerve trunks. Of these, the splanchnic nerves carry the sensory innervation of many viscera of the upper abdomen. Yet, the actual number of splanchnic afferent fibres is very small compared to the corresponding number of somatic afferent fibres. The greater splanchnic nerve of the cat contains no more than 3000–3500 afferent fibres, 90% of which are unmyelinated (Kuo *et al.* 1982). These few visceral afferents enter the spinal cord between the T-2 and the L-2 segments (McSwiney & Suffolk 1938; Hazarika *et al.* 1964; Mei *et al.* 1970), which suggests that the number of visceral afferent fibres projecting to each individual segment of the thoracic cord must be extremely small.

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Cervero *et al.* (1984) have quantified the proportions of somatic and visceral primary afferents within the lower thoracic dorsal root ganglia (d.r.g.) of the cat. Using anterograde transport of horseradish peroxidase (HRP) through somatic and visceral nerves they described a very small number of visceral d.r.g. cells in these ganglia. Fewer than 7% of the total number of d.r.g. cells in the T-8 and T-9 ganglia were labelled after application of HRP to the central end of the splanchnic nerve. Therefore, more than 90% of the afferent fibres that reach the spinal cord at the segments of projection of the splanchnic nerve are of somatic origin and only a very small minority of the afferent input is made up of visceral afferent fibres.

Spinal cord endings of visceral afferent fibres

Noxious stimulation of viscera results not only in the perception of unpleasant sensory experiences but also in the production of many other general reactions including increases in sympathetic and motor activity. It is therefore surprising that these large and generalized effects can be triggered by such a small number of visceral primary afferent fibres. Recent morphological studies on the mode of termination of visceral afferent fibres within the spinal cord indicate that the widespread effects caused by the activation of visceral afferents are not mediated by extensive anatomical divergence of the visceral projection but are probably the consequence of functional divergence of visceral impulses within the spinal cord.

The pattern of termination of visceral afferent fibres within the spinal cord has been the object of recent HRP studies. Sacral, lumbar and thoracic regions of the spinal cord have been examined in several animal species (Morgan *et al.* 1981; Neuhuber 1982; Ciriello & Calaresu

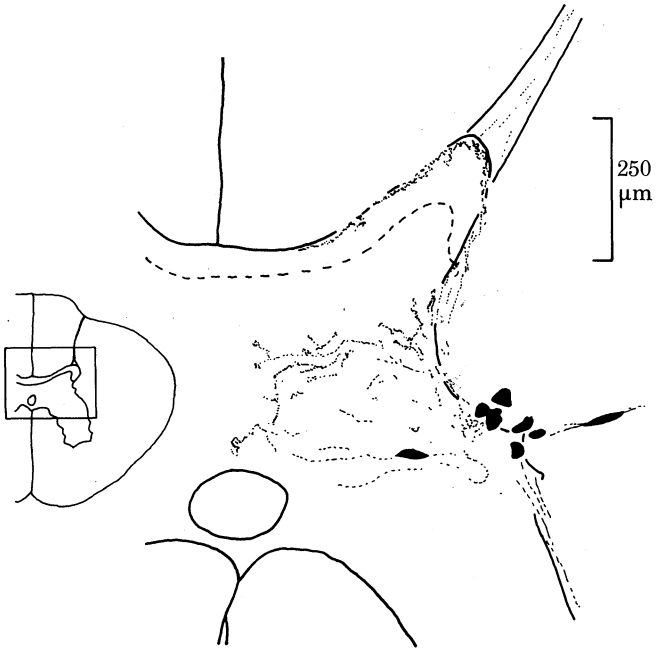

FIGURE 2. Reconstruction from seven 80 μm transverse serial sections of the projection of visceral afferent fibres to the dorsal horn of the T-9 segment of the spinal cord. The dotted line indicates the ventral border of the substantia gelatinosa. HRP was applied to the central end of the splanchnic nerve. The spinal cord area represented in the reconstruction is indicated in the small diagram of the spinal cord. Some profiles of HRP-labelled sympathetic preganglionic neurons have also been included in the reconstruction. (From Cervero & Connell (1984*b*).)

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1983; Nadelhaft *et al.* 1983; Kuo *et al.* 1983; Cervero & Connell 1984*a*, *b*). It is clear from all these studies that visceral afferent fibres display a consistent pattern of central termination throughout the spinal cord with areas of projection in laminae I and V but sparing the intermediate dorsal horn (laminae II, III and IV). Contralateral projections of visceral afferent fibres have also been described (Kuo *et al.* 1983). In a comparative study of the distribution of the somatic and visceral primary afferent input to the thoracic spinal cord of the cat, Cervero & Connell (1984*a*, *b*) observed that the density of the visceral projection to the dorsal horn was substantially lower than that of the somatic projection. This indicates that the few visceral afferents that project to each thoracic segment do not branch extensively within the cord.

Visceral afferent fibres reach the dorsal horn via Lissauer's tract and join medial and lateral bundles of fine fibres that run along the edges of the dorsal horn (figure 2). Fibres from these bundles penetrate the grey matter and terminate within laminae I and V of the dorsal horn. The substantia gelatinosa (lamina II) does not receive a direct visceral projection. Since the majority of visceral afferent fibres are unmyelinated, this observation calls into question the generally accepted belief that most afferent C-fibres terminate in the substantia gelatinosa of the dorsal horn. It would appear that neurons within the substantia gelatinosa are only responsible for the integration of cutaneous sensory signals and not for the relay and processing of all sensory messages.

5. Viscero-somatic convergence in the spinal cord

Dorsal horn and other spinal cord neurons can be classified into two groups depending on the presence or absence of an excitatory visceral input. Some neurons are not driven by visceral afferent fibres and can only be excited from their somatic receptive fields (somatic neurons). Other cells have, in addition to their somatic input, an excitatory visceral drive (viscero-somatic neurons). This form of distribution of the visceral afferent input to the spinal cord has been described in practically all regions of the spinal cord and in many animal species (Pomeranz *et al.* 1968; Gokin 1970; Guilbaud *et al.* 1977; Foreman & Ohata 1980; Cervero 1982*b*, 1983*a*, *b*). Thus, it is possible to conclude that visceral sensation can only be mediated through convergent signals via somato-sensory pathways. No evidence has been found for the presence of a sensory pathway exclusively concerned with the transmission of visceral sensory signals.

In agreement with the anatomical data on the mode of termination of somatic and visceral afferent fibres within the spinal cord, the locations of the recording sites of somatic and of viscero-somatic neurons show a differential distribution in the grey matter (figure 3). Somatic neurons are mainly located in laminae II, III and IV of the dorsal horn whereas viscero-somatic cells are located in lamina I, lamina V and in the ventral horn.

A fundamental difference has been found in the kinds of cutaneous input of somatic neurons from those of viscero-somatic neurons (see table 1). The majority of somatic cells are mechanoreceptive, that is, activated only by low threshold cutaneous mechanoreceptors whereas most viscero-somatic neurons are driven by nociceptors either specifically (nocireceptive) or in addition to their low threshold inputs (multireceptive). As for the nature of the visceral input to viscero-somatic neurons no evidence has so far been produced for a spinal cord projection of the larger Aβ fibres in sympathetic nerves. These fibres, connected to mesenteric Pacinian corpuscles, are known to project to other areas of the c.n.s. via the dorsal columns, but the available evidence indicates that they do not send collaterals to the dorsal horn.

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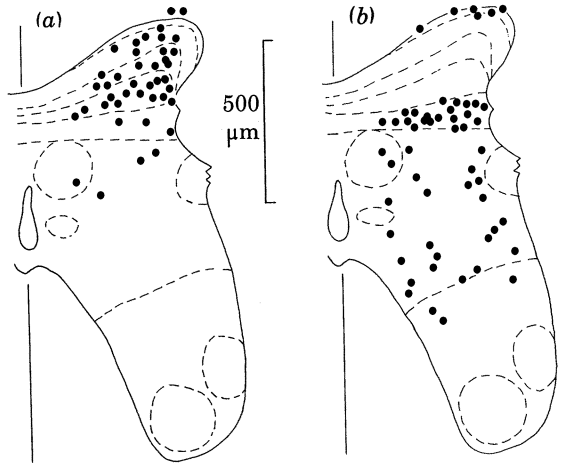

FIGURE 3. Location of the recording sites of (*a*) 41 somatic neurons and (*b*) 55 viscero-somatic neurons plotted on a diagram of the grey matter of the T-11 segment of the spinal cord of the cat. (From Cervero (1983*b*).)

TABLE 1. CUTANEOUS AND VISCERAL INPUTS OF A SAMPLE OF 182 THORACIC SPINAL CORD NEURONS: NUMBERS OF NEURONS (PERCENTAGES)

	visceral input		
skin input	no	yes	total
mechanoreceptive	32 (17.5)	9 (5)	41 (22.5)
multireceptive	20 (11)	74 (40.5)	94 (51.5)
nociceptive	9 (5)	38 (21)	47 (26)
total	61 (33.5)	121 (66.5)	182 (100)

Viscero-somatic neurons are driven by the fine Aδ and C afferent fibres of sympathetic nerves. When natural stimulation of viscera was used to ascertain the nature of the visceral input it was found that noxious intensities of visceral stimulation were necessary to drive viscero-somatic neurons. Foreman & Ohata (1980) have shown that only noxious stimulation of the heart was effective in exciting thoracic spinal cord neurons driven by cutaneous and by cardiac afferent fibres. Similarly, Cervero (1982*b*, 1983*a*) found that noxious intensities of mechanical stimulation of the biliary system were necessary to activate viscero-somatic neurons in the thoracic spinal cord of the cat and Milne *et al.* (1981) have described that viscero-somatic neurons of the spino-thalamic tract in the sacral cord of monkeys could be excited by noxious intensities of mechanical stimulation of the testes.

Not all somato-sensory spinal cord pathways contain axons of viscero-somatic cells. In fact, a clear segregation exists between pathways of projection of somatic and of viscero-somatic neurons. The latter have been found to project through pathways in the ventro-lateral funiculus of the cord, including the spino-thalamic and spino-reticular tracts (Hancock *et al.* 1975; Foreman & Weber 1980; Cervero 1983*b*). On the other hand, pathways such as the spino-cervico-thalamic tract and the post-synaptic dorsal column pathway appear to contain exclusively somatic neurons (Cervero & Iggo 1978; Cervero 1983*b*).

The observations that visceral afferent fibres converge onto somato-sensory spinal cord neurons, that most of these neurons have a somatic nociceptive input, that the visceral input

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to these cells is also of nociceptive nature and that some of these viscero-somatic neurons project through nociceptive pathways provide strong experimental support for all the main postulates of the 'convergence-projection' theory of referred visceral pain (Ruch 1947). The referral of the visceral sensation is therefore the consequence of the activation of pathways normally concerned with the integration of somatic nociceptive signals. These pathways will be activated by their visceral inputs with a different spatial and temporal pattern than that normally generated by their cutaneous drives. Therefore, the sensation produced by visceral stimulation is that of a vaguely localized pain referred to the somatic structures whose afferent fibres project to the same spinal cord area.

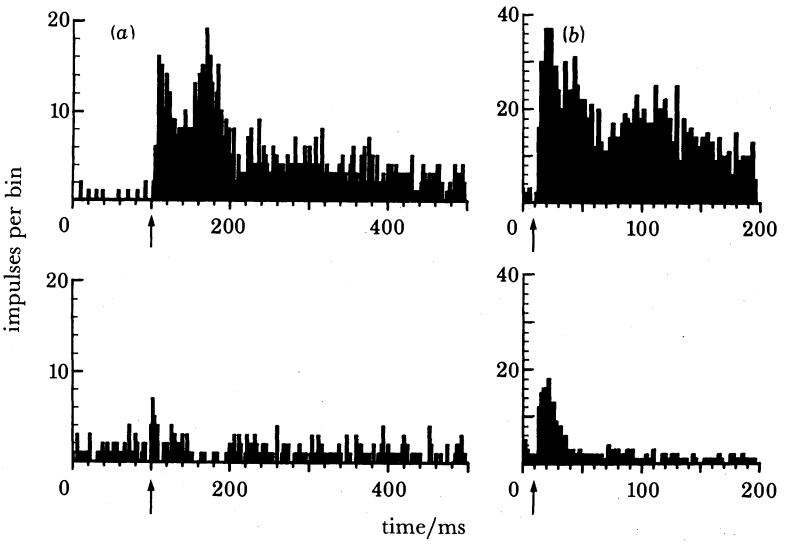

FIGURE 4. Reduction in the responses to splanchnic nerve stimulation of two viscero-somatic neurons in the T-11 segment of the spinal cord of the cat after cold block of the cord at T-7 level. Top, cord intact; bottom, cord blocked. Each histogram is a peri-stimulus–time histogram of 20 stimuli (indicated by arrows). The neuron illustrated in (*a*) shows an increased level of background activity in the spinal state but an almost complete abolition of the response to visceral stimulation. The neuron illustrated in (*b*) shows a reduction in the visceral response after cold block of the cord. (From Cervero (1983*b*).)

The proportion of viscero-somatic neurons found within the spinal cord areas of projection of sympathetic nerves has consistently been reported to be larger than that of somatic cells. This is a clear indication that the few visceral afferent fibres that project to each spinal cord segment are able to produce widespread effects by extensive functional divergence through polysynaptic networks. Moreover, evidence has been recently found suggesting that the visceral input to some viscero-somatic neurons, particularly to those in the ventral horn, can be mediated or reinforced via long supraspinal loops (Cervero 1983*b*). The powerful excitation of some viscero-somatic neurons in the thoracic spinal cord evoked by the stimulation of the splanchnic nerve was reduced or abolished after reversible spinalization of the animals (figure 4).

These findings point to a fundamental difference in the type of central processing of somatic and of visceral sensation. The former is mediated by large numbers of afferent fibres whose central projections show a great deal of anatomical and functional organization. The resulting sensory experience is well localized and highly discriminative. In contrast, visceral sensation

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is mediated by a few afferent fibres that evoke diffuse and widespread effects involving several systems and long supraspinal loops. It is therefore no surprise that the sensory experiences evoked from viscera are poorly localized, dull and diffuse and are accompanied by autonomic and somatic reflexes including increases in motor output and sympathetic outflow.

6. Central organization of visceral nociception

Little is known about the physiology of the supraspinal systems involved in the central integration of visceral nociceptive signals. Neurons in the reticular formation have been shown to respond to noxious stimulation of abdominal viscera (Gokin *et al.* 1977). On the other hand, Carstens & Yokota (1980) have described that many neurons in the thalamic nuclei where the spino-thalamic tract terminates respond to noxious cutaneous inputs as well as to noxious stimulation of the intestine. Viscero-somatic convergence has also been found on neurons of the motorsensory cortex of the cat (Tyner 1979). These cells had a bilateral, long-latency input from small afferent fibres in the splanchnic nerve. The relevance of these findings to the mechanisms of central processing of visceral nociception remains to be studied in further detail.

7. Conclusions

Visceral nociception and visceral pain show some characteristics that are fundamentally different from those of cutaneous and somatic pain. Visceral pain is poorly localized, often referred to distant somatic structures, has little discrimination and in many cases manifests itself by a dull and vague sensation of unpleasantness or diffuse discomfort. Noxious stimulation of viscera induces general reactions and reflexes including increases in somatic and sympathetic outflow. The available experimental evidence suggests that these properties of visceral pain may be the consequence of the diffuse activation, by a few visceral afferents, of somato-sensory nociceptive systems. This form of activation prevents accurate discrimination and localization of the stimuli and evokes general reactions of alertness in the animal.

All these characteristics of visceral pain fit with the traditional view of protopathic sensation (Rivers & Head 1908). Head's proposal was extended by Ranson (1915) who suggested that protopathic sensation was a feature of those sensory systems activated by impulses in unmyelinated afferent fibres. Ranson (1915) proposed that visceral pain could thus be considered an almost pure form of protopathic sensory experience. Our current experimental observations seem to fit well with this proposal. It would appear that impulses in afferent C-fibres evoke a special form of sensory experience (protopathic, in Head's nomenclature) whose features include not only the experience of discomfort and pain but the triggering of general reactions of alertness. Afferent C-fibres could be considered as the peripheral component of a mechanism of general arousal in which the experience of an aversive sensation represents only a proportion of the total response of the system.

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