

MINIREVIEW

The Modulation of Visceral Functions by Somatic
Afferent Activity

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It is of great clinical and theoretical interest to understand how visceral organ functions can be modulated by stimulation of the skin or muscle. For example, in Japan, from the 7th to the 19th century, physical stimulation to the skin and muscles with acupuncture, moxibustion, etc. were commonly used to treat disorders of various visceral organ functions. Many of the therapeutic methods of modern rehabilitation medicine seem to be based on physiological effects of somatic afferent stimulation on autonomic functions. However, it seems that not enough attention has been paid to the clarification of the physiological basis of somato-autonomic reflexes.

The first extensive physiological study of the effects of somatic afferent stimulation on various visceral functions was initiated early in this century. However, analysis of the neural mechanisms of these somato-autonomic reflexes had to await the development of electrophysiological techniques in the early 1930s when ADRIAN *et al.* [1] first recorded autonomic nerve activity. Next, about 20 years ago, both an averaging technique for the analysis of the sympathetic reflex mass discharge activity and a poststimulus time histogram technique for analysis of the unitary activity of surgically dissected sympathetic nerve filaments were introduced. Since then a great deal of new evidence concerning neural mechanisms of the somato-sympathetic reflexes at the level of the sympathetic efferent nerve has been obtained: the central reflex pathway, somatic afferent characteristics, excitatory, and inhibitory reflex characteristics, generalized and segmental reflex organization in the central nervous system, etc. Previous results on the neural mechanisms of somato-sympathetic reflexes at the sympathetic nerve level have already been reviewed by KOIZUMI and BROOKS [30] and SATO and SCHMIDT [53].

Further investigations along this line have been made to analyze neural mechanisms of the somato-autonomic reflexes at the level of various autonomic

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effector organs, such as the heart, gastrointestinal tract, urinary bladder, sweat gland, adrenal medulla, etc. These studies have used combinations of recordings of visceral organ parameters and autonomic neural activities influencing those organs. In this minireview, we will focus on recent neurophysiological studies of somato-autonomic reflexes that involve recordings of autonomic efferent nerve activity in combination with effector responses of the visceral organ.

HISTORICAL BACKGROUND

(1) *Somato-sympathetic reflexes*

About a century ago Carl Ludwig and his coworkers recorded blood pressure changes in response to electrical stimulation of limb afferent nerves and studied the modification of these responses after transections of the brain stem in anesthetized animals. They concluded that the pathway of somato-sympathetic reflexes runs from the spinal cord up to the medulla oblongata and back to the preganglionic neurons in the spinal cord. In 1916 Ranson and Billingsley reinvestigated the problem and they introduced the concept of the medullary pressor and depressor centers. Sherrington in 1906 and Brooks in 1933 described a propriospinal reflex pathway for the somato-sympathetic reflexes based on the blood pressure responses of spinalized animals. ADRIAN *et al.* [1] seem to be the first to have succeeded in recording efferent nerve activity directly from the sympathetic nerves. ALEXANDER [2] recorded somatically evoked sympathetic reflex discharges directly from the sympathetic nerves. Schaefer and his colleagues (1958, 1963) [60, 64] reported that somatic afferent stimulation usually elicited generalized massive reflex efferent discharge in all types of sympathetic nerves followed by a generalized postexcitatory depression. Their work established the brain stem as the primary center of the somato-sympathetic reflexes.

BEACHAM and PERL [5] first recorded a sympathetic reflex discharge of spinal origin from thoracic and lumbar white rami (i.e., preganglionic neurons) evoked by single shocks to dorsal roots, spinal nerves, and limb nerves in unanesthetized, spinalized cats. A similar spinal reflex was also evoked by single shocks to visceral nerves in unanesthetized spinal cats [17]. A spinal reflex was recorded from some postganglionic branches in the spinal cat [16]. In anesthetized cats with the central nervous system intact, SATO *et al.* [55] and COOTE and DOWNMAN [7] demonstrated two kinds of sympathetic reflex discharges evoked by somatic afferent nerve stimulation, namely early spinal and late supraspinal reflexes. In this way a spinal reflex pathway for somato-sympathetic reflexes has been established in addition to the supraspinal one described earlier. Such a spinal path had already been predicted by Sherrington (1906) and Brooks (1933).

SATO and SCHMIDT [51] introduced an averaging recording technique for the study of somato-sympathetic nerve reflexes, making it possible to measure the magnitude of reflex responses quantitatively. Then, they stimulated various spinal afferent nerves at different spinal levels and recorded mass reflex discharges from

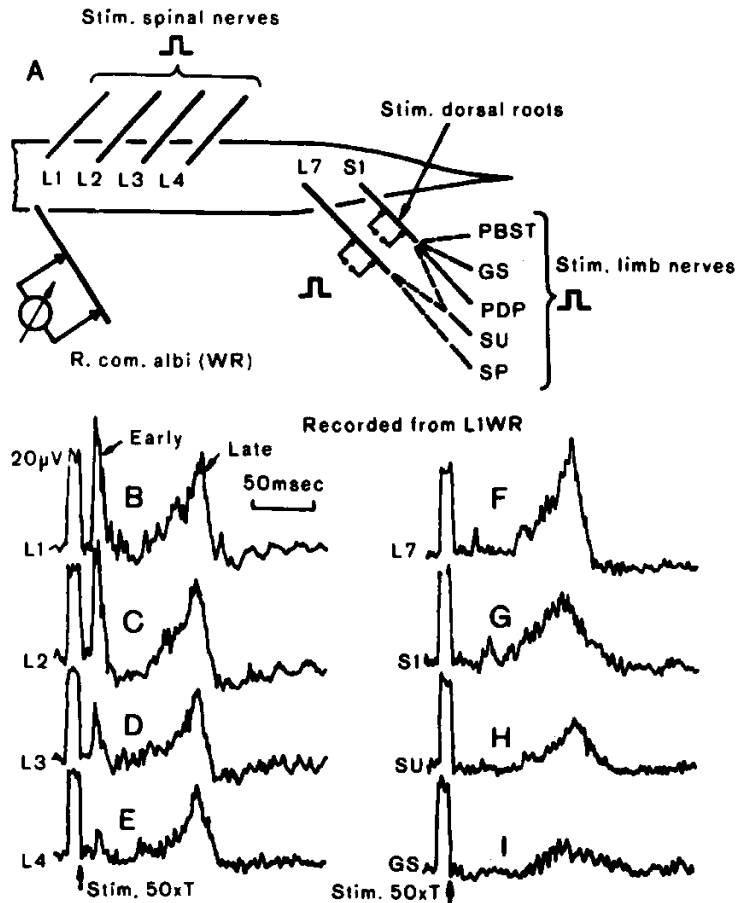


Fig. 1. A: schematic diagram of the arrangement of the stimulation and recording electrodes when recording sympathetic mass reflex discharges from the lumbar white ramus (WR) in cat. The stimuli were delivered to the spinal nerves L1-L4, the dorsal roots L7, S1, and also to cutaneous and muscle hindlimb nerves. B-I: sympathetic reflexes recorded from L1 WR. Single stimuli (indicated by arrows) were given at the end of the calibration pulses to the spinal nerves L1, 2, 3, 4, 7, and S1 (B-G) and to the limb cutaneous nerve (sural nerve or SU, H) and muscle nerve (gastrocnemius and soleus nerve or GS, I) with 50-fold threshold ($50 \times T$) intensity at a repetition rate of 1/4 s. Each specimen is the average of ten individual reflexes. Early means an early spinal reflex component. Late means a late supraspinal reflex component (from SATO and SCHMIDT [52]).

sympathetic preganglionic fibers in anesthetized cats with an intact central neuraxis [52]. Figure 1 illustrates the two different reflex components: (1) the early spinal reflex with a short latency and (2) the late supraspinal (medullary) reflex with a long latency. The figure also shows that the large, early reflex was elicited only by

stimulation of spinal nerves that entered the cord at the same or a nearby segment from which the sympathetic white ramus, which was used for recording, emerged, whereas the large late reflex could be elicited by stimulation of any spinal or hindlimb nerve. This was the first demonstration that the spinal reflex component of the somato-sympathetic reflex response had a strong segmental organization, whereas the supraspinal (medullary) reflex component was generalized. This supraspinal reflex component conforms with investigations in which somatically evoked reflexes were recorded from more peripheral sites of the sympathetic nervous system, such as the renal and cardiac sympathetic nerves [7, 29, 60, 64].

Myelinated and unmyelinated somatic afferents evoke sympathetic reflexes. SATO and SCHMIDT [51] demonstrated that a single volley in hindlimb cutaneous group II ($A\beta$) and III ($A\delta$) fibers were sufficient to induce cervical sympathetic reflex discharges in anesthetized cats. The group II afferent contribution was more dominant than that of group III. The effects of muscle afferent volleys were distinctly different from those from the skin. When stimulating muscle nerves the sympathetic reflex never appeared at a stimulus strength sufficient to excite nearly all group Ia and Ib fibers from the primary muscle spindle receptors and the Golgi tendon organs, respectively. Only when the stimulus strength included most of the group II fibers and extended into the group III range of flexor afferent nerves, a large sympathetic reflex was observed. Volleys in extensor muscle afferents usually evoked a smaller sympathetic reflex discharges.

There have been demonstrations of sympathetic reflex discharges induced by unmyelinated group IV (or C) somatic afferent volleys (the group IV-sympathetic reflex or C-reflex, as it may be called) [14, 31, 59] in addition to the early spinal and late supraspinal reflexes evoked by the myelinated afferents. The group IV-sympathetic reflex usually requires a temporal facilitation of afferent volleys in anesthetized cat. The much longer latency of the group IV-reflex relative to those induced by group II and III afferent stimulation is almost entirely due to the low conduction velocity of the unmyelinated afferents. The group IV-sympathetic reflex discharges are of both spinal and supraspinal origin [41].

It has long been suggested that the spinal reflex component of the somato-sympathetic reflex is depressed tonically at the spinal sympathetic prepanglionic level by inhibitory descending nerve impulses from the brain stem. This was because the spinal reflex component recorded from cardiac and renal sympathetic nerves was often difficult to evoke and appeared more dominant after spinalization at the cervical level [7]. COOTE and SATO [8] demonstrated in addition that the spinal reflex component evoked by intercostal afferent nerve stimulation was tonically inhibited by fibers descending in the ventral quadrant of the ipsilateral spinal cord in cats. Activation of arterial baroreceptor afferent nerves was suggested to contribute to the descending inhibition of the somato-sympathetic reflexes [29]. DEMBOWSKY *et al.* [13] also showed that the spinal component of the somato-sympathetic reflex was modulated by a descending tonic inhibition in the dorsolateral funiculus of the spinal cord. They suggested that these descending inhibitory pathways originated in

the cranial part of area A1 and/or area A5.

As the size of preganglionic sympathetic neurons is smaller than that of motor neurons, systematic intracellular recording has not been easy in sympathetic reflex research. COOTE and WESTBURY [9] first succeeded in recording intracellularly the cat sympathetic preganglionic neuronal activity at the thoracic level and in finding a reflex excitatory postsynaptic potential (EPSP) after visceral afferent stimulation. DEMBOWSKY *et al.* [12] also observed EPSPs after stimulation of the somatic afferent fibers from the thoracic sympathetic preganglionic neurons.

(2) *Somato-parasympathetic reflexes*

IRIUCHIJIMA and KUMADA [20] reported the inhibitory effect of somatic afferent nerve stimulation on spontaneous cardiac vagus nerve activity in anesthetized dogs. TERUI and KOIZUMI [62] further demonstrated that cutaneous somatic afferent nerve stimulation initially inhibited cardiac vagus nerve activity and excited the cardiac sympathetic nerve. These initial responses were followed by the opposite responses, i.e. excitation of the vagus nerve and long-lasting inhibition of the sympathetic nerves. They concluded that the somato-vagal and somato-sympathetic reflex responses were opposing.

The effects of somatic afferent nerve stimulation on parasympathetic pelvic efferent discharges innervating the bladder were studied by BRADLEY and TEAGUE [6] and SATO *et al.* [46] in anesthetized cats. In the cats with central neuraxis intact, single or short tetanic volleys in hindlimb afferents nerves induced reflex discharges in a pelvic vesical efferent nerve branch with 3 distinct reflex components [46]. These 3 reflex components were best observed during micturition contractions, but less so during a pelvic silent phase between vesical contractions or when the bladder was empty and quiet. The latencies of the 3 reflex components were 90, 320, and 770 ms, respectively. The two early reflex components (A1- and A2-reflexes) were evoked by stimulation of group II and III hindlimb somatic afferents. The late third reflex component (C-reflex) was induced by group IV afferent stimulation. MCMAHON and MORRISON [36] recorded an early and a late wave from the pelvic nerve after stimulation of the ventrolateral part of the cervical cord in anesthetized cats. The latency of the early wave was 39 ms, while that of the late wave was 250 ms. The somato-pelvic A2-reflex may use the slow descending tract related to the late wave while the A1-reflex may use the fast descending pathway related to the early wave described by McMahon and Morrison.

SOMATO-CARDIAC REFLEXES

It has long been known from clinical studies that heart rate can be changed by somatic afferent stimulation. Systematic electrophysiological studies of this subject were started by Schaefer's group [60, 64] who first found that the central reflex pathway for the somato-cardiac sympathetic reflex discharges was supraspinal. Their studies were continued by COOTE and DOWNMAN [7] who then observed a

cardiac spinal sympathetic reflex component.

(1) *Cutaneo-cardiac reflexes*

(a) *Mechanical stimulation.* In a majority of anesthetized cats [28] and rats [49] at normal core body temperature, a reflex increase in the heart rate is elicited after natural stimuli, such as pinching (noxious mechanical stimulation) or rubbing (innocuous mechanical stimulation) anywhere on the surface of the body. Innocuous stimulation produces a weak and inconsistent increase in heart rate while noxious stimulation causes a consistent marked reflex increase in heart rate. This cutaneo-cardiac acceleration reflex is produced mainly by a reflex increase in cardiac sympathetic efferent nerve activity. In spinal animals, stimulation of only the chest skin produces a small reflex increase in heart rate. A possible explanation for this difference between animals with an intact central nervous system and spinal animals is that a spinal, segmentally organized sympathetic reflex component of the cutaneo-cardiac acceleration reflex is dominated by a supraspinal, diffusely distributed sympathetic reflex component of the cutaneo-cardiac reflex in the animals with intact central nervous system.

(b) *Thermal stimulation.* A reflex increase in heart rate occurs in anesthetized cats after thermal stimulation at various temperatures to a small areas of skin by use of a thermoprobe [28]. The threshold temperature for evoking cardiac acceleration is between 13 and 19°C for cold stimulation, and around 40°C for warm stimulation. Either innocuous warm (< 45°C) or cool (> 10°C) stimulation causes a small reflex increase in heart rate. Stimulation by heat and cold in the noxious ranges produces a larger increase in the heart rate.

(2) *Musculo-cardiac reflexes*

Injection into a muscle artery of the hindlimb, of algescic substances such as KCl or bradykinin, that are known to excite the thin myelinated group III and unmyelinated group IV muscle afferents [37, 38], can change heart rate [42]. Injection of KCl regularly induces acceleration of heart rate and an increase in blood pressure. With bradykinin both accelerations and decelerations are observed.

(3) *Electrical stimulation of cutaneous and muscle afferents*

In anesthetized cats the heart rate changes when cutaneous and muscle afferents of the hindlimb nerve are stimulated electrically [42]. Repetitive stimulation of cutaneous group II afferents of the hindlimb does not change the heart rate. Cutaneous group III afferent activity leads to an increased heart rate in about 70% of all trials. Increases in heart rate are invariably seen when repetitive group IV cutaneous volleys are elicited. Volleys in group I and II muscle afferents are ineffective, whereas group III muscle volleys provoke bradycardia (in about 40% of all trials) or tachycardia (in about 30%). The nature of the response depends on the experimental situation but is difficult to predict or to modify. Stimulation of group IV muscle afferents invariably induces definite increases in heart rate.

(4) *Articulo-cardiac reflexes*

Movements of the knee joint, especially noxious movements, are known to induce increases in the heart rate in non-anesthetized decerebrated cats [4]. Recently it was shown that activation of small-diameter knee-joint afferents influences such cardiovascular functions as heart rate, blood pressure, and cardiac sympathetic efferent nerve activity in anesthetized cats [44, 57]. These effects are particularly pronounced when the joint receptors are sensitized by inflammation. While movements of a normal knee joint through the normal range do not have any significant influence on heart rate, movements of normal joints beyond this range induce heart rate changes of the same order of magnitude as those elicited by severe pinching of a paw or the skin. In inflamed joints, movements in the normal working range of the joint are just as powerful in their cardiovascular effects as noxious stimuli in normal joints. Forceful movements of inflamed joints are even more powerful in increasing heart rate than intense noxious stimulation of normal tissue.

SOMATO-GASTROINTESTINAL REFLEXES

Somato-gastrointestinal reflexes are well known clinically, and the influence of somatic afferent stimulation on gastro-intestinal motility has been reported for dogs, cats, monkeys, and humans (see KAMETANI *et al.* [27]). The neural mechanisms of cutaneo-gastric reflexes have been investigated in anesthetized rats by recording gastric motility and autonomic efferent nerve activity [27, 47]. Gastric motility was recorded by the intragastric balloon method. When the balloon pressure inside the pyloric antrum was increased to about 100–130 mmH₂O by expansion with water, rhythmic contractile waves at a frequency of 5–6/min corresponding to gastric peristaltic movements could be recorded. Pinching of the abdominal skin often inhibits gastric motility, while pinching of the hindpaw sometimes facilitates gastric motility in anesthetized rats. However, in anesthetized cats these reflex responses are less marked and the facilitatory response cannot be observed [23].

The neural mechanisms involved in both reflex inhibition and facilitation of rat gastric motility by stimulation of the abdominal skin and hindpaw have been determined [27]. Abdominal skin stimulation markedly and consistently increases gastric sympathetic efferent nerve activity without affecting significantly the gastric vagal efferent activity. The increase in gastric sympathetic efferent activity caused the reflex inhibition of gastric motility produced by pinching the abdominal skin. Hindpaw stimulation increases gastric vagal efferent nerve activity whereas gastric sympathetic efferent nerve activity is only slightly increased. The increase in gastric vagal efferent nerve activity seems to be responsible for the reflex facilitation of gastric motility produced by hindpaw pinching.

The inhibition of gastric motility caused by pinching the abdominal skin is almost identical under spinalized and nonspinalized conditions [27, 47]. This supports the concept of a strong segmental organization of the somato-gastric inhibitory reflex response. A dominant segmental organization for both the

inhibitory cutaneo-duodenal reflex [58] and the inhibitory cutaneo-intestinal reflex [33] evoked by abdominal cutaneous pinching has been found in accordance to the segmental organization of the inhibitory cutaneo-gastric reflex in the anesthetized rats. Single electrical stimulation of the lower intercostal afferent nerve produces an early spinal reflex discharge via group II and III afferent excitation and a late spinal reflex discharge via group IV afferent excitation in a splanchnic nerve in both central intact and spinalized rats [39]. Both the early spinal and late spinal splanchnic efferent reflex discharges seem to contribute to the spinal inhibitory reflex responses of gastrointestinal motility due to a rise in gastrointestinal sympathetic nerve activity after pinching stimulation of the abdominal skin.

SOMATO-VESICAL REFLEXES

Cutaneous stimulation of the perineal area evokes micturition in chronic spinal patients and animals (see SATO *et al.* [50]). Stimulation of the perineal skin evokes contraction of the quiescent bladder [10, 48, 50], while inhibiting the large rhythmic micturition contractions [11, 48, 50]. The following is a summary of the results of recent studies on the somato-vesical reflex response in anesthetized rats and cats.

(1) *Cutaneo-vesical reflexes*

(a) *Mechanical stimulation.* When the urinary bladder is slightly expanded, it has a quiescent, or small, rapidly fluctuating tonus in anesthetized rats [48] and cats [50] with central neuraxis intact. Innocuous or noxious mechanical stimulation of the perineal skin produces a transient increase in intravesical pressure as a result of a reflex increase in efferent discharges of the vesical branch of the pelvic nerve. Hypogastric nerves do not seem to be essential for this vesical reflex response. Perineal stimulation produces this vesical excitatory reflex response regardless of whether the spinal cord is intact or transected above the sacral level [48, 50]. This may indicate that the excitatory cutaneo-vesical reflex is a propriospinal and segmentally dominated reflex.

When the urinary bladder is expanded further large, slow, rhythmic micturition contractions synchronized with burst discharges of the parasympathetic pelvic efferent nerve, are initiated. These micturition contractions are completely abolished either by bilateral denervation of the pelvic nerve branches or acute spinal transection at the cervical or middle thoracic level. Therefore, these rhythmic micturition contractions must be initiated by pelvic efferent nerve activity subsequent to integration in supraspinal structures. Noxious stimulation of perineal, abdominal, or chest skin produces in this order of inhibiting effectiveness a reflex inhibition of micturition contractions [48, 50]. The inhibition results from the depression of the burst discharges in the pelvic efferent nerve. The wide input area indicates that there is an intermediate degree of segmental organization of the somato-pelvic reflexes as compared with the other responses mentioned above. Again, sympathetic hypogastric nerves do not seem to be essential for producing this

cutaneo-vesical inhibitory reflex response.

(b) *Thermal stimulation.* Thermal stimulation applied at various temperatures to the perineal skin with a thermoprobe produces responses similar to those evoked by mechanical stimulation [50]. Thermal stimulation in the non-noxious range causes a small and inconsistent response, while thermal stimulation in the noxious range generates a consistent inhibitory response.

(2) *Musculo-vesical reflexes*

Micturition contractions are also inhibited when muscle afferent activity in hindlimb nerves is evoked by close i.a. injection of algescic substances, such as KCl and bradykinin [43]. This inhibition is brought about by the depression of the rhythmic burst discharges of the parasympathetic pelvic efferent nerves. On the other hand, when the bladder is quiescent, the effect on the bladder of algescic chemical stimulation of the hindlimb muscle afferents is excitatory, caused by a reflex increase in pelvic efferent nerve activity.

(3) *Electrical stimulation of somatic afferents*

Repetitive electrical stimulation of group III and IV cutaneous and muscle afferents had an excitatory effect on the quiescent bladder and an inhibitory effect on the bladder during the large, rhythmic micturition contractions, whereas the stimulation of group I (muscle afferent) and II (cutaneous and muscle) afferents was ineffective [43]. When the stimulus intensity was increased gradually, excitatory, and inhibitory effects appeared in the range in which group III afferents were excited, and became more dominant in the range in which group IV afferent stimulation occurred.

(4) *Chronic spinal cats*

Somato-vesical reflexes were studied in chronic spinal cats whose spinal cord was transected at the midthoracic level many months earlier. When the bladder was empty and quiescent, brief repetitive electrical stimulation of a hindlimb somatic nerve increased the pelvic efferent nerve activity which in turn resulted in vesical reflex contractions [46].

When the bladder was expanded, there were spontaneous, large, rhythmic micturition contractions. These observations contradicted the view held since Barrington (1925) that the center for generating the rhythmic micturition contractions is in the brain stem, vesical micturition contractions in chronic spinal cats were still induced by rhythmic burst discharges transmitted in the pelvic efferent nerves from the lower spinal cord. Electrical stimulation of hindlimb nerves produced an initial transient vesical contraction, followed by a long-lasting inhibition of the rhythmic micturition contractions of the expanded bladder consequent to the depression of the pelvic rhythmic burst discharges [46].

SOMATO-SUDOMOTOR REFLEXES

Activation of sweat glands produces changes in both the voltage and impedance of the skin. Reflex changes in skin potential or impedance produced by various stimuli including emotional ones have been called the "galvanic skin reflex" (GSR) or "electrodermal reflex" (EDR) (see a review by WANG [63]). Cat paws have sweat glands, and the cat has often been used to study the GSR.

In spinal cats the GSR can be either excited or inhibited by pinching of the skin or stimulation of cutaneous afferent nerves originating from various spinal segments [22]. Generally speaking, there is a tendency for the GSR to be inhibited when the afferent input enters spinal segments near the outflow of the sudomotor sympathetic nerve fibers to the corresponding paw, whereas excitation occurs when the input is to distant segments. Interestingly, an inhibitory GSR is produced more frequently by ipsilateral than by contralateral cutaneous stimulation. It seems reasonable to assume that this phenomenon results from a mechanism similar to the one which produces the hemihidrosis discovered by TAKAGI and SAKURAI [61] in human beings. Hemihidrosis in humans is a condition where there is excessive perspiration contralateral to the side pressed and reduced perspiration ipsilateral to the side pressed.

SOMATIC AFFERENT MODULATION OF THE SYMPATHETIC
OUTFLOW SUPPLYING THE MUSCLE, SKIN, AND JOINT

JÄNIG *et al.* [26] and KOIZUMI and SATO [32] first demonstrated that a single sympathetic fiber included among the cutaneous and muscle nerves can be reflexly excited or inhibited by electrical stimulation of hindlimb somatic afferent nerves. Especially, it was noted that stimulation of the group IV afferents caused a strong excitatory reflex discharge. Jänig and his coworkers (see a review by JÄNIG [25]) continued research along this line and found that cutaneous noxious stimulation excited sympathetic muscular vasoconstrictor activity, while inhibiting sympathetic cutaneous vasoconstrictor activity. They further demonstrated that most of the reflexes elicited in muscle vasoconstrictors and cutaneous vasoconstrictors by cutaneous stimulation were preserved in chronic spinal cats. Furthermore, noxious stimulation of the skin of the ipsilateral hindpaw elicits inhibition of ongoing activity in cutaneous vasoconstrictor neurons, and this inhibition lasts longer in spinal animals.

SATO and SCHAIBLE [56] demonstrated in anesthetized cats that the spontaneous ongoing activity of the sympathetic postganglionic neurons in a medial articular nerve to the knee joint is not influenced by moving this joint within its normal working range, whereas the neuronal discharges are reflexly increased by noxious movements of the same joint. The response pattern of the articular sympathetic neurons to somatic afferent stimulation appears to correspond to that of muscular sympathetic efferent neurons rather than that of cutaneous sympathetic efferents.

SOMATO-ADRENAL MEDULLARY REFLEXES

Visceral function is influenced by circulating hormones in addition to activity in autonomic nerves. Although recent studies have dealt with the effects of somatic afferent stimulation on autonomic nerve activity, the possibility of similar somato-hormonal secretion reflexes has received little attention. Recently, a new approach was begun in Sato's laboratory using anesthetized animals to study somato-hormonal reflexes. This approach eliminates emotional factors, and it was used to demonstrate that adrenal sympathetic nerve activity and catecholamine secretion from the adrenal gland can be modulated reflexly by somatic afferent activity.

(1) *Cutaneo-adrenal reflexes*

(a) *Mechanical stimulation.* Noxious pinching of the lower chest or hindpaw produces reflex increases in both adrenal sympathetic efferent nerve activity and the catecholamine secretion from the adrenal medulla in anesthetized rats [3] and cats [45]. It has been noted that pinching of the lower chest elicits a longer-lasting response than hindpaw stimulation, i.e., 7–17 min (for lower chest pinching) and 1 min (for hindpaw pinching) after cessation of the stimulation. After spinal transection at the C1-2 level, only lower chest stimulation is capable of producing a reflex response.

Contrary to the responses elicited by pinching, innocuous brushing of the lower chest or hindlimb skin in the same anesthetized rats with intact central nervous system produces reflex inhibition in both adrenal sympathetic nerve activity and catecholamine secretion restricted to the stimulation period. Some slight increases in both nerve activity and secretion rates follow after cessation of the stimulation as a rebound response. It is interesting to note that these depressor reflex responses can not be produced in anesthetized cats with an intact neuraxis [45]. In spinalized rats, brushing of the lower chest or hindlimb skin does not produce the reflex decrease, but, rather has the opposite effect, i.e., a reflex increase in both nerve activity and catecholamine secretion. It was concluded that noxious or innocuous cutaneous stimulation can reflexly modulate the secretion of adrenal medullary hormones via the central nervous system by producing increases or decreases in activity in the adrenal sympathetic efferent nerve. It was shown that a majority of single nerve filaments of the adrenal nerve responded to cutaneous stimulation in a manner similar to the mass nerve discharge responses [24].

(b) *Thermal stimulation.* KUROSAWA *et al.* [34] showed that both cold and warm stimulation of a restricted area of abdominal skin with a thermoprobe in the noxious ranges (below 10°C or above 43°C) caused noticeable reflex increases in both adrenal nerve activity and adrenal catecholamine secretion. Conversely, stimulation in the innocuous range (between 13 and 40°C) did not produce significant changes in these variables. In contrast to the responses to mechanical stimuli, there was no inhibitory adrenal medullary reflex response to innocuous thermal stimulation. This suggests same degree of modality specificity in the type of

somatic afferent fibers capable of producing inhibitory adrenal medullary reflex responses.

(2) *Articulo-adrenal medullary reflexes*

The effects of articular stimulation on adrenal catecholamine secretion and adrenal sympathetic efferent nerve activity have been studied using halothane anesthetized cats [45]. Rhythmic flexions and extensions as well as rhythmic inward and outward rotations of a knee joint within their physiological ranges of motion did not change either the nerve activity nor the adrenal catecholamine secretion. Static outward rotation in the normal working range also had no effect. However, as soon as this static rotation was extended into the noxious range, significant increases in both of these variables were elicited. It was concluded that the adrenal sympathetic nerve response to articular afferent stimulation was responsible for the adrenal catecholamine secretion response. Furthermore, it was demonstrated that these articulo-adrenal medullary reflexes were greatly augmented in animals whose knee joints were artificially inflamed by kaolin and carrageenan. In these animals, reflex responses were elicited by knee joint movements within the normal ranges. There is apparently a supraspinal contribution to the reflex response of the sympatho-adrenal medullary function evoked by knee joint stimulation, as spinal transection at the C2 level completely abolished the response.

Mechanical stimulation of the thoracic or lumbar vertebral joint in anesthetized rats caused an initial decline in adrenal nerve activity followed by a subsequent increase which is due to a reflex depressor response of blood pressure [54].

(3) *Electrical stimulation of somatic afferent nerves*

Electrical stimulation of somatic afferent nerves was used to demonstrate the afferent fiber categories involved in adrenal sympathetic efferent nerve responses in anesthetized rats [21]. In general, high intensity repetitive electrical stimulation, activating both myelinated ($A\beta$ and $A\delta$, or groups II and III) and unmyelinated (C, or group IV) afferent fibers, produced increases in adrenal nerve activity nearly identical to those induced by noxious mechanical or thermal stimulation of the skin innervated by the nerves stimulated electrically. On the other hand, low intensity repetitive electrical stimulation, activating myelinated afferent fibers alone, produced inhibitory responses, similar in character and duration to the responses evoked by innocuous mechanical stimulation of the skin in rats.

Single-shock stimulation of the 13th thoracic nerve evokes various reflex components in the adrenal nerve in rats [21]. These components, in the temporal order in which they appear, are: 1) initial depression of spontaneous activity (the early depression), 2) reflex discharge due to activation of A afferent fibers (the A-reflex), 3) subsequent reflex discharge due to activation of C afferent fibers (the C-reflex), and 4) postexcitatory depression. It was suggested that the decrease in sympathetic activity that occurs during repetitive electrical stimulation of myelinated afferent fibers was due to summation of both the early and postexcitatory

depression components evoked by a single shock stimulation, while the increase in activity during repetitive stimulation of both myelinated and unmyelinated afferent fibers was due to summation of the C-reflex components elicited by a single-shock stimulation. In cats, A-reflex, C-reflex, and postexcitatory depression appear upon a single electrical stimulation; however, no early depression was observed (Sasaki, Sato, Sato, and Schmidt, not published). The lack of the early depression may relate to the fact that neither brushing of the skin nor innocuous movements of the normal knee joint produce any significant inhibitory response in cats.

SOMATO-PITUITARY HORMONE REFLEXES

The milk ejection reflex is well known and its neural and hormonal mechanisms have been well characterized (see review by POULAIN and WAKERLEY [40]). For this reflex, an increase in oxytocin secretion from the posterior pituitary gland after cutaneous stimulation of the breast is essential. This indicates that hypothalamic oxytocin-secreting neuronal activity is modulated by cutaneous breast stimulation [35]. It is therefore of interest to analyze the somatically induced reflex characteristics of various hypothalamic nerve cell activities in association with the secretion of hormones or the hormone releasing factors using anesthetized animals. In anesthetized rats, various segmental cutaneous stimuli can change the activity of hypothalamic oxytocin releasing nerve cells as a reflex response (Akaishi, Robbins, Sakuma, and Sato, not published).

In this respect, although not an oxytocin-secreting neuron, certain supraoptic vasopressin secretory cells have been shown by HAMAMURA *et al.* [19] to be excited by tail pinching and/or by noxious heat stimuli to the hindpaw. Furthermore, it has been shown in anesthetized rats by FELDMAN *et al.* [15] that repetitive electrical stimulation of the afferent sciatic nerve produces a reflex increase in plasma corticosterone via hypothalamopituitary involvement.

SUMMARY

We began by briefly reviewing the historical background of neurophysiological studies of the somato-autonomic reflexes and then discussed recent studies on somatic-visceral reflexes in combination with autonomic efferent nerve activity and effector organ responses. Most of the studies that have advanced our knowledge in this area have been carried out on anesthetized animals, thus eliminating emotional factors. We would like to emphasize again that the functions of many, or perhaps all visceral organs can be modulated by somato-sympathetic or somato-parasympathetic reflex activity induced by a appropriate somatic afferent stimulation in anesthetized animals. As mentioned previously, some autonomic nervous outflow, e.g. the adrenal sympathetic nerve activity, is involved in the control of hormonal secretion. John F. Fulton wrote in his famous textbook "Physiology of the Nervous System" (1949) [18] that the posterior pituitary neurosecretion system

(i.e. for oxytocin and vasopressin) could be considered a part of the parasympathetic nervous system. In the study of body homeostasis and environmental adaptation it would seem very important to further analyze the contribution of somatic afferent input to the autonomic nervous and hormonal regulation of visceral organ activity. Also, some immunological functions have been found to be influenced by autonomic nerves or hormones (e.g. adrenal cortical hormone and catecholamines). Finally, we must take into account, as we have briefly discussed, that visceral functions can be modulated by somatic afferent input via various degrees of integration of autonomic nerves, hormones, and immunological processes. We trust that such research will be expanded to higher species of mammals, and that ultimately this knowledge of somato-visceral reflexes obtained in the physiological laboratory will become clinically useful in influencing visceral functions.

Key words: visceral reflex, somatic afferent, autonomic reflex, somato-autonomic reflex, somato-hormonal reflex.

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