

NEURAL MECHANISMS OF AUTONOMIC RESPONSES ELICITED BY SOMATIC SENSORY STIMULATION

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The nonconditioning reflex is known to have the five components of the classical reflex arc: receptors, afferents, reflex center, efferents, and effectors. In most studies of reflex regulation of the autonomic nervous system, both afferent and efferent pathways have been contained within the autonomic nerves.

The function of many visceral organs is regulated by the autonomic nervous system, while the function of skeletal muscles is regulated by the somatic nervous system. Both autonomic and somatic nervous regulation consist of central descending control starting in the brain, and reflexogenic control. The reflex mechanisms have usually been studied separately or independently in each of the autonomic and somatic nervous systems.

In autonomic reflex regulation, insufficient attention has been paid to the role of somatic afferents. I have been especially interested in the somatosensory regulation of various visceral functions, and I would like to give a brief overview of this subject, focusing upon the results obtained mainly in my laboratory, where we have used anesthetized animals in most cases, thus eliminating the emotional responses following somatic afferent stimulation.

Neurophysiological study of the somato-autonomic reflex, especially of the somato-sympathetic reflex, was first reported by Hans Schaefer and his colleagues in the late 1950's [27]. They stimulated various somatic afferent nerves electrically in anesthetized cats, and they recorded the reflex action potentials (or discharges) from cardiac and renal sympathetic efferent nerves. They found that these reflex discharges involved a central reflex pathway through the brain stem, but not a propriospinal reflex pathway.

In 1965, my colleagues and I found both early spinal reflex components of shorter latency and the late supraspinal central reflex components of longer latency in the lumbar sympathetic trunk following a single electrical shock to a hindlimb sciatic nerve in anesthetized cats [26]. The early spinal reflex persists in spinalized cats.

The somato-sympathetic reflex characteristically has great variability; this has made it difficult to analyze it quantitatively. In 1966, Dr. Robert F. Schmidt and I first introduced the averaging technique, for the study of somato-sympathetic reflex discharges [22]. That method enabled us to find that stimulation of different spinal afferent nerves elicited both early spinal and late supraspinal sympathetic reflex discharges in the lumbar white ramus, and that the late supraspinal reflex component was broadly elicited, while the early spinal reflex component could only be elicited by stimulation of spinal nerves at appropriate spinal levels [23]. In 1973 Schmidt and I introduced a diagram in *Journal of Physiological Reviews* for the reflex pathways involved in the somato-sympathetic reflexes with special reference to somatic afferent characteristics such as the myelinated and unmyelinated, and central reflex components such as the spinal and supraspinal [24] (Fig. 1).

For further analysis of the somato-autonomic reflex, it was necessary to study the reflex responses of various autonomic effector organs in parallel with sympathetic and parasympathetic nerve activity. Based on this necessity, my wife, Yuko Sato, and I, began to work, in 1973, on somato-autonomic reflex responses at the level of various effector organs. Our approach towards this subject was to experiment upon anesthetized animals thereby eliminating emotional responses due to somatic sensory stimulation [25]. In some cases, the autonomic nervous system is closely coupled with the endocrine and immune systems.

For this type of study, we selected gastric motility, urinary bladder contractility, heart rate, cerebral circulation, peripheral nerve circulation, adrenal medullary function, and cytotoxic activity of the splenic natural killer cells. The respective effector organs have a variety of autonomic innervation from the brain and different spinal segmental levels. For this study it was our principal paradigm to use quantitative electrical and qualitative natural stimulation of somatic afferents

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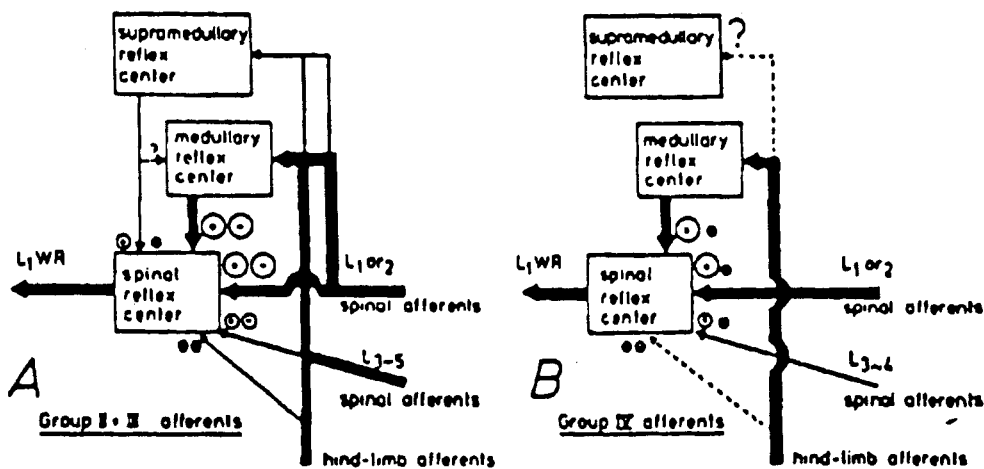


Fig. 1. Central reflex pathways of somato-sympathetic reflexes. A) Central pathways of those reflexes induced by myelinated somatic afferents; B) corresponding pathways for unmyelinated afferents. Thicknesses of various pathways are a measure of their potency. Excitatory or inhibitory effects indicated by + and - signs, respectively. Sizes of signs provide a rough measure of effectiveness of excitatory or inhibitory action (from [24]).

of the skin, muscles, and joints. Further, we always analyzed the efferent pathways of the reflexes, by recording activity from the sympathetic and parasympathetic nerves that innervate the effector organs, and we analyzed the correlation of autonomic nerve activity with the responses of various visceral effector organs during somatic sensory stimulation. In the following, I would like to introduce some results of our studies.

1. SOMATO-GASTROINTESTINAL REFLEXES

Somato-gastrointestinal reflexes are well known clinically. When patients have stomach pain, they often press the abdominal wall. This procedure is thought to decrease gastric motility. On the other hand, stimulation of the legs has long been considered to facilitate gastric motility.

In order to study the neural mechanisms of cutaneo-gastric reflexes, we recorded gastric motility in anesthetized rats using the balloon method. When the balloon pressure inside the pyloric antrum was increased to a certain level, 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 consistently inhibits gastric motility, while pinching of paws sometimes facilitates gastric motility, as shown in the sample recordings of Fig. 2A-F [10]. In Fig. 2G and H circles on the rat indicate the effect on gastric motility of pinching various skin areas. Open circles indicate reflex excitation and filled circles indicate inhibition. The various response magnitudes are indicated by different circle sizes. Clearly, pinching of the abdominal skin produced strong inhibition. Pinching of the middle and caudal ventral, and the dorsal thorax produced moderate or weak inhibition. On the other hand, pinching of the paws produced excitation. Pinching of the nose, forearms, and tail produced a moderate excitation, and pinching of the face, ears, neck, legs, and sacral area produced weak excitation.

The inhibitory response persisted after spinal transection at the cervical level, but disappeared after bilateral severance of the gastric sympathetic nerves [9]. Therefore, the spinal sympathetic reflex seems to be responsible for this inhibition. On the other hand, the facilitatory response disappeared, either after spinal transection at the cervical level, or after bilateral severance of the vagal nerves. Thus, the gastric vagal reflex seems to be responsible for this facilitation.

In fact, whenever abdominal skin stimulation produced gastric inhibition, gastric sympathetic efferent nerve activity was markedly increased, but gastric vagal efferent activity was not significantly affected [9] (Fig. 2L). On the other hand, when hindpaw stimulation increased gastric motility, gastric vagal efferent nerve activity was slightly increased, whereas gastric sympathetic efferent nerve activity was only marginally increased (Fig. 2M).

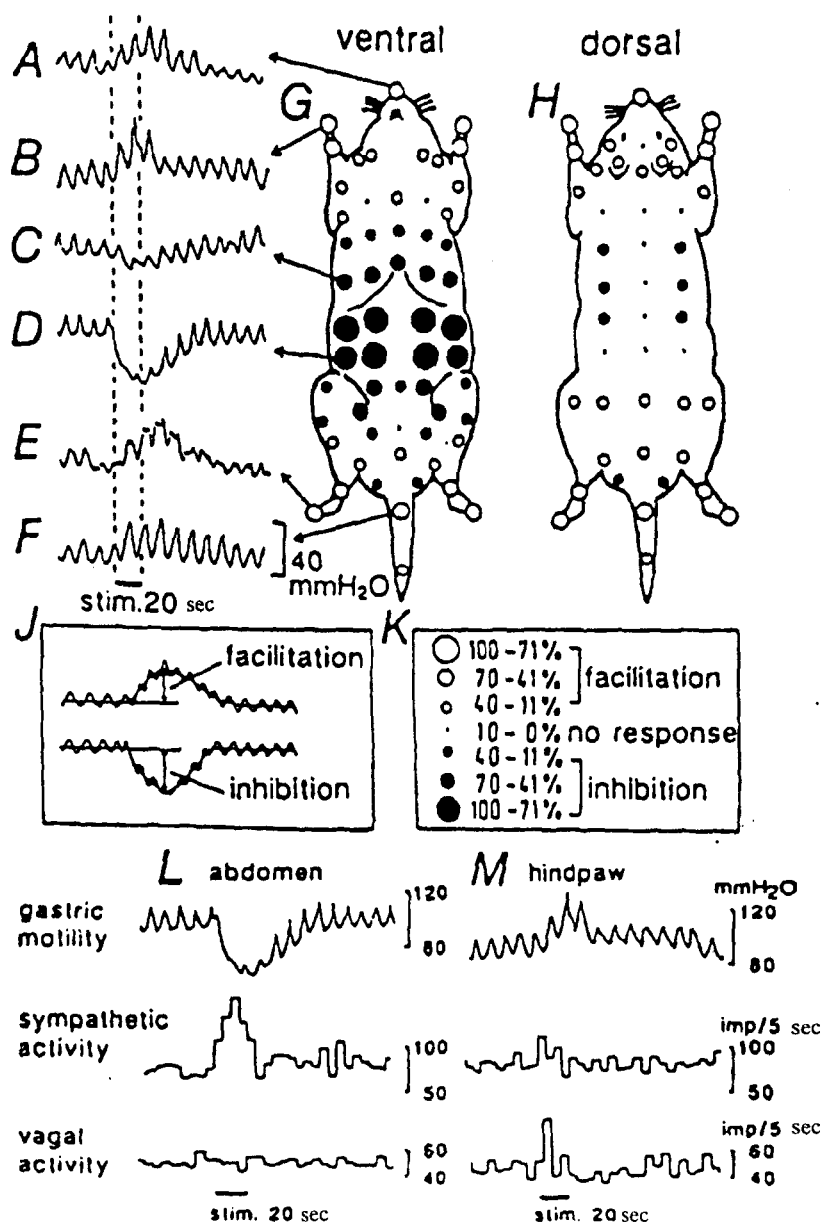


Fig. 2. Effect on gastric motility of pinching various skin areas in rats. A-F) specimen records of gastric motility response. Pinching of 20 sec duration is shown by the bar and vertical dotted lines. G and H) schematic diagrams relating the skin areas pinched to the reflex changes in gastric motility; J) model illustrating the method of estimating the magnitude of the reflex response; K) open circles indicate excitation; filled circles indicate inhibition; circle size indicates magnitude; L and M) effects of pinching abdominal skin (L) and hindpaw (M) on gastric motility and on gastric sympathetic and vagal parasympathetic efferent nerve activity (A-K, from [10]; L and M, from [9]).

Somatic afferents producing gastric reflex responses are not necessarily only cutaneous afferents; muscle afferents are also important. Recently we examined the effects of acupuncture-like stimulation of various segmental areas on gastric motility, using an acupuncture needle, in anesthetized rats [20]. We inserted an acupuncture needle (diameter 340 μ m) into the abdominal or hindpaw skin and underlying muscles at a depth of 4-5 mm and twisted right and left once every second. This stimulation excited both cutaneous and muscle afferent nerve activity, and we obtained almost identical results, whenever we stimulated either skin alone or underlying muscle alone, as we did by cutaneous pinching.

We concluded that the inhibitory gastric response elicited by abdominal skin and muscle stimulation is a reflex response. Its afferent nerve pathway is composed of abdominal somatic afferent nerves, the efferent nerve pathway is the gastric sympathetic nerve, and the reflex center is within the spinal cord. The excitatory gastric response elicited by somatic stimulation of a hindpaw is also a reflex response. Its afferent nerve pathway is composed of hindpaw somatic afferent nerves, the efferent nerve pathway is the gastric vagal efferent nerve, and its reflex center requires the presence of the brain.

2. SOMATO-VESICAL REFLEXES

Clinically, urinary bladder function is also known to be controllable by cutaneous stimulation, and is used to facilitate or prevent urination. We examined the effect of stimulation of various skin areas on the function of the bladder in anesthetized animals. We measured intra-bladder pressure using the intravesical balloon method.

The nearly empty or slightly expanded urinary bladder is quiescent or under only small pressure. Innocuous or noxious mechanical stimulation of the perineal skin provokes a transient increase in intravesical pressure associated with a reflex increase in pelvic parasympathetic efferent nerve activity [18] (Fig. 3I). This response of the bladder exists after spinal transection at the cervical level, but disappears after bilateral severance of pelvic parasympathetic nerves. Stimulation of other skin areas is not effective (Fig. 3A-C). Therefore, this excitatory response is a spinal reflex, and the efferent path is a pelvic parasympathetic nerve.

Further expansion of the urinary bladder produces larger, slower, rhythmic micturition contractions of a frequency of approximately once every minute, synchronized with rhythmic burst discharges of the pelvic parasympathetic efferent nerve. This micturition contraction usually requires the presence of the brainstem. This contraction disappears after acute spinal transection above the sacral level. In chronic spinalized animals, however, the micturition contraction can be generated from the sacral spinal cord. Noxious stimulation of the perineal skin inhibits micturition contractions [18]. The inhibition of the bladder contraction is a consequence of a reflex inhibition of the rhythmic burst discharges of the pelvic parasympathetic nerve (Fig. 3II, III). Again, the efferent path of the inhibitory response is the pelvic nerve.

Similar responses of pelvic nerve activity and bladder contraction were confirmed when acupuncture needle stimulation was delivered either to the perineal skin alone or to the underlying muscles alone [19].

We can summarize by saying that, in anesthetized animals, perineal somatic afferent stimulation elicits two types of reflex responses of bladder contraction, and that the efferent path of these reflexes is in the pelvic parasympathetic nerves. The two types of reflex responses depend on the degree of bladder expansion. When the bladder is quiescent, there is an excitatory spinal reflex response. When the bladder is expanded to a certain degree, the large rhythmic micturition contractions appear as a result of rhythmic burst discharges in the pelvic nerve. Perineal afferent stimulation causes a reflex inhibition of the pelvic nerve burst discharges and results in inhibition of the micturition contractions of the bladder.

3. SOMATO-CARDIAC REFLEXES

Heart rate is very sensitive to various kinds of stimulation, including somatic afferent stimulation. Figure 4A-D shows that pinching stimulation of various skin areas increases the heart rate in anesthetized cats [11]. This response can be regarded as a generalized response and is not affected by bilateral severance of the cardiac vagal nerves (Fig. 4E-H). On the contrary, bilateral severance of the cardiac sympathetic nerves abolishes the heart rate response (Fig. 4J-M). Major involvement of cardiac sympathetic nerves in the response was proved indirectly by cutting the cardiac autonomic nerves and directly by recording cardiac autonomic nerve activity. Direct recording of cardiac sympathetic efferent nerve activity shows that this activity is increased whenever the heart rate is increased [17] (Fig. 4N).

A single electrical shock to a fore- or hindlimb somatic afferent nerve can evoke a reflex discharge of supraspinal origin in a cardiac sympathetic nerve [7]. In anesthetized cats, the latency of this reflex discharge is about 80 to 120 msec. A single shock to a thoracic spinal afferent nerve can produce another reflex discharge of spinal origin in the same cardiac sympathetic nerve. This spinally-mediated reflex has a much shorter latency of about 30-50 msec. This spinal reflex is usually suppressed strongly by the supraspinal structures when the spinal cord is intact. Spinal transection can activate this spinal component.

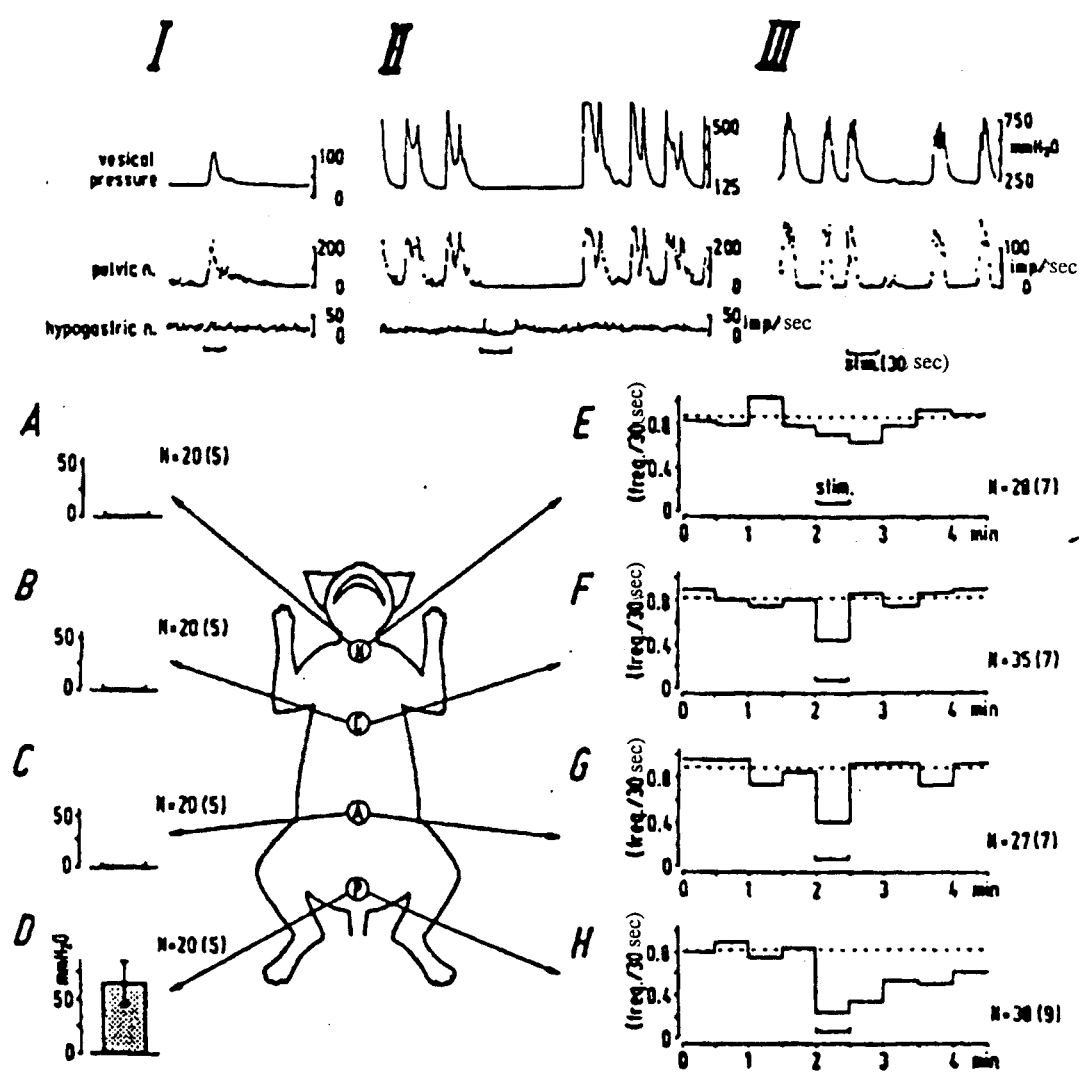


Fig. 3. Effects of pinching the skin on vesical pressure and vesical autonomic efferent nerve activity in cats. I, II, III) Simultaneous recordings of intravesical pressure, pelvic parasympathetic efferent nerve activity, and hypogastric sympathetic efferent nerve activity; stim., pinching for 30 sec. A-D) Reflex changes in the peak amplitude of vesical pressure after pinching the skin when the bladder was quiescent; E-H) peristimulus-time histograms of large rhythmic micturition contractions. Ordinates) frequency of large micturition contractions per 30 sec. Pinched skin areas) neck (A, E), chest (B, F), abdomen (D, G), and perineum (D, H) (from [18]).

In anesthetized rats, the effects on heart rate of pinching stimulation of various segmental skin areas were examined with the spinal cord intact or in the acutely spinalized preparation. In the spinal cord-intact rats, pinching of any segmental skin area is effective, although stimulation of a fore- or hindpaw produces the largest responses. In acutely spinalized rats, pinching applied to the thoracic segmental skin areas produces the larger response of heart rate, while pinching of a fore- or hindpaw becomes ineffective.

These results indicate that a strong segmental organization of the cardiac reflex response exists in spinal rats, and this segmental organization is suppressed by supraspinal structures when the spinal cord is intact. In the spinal cord intact preparation, somatic afferents from various segments ascend the spinal cord to the brainstem, and then descend the spinal cord to the thoracic segments and stimulate the cardiac sympathetic neurons.

4. EFFECTS OF SOMATIC AFFERENT STIMULATION ON CEREBRAL BLOOD FLOW

It may be interesting to question whether somatic afferent stimulation can produce any reflex response in cerebral blood flow, because cerebral blood flow is very important for neuronal activity of the brain. The brain is full of neurons, glia cells, and small blood vessels.

Pinching of a forepaw in the anesthetized rat can increase blood flow in the cortex as shown in Fig. 5A. The flow was measured by laser Doppler flowmetry in this case. After spinal transection at the upper thoracic level, the same stimulation produced the same increase in the cortical blood flow without changing systemic blood pressure (Fig. 5B) [1]. The response of cortical blood flow exists even after total severance of sympathetic and parasympathetic nerves to the brain. Therefore, other unknown vasodilative fibers in the brain were proposed. The result of cortical blood flow in the spinal animal following forelimb pinching was confirmed using the [¹⁴C]iodoantipyrine method.

Concerning the intracranial vasodilative fibers, we proposed intracranial cholinergic fibers originating in the nucleus basalis of Meynert or substantia innominata and projecting to the cerebral cortex [16]. This nucleus is now well known for its profound degeneration during aging or in Alzheimer's disease in human beings. Using anesthetized rats, we found that focal stimulation, either electrical or chemical, of this nucleus, increased cortical cerebral blood flow without any changes in blood pressure. This response is reduced by both muscarinic and nicotinic cholinergic receptor antagonists [5]. Furthermore, during focal stimulation of this nucleus, acetylcholine (ACh) release in the cortex is increased [13]. The cortical extracellular ACh was collected using the microdialysis technique and ACh was measured by high performance liquid chromatography using electrochemical detection. Therefore, it is clear that these intracranial cholinergic fibers can dilate small cortical blood vessels and increase cortical blood flow.

The neurons in this nucleus are excited by pinching of a paw [2]. The excitation of these neurons is particularly strong when pinching a fore- or hindlimb, compared with pinching the face or back. These data of neuronal activity are well in accord with responses of cortical blood flow and ACh content. Both responses of blood flow and ACh are much larger when stimulation is delivered to either a fore- or hindpaw [1, 14] (Fig. 5C, D).

We can conclude that the intracranial cholinergic neurons of the nucleus basalis of Meynert play a vasodilative role in the regulation of cortical cerebral blood flow, and can respond to somatic afferent stimulation and produce the observed responses of cortical blood flow. The somatic afferent regulation of cerebral cortical blood flow might be clinically applied for improvement of disturbed or insufficient cortical blood flow.

5. EFFECTS OF SOMATIC AFFERENT STIMULATION ON PERIPHERAL NERVE BLOOD FLOW

Peripheral nerves receive their oxygen and nourishment, mainly glucose, from blood flowing in the nerve blood vessels, the vasa nervorum. Histochemical studies have demonstrated that the nerve fibers innervating the vasa nervorum contain noradrenaline, acetylcholine, serotonin, and various polypeptides.

Our recent study in rats demonstrates that nerve blood flow in the sciatic nerve is regulated by (1) sympathetic noradrenergic vasoconstrictors emerging from the ventral roots of the spinal cord via the T11-L1 segments, (2) parasympathetic cholinergic vasodilators emerging from the ventral roots of the spinal cord via the L6 segment, and (3) afferent, calcitonin gene-related peptide (CGRP) containing vasodilators entering the dorsal roots of the spinal cord via the L3-S1 segments [8, 21].

In the spinalized rats, somatic afferent stimulation, for example pinching of a hindpaw, can stimulate sympathetic vasoconstrictor fibers and produce a reflex decrease in nerve blood flow, without changing blood pressure [6].

When we cut the dorsal roots, stimulation of the dorsal roots between the L3 and S1 segments for only 10 sec produced a long-lasting, almost 5-6 min, increase in nerve blood flow, independent of changes in mean arterial blood pressure. This long-lasting increase in nerve blood flow appears to be mediated by activation of CGRP containing afferent fibers, innervating the vasa nervorum, because the response was abolished by topical application of a CGRP receptor antagonist [21].

Quite interestingly, nerve blood flow was increased by pinching of the same skin areas, for example a hindlimb, even after destroying the spinal cord totally below the 10th thoracic level. In this preparation, there is no longer a reflex center.

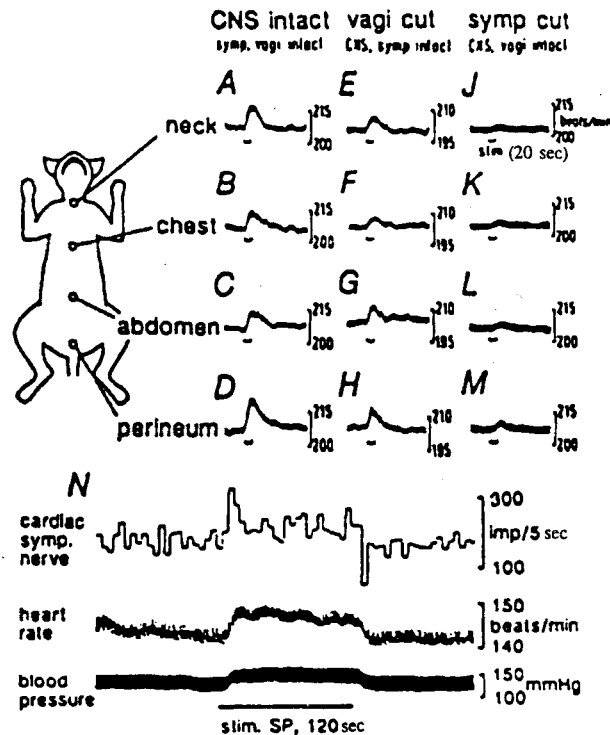


Fig. 4. Effects of pinching the skin on heart rate and cardiac sympathetic efferent nerve activity in cats. A-M) Effects of pinching various skin areas under different conditions. The animal's condition is indicated above the respective recordings. The skin was pinched for 20 sec on the neck, chest, abdomen, and perineum. N) Simultaneous recording of cardiac sympathetic nerve activity, heart rate, and blood pressure during electrical stimulation of hindlimb nerve (superficial peroneal nerve; SP) at 200 times threshold intensity at 10 Hz for 120 sec (A-M, from [11]); N, from [17]).

For this response without the spinal cord, we assume that CGRP-containing afferent fibers are branching at least to both the skin and nerve blood vessels. Stimulation of one branch can excite the other branch, releasing CGRP and resulting in vasodilation of the nerve. This type of response should be a consequence of the axon reflex, as Prof. Nozdratchev mentioned before. This finding is still very new in our line of study. We may need more careful study of the axon reflex between the skin or muscle, and other visceral organs.

6. SOMATO-ADRENAL MEDULLARY REFLEXES

Some of the endocrine organs are regulated by autonomic nerves. For example, chromaffin cell functions of the adrenal medulla are regulated by adrenal sympathetic nerves. Our laboratory has demonstrated that adrenal sympathetic nerve activity is reflexly modulated by somatic afferent stimulation in anesthetized rats. Pinching various segmental skin areas (neck, forepaw, lower chest, abdomen, thigh, hindpaw) produces reflex increases in nerve activity, while brushing various segmental skin areas produces reflex decreases in nerve activity [3, 15].

We measured secretion rates of adrenaline and noradrenaline from the adrenal medulla by collecting blood samples from the adrenal vein. Pinching of the skin increases secretion of both catecholamines, and brushing of the same skin decreases secretion of both [4]. The excitatory and inhibitory responses of catecholamine secretion and nerve activity were in parallel in their responses to pinching and brushing of the skin (Fig. 6).

In central-nervous-system-intact rats the reflex response of adrenal sympathetic nerve activity following pinching of various segmental skin areas is a generalized response, requiring the brain. However, after spinal transection at the cervical

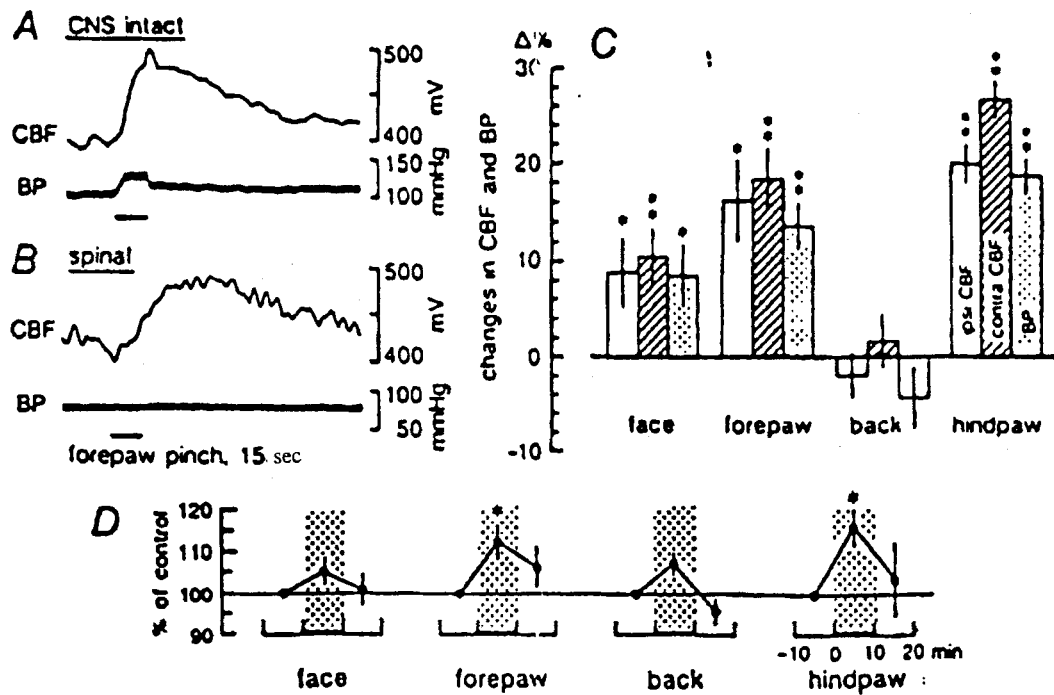


Fig. 5. Effects of pinching various skin areas on cerebral cortical blood flow (CBF) and acetylcholine release in the parietal cortex in rats. A, B) CBF and blood pressure (BP) following pinching of a forepaw for 15 s before (A) and after (B) spinal transection; C) summary of the responses of CBF and BP to pinching of various skin areas in central-nervous-system-intact rats. The changes in maximum responses of CBF and BP within 3 min after onset of stimulation were expressed as percentages of the prestimulus control values (mean \pm S.E.M.); D) responses of acetylcholine release in the parietal cortex to pinching of various skin areas for 10 min. The responses are expressed as percentages of the prestimulus control value (mean \pm S.E.M.). * $P < 0.05$, ** $P < 0.01$; significantly different from prestimulus control values using paired t-test (A-C, from [1]; D, from [14]).

level, skin areas producing the response become quite restricted to the thoracic segments [3, 4]. Considering the reflex pathways of the adrenal medullary responses elicited by pinching of various segmental areas, a strong segmental excitatory reflex within the spinal cord is mixed with a generalized supraspinal reflex in the CNS intact animals.

In the case of brushing stimulation, effective skin areas are also restricted to the thoracic segments after spinal transection at the high spinal level [4, 15]. Interestingly the inhibitory reflex response seen before spinal transection reversed to an excitatory one after spinal transection. The result of non-noxious brushing stimulation can be summarized by saying that the spinal reflex is excitatory in the spinal animal, and this excitatory spinal reflex is modulated to a generalized inhibitory reflex in the central-nervous-system-intact animal.

7. SOMATO-IMMUNE REFLEXES

Another interesting question might be whether somatic afferent stimulation can affect immune function through sympathetic or parasympathetic efferent nerves that innervate the immune-related lymphatic organs, such as the thymus, spleen, lymph nodes, and bone marrow. The spleen, for example, receives sympathetic innervation. Stimulation of a splenic sympathetic nerve can constrict splenic blood vessels, reduce blood flow, and also decrease activity of the splenic natural killer cells that are immune-associated cells.

Our study in anesthetized rats demonstrates that pinching the hindpaws increases splenic sympathetic efferent nerve activity [12] (Fig. 7A, left column). Splenic blood flow is reduced by pinching of the hindpaws (Fig. 7A, middle column). We

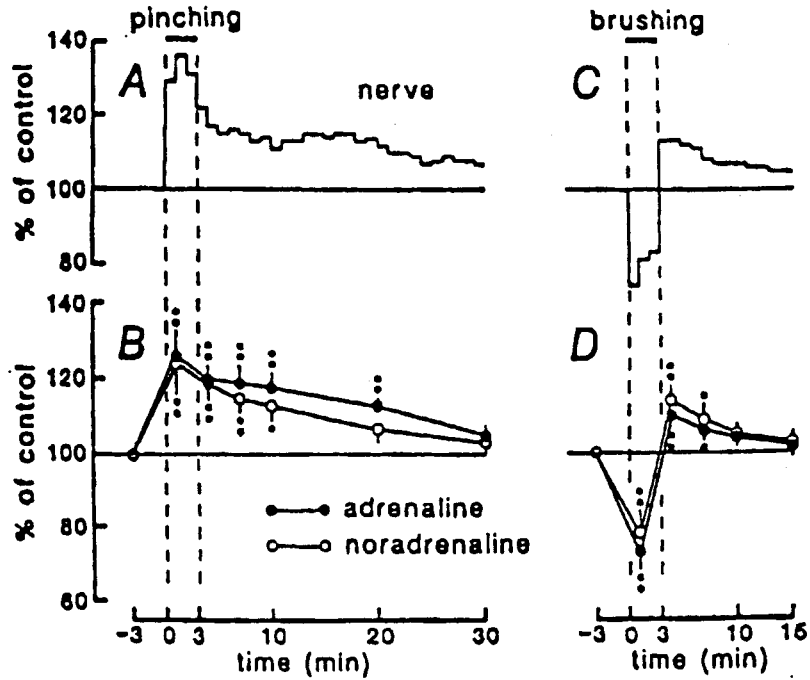


Fig. 6. Effects on adrenal sympathetic nerve activity (A, C) and adrenal catecholamine secretion (B, D) during stimulation of lower chest skin by pinching (A, B) or by gentle brushing (C, D) in rats. In A and C, values indicate means of the mean response of each animal. In B and D, values indicate mean \pm S.E.M. of the mean response of each animal. * $P < 0.05$, ** $P < 0.01$, significantly different from prestimulus control values, using paired t-test (from [4]).

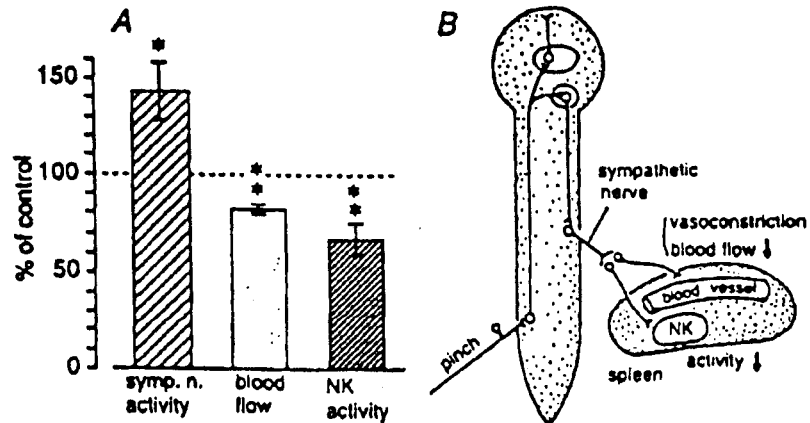


Fig. 7. Effect of hindpaw pinching for 30 min on splenic sympathetic nerve activity (A, left column), splenic blood flow (A, middle column), and cytotoxic activity of NK cells (A, right column) in rats. The responses are expressed as a percentage of the prestimulus control value (mean \pm S.E.M.). * $p < 0.05$, ** $p < 0.01$, significantly different from the prestimulus level or non-stimulated group. B) Schematic diagram of the reflex pathway for splenic NK cell activity and blood flow responses elicited by hindpaw pinching (from [12]).

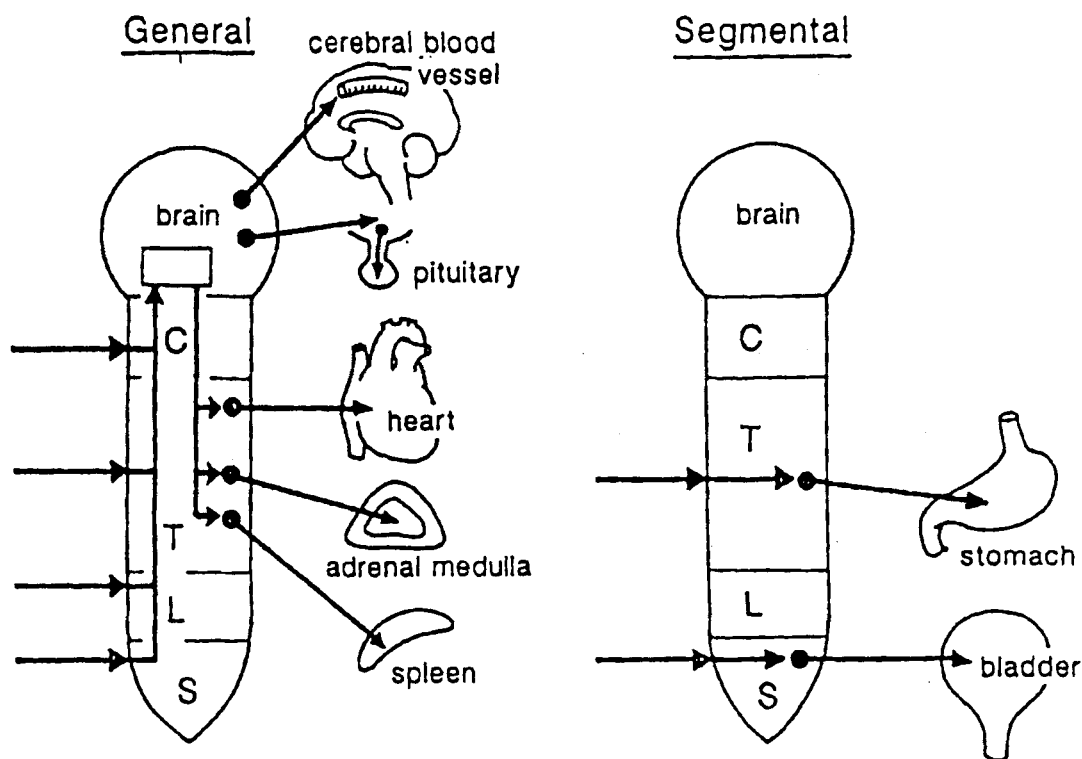


Fig. 8. Schematic diagram of somato-autonomic reflex responses. The responses in cerebral cortical blood flow, heart rate, adrenal medullary hormonal secretion, and splenic immune function are general, whereas the responses in gastric motility and urinary vesical contractility are segmental.

also investigated the effects of brushing and pinching stimulation of the skin on the cytotoxic activity of the natural killer (NK) cells. Brushing of the body surface for 30 min duration did not significantly influence cytotoxic activity of the NK cells. Cytotoxic activity of the NK cells is significantly reduced following pinching of the hindpaws for 30 min (Fig. 7A, right column); pinching for 20 min is ineffective. The response of NK cells is abolished, either after bilateral severance of the splenic sympathetic nerves or after spinal cord transection at the cervical level [12].

To summarize, afferent information from the hindpaws can reflexly excite splenic sympathetic efferent fibers through the brain, resulting in splenic vasoconstriction and decrease in cytotoxic activity of the natural killer cells in the spleen (Fig. 7B).

8. SUMMARY AND CONCLUSION

All evidence introduced here indicates that, in anesthetized animals in which emotional factors have been eliminated, somatic afferent nerve stimulation can regulate various visceral functions by responses that are reflex in nature.

One conclusion emerging from the evidence presented is that the effects of somatic afferent stimulation are dependent upon the particular organs and on the spinal afferent segments. When the central nervous system is intact, the responses are sometimes general, as seen in cerebral cortical blood flow, heart rate, and adrenal medullary hormonal secretion and splenic immune function, whereas sometimes they have a strong segmental organization, as seen in gastric motility and urinary vesical contractility (Fig. 8). Needless to say, in the spinalized preparation all responses are strongly segmental.

The contribution of the sympathetic and parasympathetic efferent nerves to the somato-visceral reflexes depends on the organs. It is difficult for us to state specifically or to generalize upon which autonomic component, the sympathetic or parasympathetic, will dominate as the efferent path in these reflexes, because this depends on the individual organ, the site being stimulated, and the nature or mode of the stimulation.

The somatically-induced reflex responses of autonomic, hormonal and immune functions demonstrated in anesthetized animals, as have been discussed herein, appear to function even during conscious states. We need further studies to evaluate the physiological meaning of these somato-autonomic reflex responses. The analysis of neural mechanisms of these reflex responses seems to be very important for clinical application to regulate visceral function by physical treatment.

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