Effects of Central Baroreceptor De-afferentation on Blood Pressure and Thermophysiological Responses to Environmental Thermal Challenges in Rats

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EFFECTS OF CENTRAL BARORECEPTOR DE-AFFERENTATION ON BLOOD PRESSURE AND THERMOPHYSIOLOGICAL RESPONSES TO ENVIRONMENTAL THERMAL CHALLENGES IN RATS

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Abstract

Recent studies have reported that the maintenance of arterial blood pressure (BP) is closely linked with the hemodynamics and energetics of thermoregulation. Those cardiovascular adjustments that occur under heat loads to facilitate heat transport jeopardize the maintenance of BP, while those responses that ensure adequate tissue oxygenation promote hyperthermia. Moreover, mechanically - and pharmacologically - evoked tonic changes in BP are accompanied by compensatory alterations in oxygen consumption, an index of heat production. The continually oscillating balance between these two co-regulated systems may, in part, account for the prevailing notion that BP is largely unresponsive to environmental thermal challenges. This balance is presumably mediated by baroreceptor reflexes.

The Nucleus Tractus Solitari (NTS) is a relay station for vagal baroreceptor afferents. Its interruption leads to exaggerated pressor reactivity to environmental stimuli that purportedly reflects enhancement of sympathetic preganglionic discharge. Accordingly, this debuffered preparation has become a popular experimental model for assessing the environmental and neurogenic contributions to clinical hypertension. To date no studies have directly assessed the consequences of baroreceptor deafferentation on physiological responses to thermal challenges. Accordingly, the following study examined the influence of NTS electrolytic lesions on BP and thermophysiological reactivity to graded, warm and cold thermal challenges in restraint-adapted, chronically-catheterized rats.

Sixteen, male, Sprague Dawley rats were adapted to a food deprivation regimen and physical restraint. They were then shaved and exposed to two

10-h thermal challenge sessions, distributed across a 48-h period (Pre-surgery). The sessions consisted of successive 90-min bouts of incremental warm (27 °, 31 °, 35 °C) or cold (19 °, 15 °, 11 °C) exposures with 60-min interpolated periods of baseline (23 °C) temperature. Half of the animals (n = 8) were then given bilateral electrolytic DC lesions of the mid-NTS, while the remaining animals served as Sham-operates (n = 8). Post-operative ventilation of the lesioned animals on high atmospheric oxygen prevented pulmonary edema and fulminating hypertension. During a 2-wk recovery period the adaptation routine was reinstated. All rats were then implanted with a chronic aortic catheter and re-exposed to the 10-h warm and cold challenge sessions (Post-surgery). The dependent variables included several indicies of body temperature, respiratory-blood gases, blood pH, evaporative heat loss, and mean arterial BP. The results showed that NTS lesions were discretely localized in the region receiving vagal afferents and that they prevented pharmacologically-evoked pressor or depressor alterations in heart rate. Such lesions were accompanied by a lower baseline BP, but they enhanced BP reactivity to thermal exposures relative to the Sham-operated animals. Phasic, hypertensive episodes were produced by incremental cold challenges, while lower amplitude BP suppression was obtained under heat challenges. Deafferentation inhibited both baseline and thermal-evoked alterations in metabolism during either warm or cold challenges and increased susceptibility to heat-induced acidosis. Few other group differences were obtained in rectal, abdominal or tail skin temperature, evaporative heat loss, or blood gas composition.

The bidirectional BP responses to thermal challenges in the NTS-lesioned rats counters prevailing notions that (a) baroreceptor

deafferentation enhances sympathetic preganglionic discharge rate and that (b) the mechanisms of BP and thermoregulation are easily dissociable. Since the NTS-lesioned rat was characterized by an enhanced hemodynamic, but suppressed metabolic, responsiveness to thermal challenges, it appears that the intact baroreceptor reflex buffers significant cardiovascular adjustments that would otherwise develop under a thermal load. The BP adjustments accompanying temperature stressors are predicated on the functional integrity of the baroreceptor reflexes and on the direction and severity of the thermal challenges. These findings support the notion that a better understanding of how BP and thermoregulation are integrated will clarify the neurogenic principles underlying stress-induced cardiovascular psychophysiology.

Introduction

The cardiovascular system is a transport system designed to accomplish two objectives: (a) to supply nutrients to the tissue and (b) to maintain an adequate body temperature. The interaction of these two objectives provided the basis for this study.

It is often assumed that blood pressure and thermoregulation are easily dissociable, both at a central and a peripheral level. Research has implied that bulbar mechanisms are responsible for the neurogenic control of blood pressure, whereas the peripheral component is comprised of skeletal muscle, renal, splanchnic and cutaneous vascular responses (Chalmers, 1975; Hurst, Logue, Schlant, & Wenger, 1974). In contrast, thermoregulation is viewed to be under hypothalamic control, whereas the peripheral responses are relegated to mainly cutaneous vascular effectors (Boulant, 1976; Hammel, 1968). This study is designed to indirectly investigate the notion that blood pressure and thermoregulation are co-regulated by a hypothalamic-bulbar longitudinal system of fibers (Ciriello & Calaresu, 1980; Saper, Loewy, Swanson, & Cowan, 1976). This notion is based on evidence that competition occurs between blood pressure and thermoregulation for regional blood flow during circumstances that relate behavior, stress, or both, to cardiovascular activity (Atterhog, Carlens, Granberg, & Wallenberg, 1975; Chapman, Munday, & Withey, 1975; Johnson, Neiderberger, Rowell, Eisman, & Brengelmann, 1973). Thus, if thermal energetics and blood pressure are neurogenically linked and if the two systems co-regulate regional blood flow, an abnormality in blood pressure regulation may be accompanied by an alteration in thermoregulation.

Basic Hemodynamics of Blood Pressure Regulation

Vascular variables. The vascular component of blood pressure is comprised of total peripheral resistance. Total peripheral resistance is a cumulative index of the resistance to blood flow offered by resistance vessels in various regions including the brain, heart, muscle, viscera, kidney and skin. Larger diameter vessels facilitate blood flow and lower total peripheral resistance, whereas smaller diameter vessels do the converse (Levine, 1976). The main role of the capacitance vessels is to ensure an appropriate return of blood to the heart. The amount of blood which is displaced from venous reservoirs towards the heart is determined by the diameter of the veins (Vanhoutte & Janssens, 1978). During vasoconstriction (or a rise in total peripheral resistance) the venous diameter decreases and a considerable amount of blood is passively expelled to the heart, while the converse also holds true during vasodilation (Shepherd & Vanhoutte, 1975). Thus, together the resistance and capacitance vessels maintain blood flow to the heart for ultimate distribution to the tissues acutely requiring nutrients, while they shunt blood flow away from tissues not being used or less essential to the survival of the organism.

The resistance vessels which control regional peripheral resistance are under direct sympathetic nervous system control (Christensen & Galbo, 1983). Sympathetic fibers induce vasoconstriction through the local release of norepinephrine at the nerve fiber endings. Such afferent fibers are important in responding to a variety of regional stimuli, and thay are the major pathway for changes in peripheral resistance produced by mechanical or chemical stimulation of the carotid

sinus and aortic arch stretch receptors (Kirchheim, 1976). Venoconstriction in the smooth muscle cells may be induced through the release of norepinephrine from the sympathetic nervous system. This neurogenic sympathetic control is rather selective in the degree of venomotor change induced in a particular region. The participation of a given venous bed in reflex changes in capacity depends upon the amount of venous smooth muscle present and upon the density of adrenergic innervation. Thus, regional venous beds are able to differentially venoconstrict in response to sympathetic nervous stimulation, which may enable the capacitance vessels to fulfill important physiological and behavioral functions (Vanhoutte & Janssens, 1978).

Influence of baroreceptor stimulation on reflex control of blood pressure. Neurogenic control of blood pressure has traditionally been linked to buffering action of baroreceptors in the carotid sinus and aortic arch. From these regions primary baroreceptor fibers course through the glossopharyngeal and vagal nerves to synapse in the medial and commissural division of the Nucleus Tractus Solitari (NTS) (Palkovits, Mezey, & Zaborszky, 1979). A portion of the primary baroreceptors, the vagal cardio-inhibitory fibers, then synapse in the dorsal vagal nucleus from which they send axons to innervate the heart. Other primary baroreceptor afferents synapse in the vasomotor center, an anatomically diffuse area where synapses occur between the primary baroreceptor afferents and the interneurons of the reflex arch. The interneurons course down the medulla into the spinal cord where they synapse on the preganglionic sympathetic cells located in the intermediolateral cell

column between the first thoracic and second lumbar segments. These preganglionic fibers terminate in either the sympathetic or peripheral ganglia on the post-ganglionic neurons which constitute the final stage in the baroreceptor reflex arch (Palkovits & Zaborszky, 1977).

Baroreceptors respond to the intensity of any mechanical deformation caused by a change in blood pressure. Common carotid occlusion distal to the site of the receptors or micro-stimulation of the medial portion of the NTS simulates an increase in blood pressure and thereby increases the firing rate of the primary baroreceptor fibers. The increased firing rate of primary fibers enhances the inhibitory action of the neurons between the NTS and the vasomotor center. This inhibitory action decreases the firing rate of the sympathetic ganglia coursing through the spinal cord and innervating the vasculature and thus causes a decrease in total peripheral resistance. Such an occlusion also activates a parasympathetically-mediated bradycardia (Randall, 1977). Conversely, reduction of blood pressure induced through lesions to the medial portion of the NTS or common carotid occlusion proximal to the site of the baroreceptors releases sympathetic inhibition and increases vascular resistance. Concurrently, there is a decrease in the inhibitory action of the vagal nerves and tachycardia occurs (Katonas, Poitras, Barnett, & Terry, 1970; Kezdi & Geller, 1968; Kunze, 1972; Palkovits & Zaborszky, 1977).

Supramedullary modulation of the baroreceptor reflex has been questioned largely because of the small effect of midcollicular decerebration on the reflex in the anesthetized animal (Chai, Share, & Wang, 1963; Katz, Kahn, & Wang, 1967). However, an increasing amoung of evidence

suggests the importance of hypothalamic modulation of this baroreceptor reflex. For example, Hilton and Spyer (1971) found that electrical stimulation of the baroreceptor afferents produce an increase in blood pressure that could be reduced by bilateral electrolytic lesions of the preoptic anterior hypothalamus (PO/AH). Kent, Drane, and Manning (1971) found that the increase in blood pressure seen immediately upon electrical stimulation of the carotid sinus was reduced and the time to onset of the response was increased following lesions to the PO/AH. McAllen (1976) further showed that electrical stimulation of the PO/AH elicited bradycardia and hypotension and inhibited baroreceptor reflexes measured by electrical activity of primary baroreceptor afferents. Thus, it appears that certain hypothalamic areas can exert cardiovascular control independent of the medulla and that they may also affect the functioning of the baroreceptor reflex.

Anatomical studies also yield evidence suggesting direct neuronal pathways coursing from the NTS to various nuclei within the hypothalamus. Through the use of retrograde labeling, neurons were found to project from the commissural portion of the NTS to the paraventricular, posterior, and lateral nuclei of the hypothalamus. Moreover, injections of isotopes into the paraventricular portion of the hypothalamus revealed a large number of silver grains in the medial portion of the NTS, suggesting that neurons projected from the hypothalamus to the NTS regions as well (Saper et al., 1976). Also, Ciriello and Calaresu (1980) electrically stimulated the paraventricular nucleus of the hypothalamus and elicited action potentials from 50 units histologically verified to be in the NTS.

These units responded with a maximal bradycardia when the carotid sinus and aortic depressor nerves were stimulated and thus were part of the baroreceptor reflex arch. The investigators found that the action potentials evoked by electrical stimulation of the paraventricular nucleus occurred with a latency consistent for any one unit. Thus, it was concluded that there are monosynaptic pathways coursing from the hypothalamus to the NTS and vice versa.

The supramedullary regions involved in the baroreceptor reflex pathway are more susceptible to the action of anesthetics than the medulla (Peis & Manning, 1964). As a result, the use of conscious or anesthetized animals has generated controversy concerning baroreceptor functioning. Gutman, Chaimovits, Ginath and Bergmann (1962) found a pentobarbital-induced reduction of pressor responses and a reversal to depressor responses observed upon electrical stimulation of the dorso-vagal and NTS regions. Baust and Niemszyk (1968) then demonstrated that potentiation of an epinephrine-induced rise in blood pressure produced by successive removal of mesencephalic brainstem structures was abolished by pentobarbital anesthesia. Jonzon, Oberg, Sedin and Sjostrand (1973) demonstrated that pentobarbital anesthesia elevated the threshold of responding to electrical stimulation of hypothalamic areas more than in the dorsal medullary reticular formation. Moreover, Korner (1971, 1974) showed that pentobarbital anesthesia blocks diencephalic regions influencing vagal afferents in rabbits and thus selectively eliminates one of the major autonomic effector components of the baroreceptor reflex arch. Accordingly, the use of anesthetics suppresses blood pressure responsiveness and in some cases may lead to

inconsistent results. Thus, it is desirable to use conscious animals in order to preclude the effects of anesthesia on baroreceptor functioning.

The function of the arterial baroreceptor reflex depends on the integrity of afferent impulses from the carotid sinus and aortic arch and the efferent bulbospinal and peripheral sympathetic nerves (Korner, 1971). Activation of baroreceptor afferents produces alterations in vasomotor tone in various vascular regions. Wang, Chai, Kuo and Wang (1970) and Brooksby and Donald (1971) obtained evidence of splanchnic and renal vasoconstriction in unanesthetized cats and dogs in response to proximal common carotid occlusion. They observed a 37% reduction in the pressor response of the splanchnic and renal vessels to proximal common carotid occlusion after the splanchnic sympathetic nerves had been eliminated either surgically or pharmacologically. They also observed a renal and splanchnic vasodilation upon distal common carotid occlusion. They concluded that the baroreceptor reflex affects the vascular response in the renal and splanchnic regions and that the response occurs to maintain cardiovascular homeostasis.

The baroreceptor reflex also alters vascular resistance in skeletal muscles. Vatner et al. (1972) reported a decrease in skeletal muscle vascular resistance during electrical stimulation of the carotid sinus nerve. However, when systemic blood pressure was allowed to fall during carotid sinus nerve stimulation, the resultant change in muscle vascular resistance depended on the degree of concommitant reflex hypotension. These investigators also reported a 37% decrease in muscle blood flow

with a fall in blood pressure of 62 mm Hg; however, a 28 mm Hg drop in blood pressure produced only a 8% decrease in muscle blood flow. Thus, again the responses that occur in the resistance vessels of skeletal muscles as a result of baroreceptor activation operate to maintain normal cardiovascular functioning.

Research has also demonstrated that baroreceptor reflexes alter cutaneous circulation. Bond, Lackey, Taxis and Green (1970) demonstrated that proximal common carotid occlusion, which simulates a decrease in blood pressure, produces cutaneous vasoconstriction in unanesthetized cats. The vasoconstriction increases total peripheral resistance by 225% of normal and thus contributes to the 60% increase in blood pressure. Bond et al. (1970) also demonstrated that distal common carotid occlusion, which simulates an increase in blood pressure, produces cutaneous vasodilation in unanesthetized cats. The cutaneous vasodilation decreases total peripheral resistance by as much as 70% and aids in reducing blood pressure by up to 45%.

In addition to the baroreflex influencing cutaneous vasomotor responses, it also indirectly regulates cutaneous venomotor responses. With cutaneous vasoconstriction produced by proximal common carotid occlusion occurs a decrease in the diameter of the surface limb veins. This decrease reduces the amount of blood stored in venous reservoirs and enhances the return of blood to the heart, thereby increasing the total volume of circulating blood. The increase in blood volume increases blood pressure and thus maintains normal cardiovascular functioning (Nadel, 1980; Vanhoutte & Janssens, 1978). The converse

occurs to venomotor tone in response to distal common carotid occlusion and hence results in a decrease in blood volume and a reduced blood pressure. Thus, both vasomotor and venomotor tone are regulated by the baroreceptor reflex arch for the proper maintenance of cardiovascular functioning.

Electrolytic Lesions to the Region of the Nucleus Tractus Solitari

The blood pressure effects of bilateral electrolytic lesions to the NTS progress from an acute to a chronic phase. The acute phase in cats is characterized by rapid development of arterial hypertension that is sustained by tachycardia and increased total peripheral resistance (Doba & Reis, 1975). In rats the tachycardia results in a reduced blood return to the heart which leads to a decline in stroke volume. The tachycardia also results in pulmonary edema and together with the reduced stroke volume the animal succumbs due to cardiac failure (Doba & Reis, 1975). The chronic phase occurring in cats is characterized by labile arterial pressure and a sustained tachycardia (Talman, Snyder, & Reis, 1980). Moreover, during the chronic phase there is an enhanced synthesis of adrenal catecholamines which contributes to an elevated total peripheral resistance (Doba & Reis, 1978).

Nathan and Buckholtz (1982) contended that with proper postoperative care, rats are able to survive the acute phase of the NTS hypertension. Following bilateral electrolytic lesions to the NTS their rats were maintained for 6-8 h on an anesthetic dose of sodium pentobarbital. The anesthesia allowed the heart to respond to vagal stimuli by attenuating the sympathetic innervation. Vagal stimulation decreases heart rate in

order to obtain adequate filling of the atria, thereby maintaining cardiac output at a normal level (Kirchheim, 1976; Laubie & Schmitt, 1979).

Bilateral electrolytic lesions interrupt baroreceptor activity arising from the carotid sinus and aortic arch and destroy the terminals of baroreceptor afferent fibers. They also destroy the neurons onto which the baroreceptor afferents terminate and eliminate supramedullary contributions to the reflex arch which operate through the NTS (Doba & Reis, 1974; Nathan & Reis, 1977). The lability of blood pressure accompanying NTS lesions reflects a neural imbalance between excitatory and inhibitory systems which modulate sympathetic discharge (Laubie & Schmitt, 1979). Following the NTS lesions, the inhibitory action of the neurons coursing from the NTS to the vasomotor center is attenuated and thus the excitatory sympathetic interneurons coursing through the intermediolateral cell column increase their firing rate. The increased activity of these interneurons leaves the sympathetic pre- and post-ganglionics more responsive to environmental stimuli by enhancing their firing rate. Thus, the relatively small increase in sympathetic activity and arterial pressure seen in response to various behaviors or stressors are unopposed by baroreceptor activity after NTS lesions. Therefore, there is an increase in sympathetic responsivity to various stimuli and a resultant lability of blood pressure (Doba & Reis, 1974; Laubie & Schmitt, 1979; Nathan & Reis, 1977).

Thermoregulation

Neurogenic control of thermoregulation. Physiological studies have

emphasized the thermoregulatory importance of the preoptic anterior hypothalamus (PO/AH). This area integrates local (Boulant, 1976), spinal (Guieu & Hardy, 1970; Jessen & Ludwig, 1971), and cutaneous (Boulant & Gonzalez, 1974; Jacobsen & Squires, 1970) thermal information to sustain an adequate body temperature. The hypothalamic control of thermoregulation has been investigated in two basic ways: (a) through local heating or cooling of the PO/AH or (b) through lesions to the PO/AH. Both methods have yielded similar results. For example, Hammel, Fusco and Hardy (1961) observed thermoregulatory responses to both local heating and cooling of PO/AH neurons in dogs resting in a neutral environment. Temperature alterations were produced by circulating either warm or cold alcohol through four thermodes simultaneously placed into the PO/AH. A drop of 1.5 ^{o}C in the PO/AH temperature elicited strong heat conserving responses such as shivering, vasoconstriction, and a drop in skin temperature in regions associated with heat dissipation. In contrast, when the PO/AH temperature was raised 1.0 ^{o}C, the animals exhibited marked heat-dissipating responses such as vasodilation, panting, and in some instances, hyperventilation.

In addition, studies which induced lesions to the PO/AH confirmed its thermoregulatory importance. Squires and Jacobsen (1968) induced functional disruption to the PO/AH region in cats by discrete electrolytic lesions. Lesions confined to the PO/AH region rendered the animal incapable of adequately thermoregulating core temperature in either hot or cold conditions. Stitt (1978) reached similar conclusions when he lesioned the PO/AH in dogs and rats, suggesting that the PO/AH is important

for normal thermoregulation.

Research has also suggested that the medulla oblongata is capable of mediating thermoregulatory responses. Chai and Lin (1972) observed that thermal stimulation of the medulla by the use of water-perfused electrodes in unanesthetized monkeys produces a variety of thermoregulatory responses: cooling the medulla caused vasoconstriction, an increase in blood pressure, shivering, tachycardia, slower respiration, and a slight increase in body temperature. Heating the medulla by the same method leads to cutaneous vasodilation, hypotension, acceleration of respiration, and a slight decrease in body temperature. Thus, there is a coordinated adjustment of body temperature and vasomotor activity upon medullary thermal stimulation.

A longitudinal system of neurons coursing from the medulla to the PO/AH seems to mediate baroreceptor reflexes and similar hierarchical connections between the hypothalamus, medulla, and spinal cord seems to operate in the control of thermoregulation. Hilton (1970) and Hilton, Marshall and Timms (1980) found that stimulation of this longitudinal neural pathway in the medullary and PO/AH area decreased blood pressure, total peripheral resistance, and heart rate. Furthermore, electrolytic lesions to the PO/AH attenuated the cardiovascular response to medullary stimulation, suggesting that baroreceptor reflexes are mediated throughout this neural pathway. Chambers, Seigel, Lui, and Lui (1974) found that spinal cooling below the level of transection in cats induced shivering and vasoconstriction of the hind limbs. Whole body cooling of spinally-transected cats elicited only slight shivering in the hind limbs and

strong shivering in the forelimbs. They also found that decerebration at the level of the rostral pons in the spinally-transected animals abolished thermoregulatory responses to whole-body cooling in the forelimbs, while shivering below the level of transection continued in response to spinal cord cooling. Furthermore, lowering the level of transection to the medulla, again in the transected animals, reinstated shivering and vasoconstriction in the forelimbs. As the level of decerebration was moved rostrally the ability to thermoregulate declined and animals with high level decerebration regulated body temperature poorly. Thus, there appears to be a functional connection from the hypothalamus to the medulla and from the medulla to the spinal cord. These functional connections are inhibitory in nature, and the hypothalamus suppresses the thermoregulatory nature of the medulla. However, if the hypothalamus is removed, the medulla is capable of initiating appropriate thermoregulatory responses, albeit a less precise control of body temperature. The same set of circumstances occurs when the spinal cord is left solely responsible for thermoregulation (Satinoff, 1978).

Components of Thermoregulation: Vascular and Metabolic Processes

Physiological thermoregulation consists of both a vascular and a metabolic component. The vascular component is comprised of circulatory-assisted heat transport--the degree to which the circulatory system controls heat dissipation from the animal's torso (Johnson, Rowell, & Brengelmann, 1974; Mount, 1979; Rowell, 1974). One factor that relates to the capacity of vessels to dissipate heat is tissue conductance. An increase in cutaneous blood flow, resulting from dilation of the vessels,

enhances tissue conductance and facilitates heat transport from the body core to the environment (Johnson et al., 1974). Therefore, the change in tissue conductance accompanying an increase in cutaneous resistance retards heat transport (Vanhoutte, 1978).

Exogenous thermal challenges can be imposed on an organism through alterations in ambient temperature. When a quadraped is placed in a warm environment, cutaneous vasodilation occurs. Vasodilation facilitates thermal conductance, minimizes heat accumulation, and enables the maintenance of a normal core temperature (Chapman et al., 1975; Nadel, 1980). The degree of this cutaneous vasodilation is proportional to the severity of heat challenge. Heat-induced vasodilation may jeopardize cardiovascular functioning if no compensatory alterations in vasomotor tone, which maintain normal blood supply to the heart, occur. (Atterhog et al., 1975; Johnson, Neiderberger, Rowell, Eisman, & Brengelmann, 1973; Nadel, 1980). However, heat challenge causes baroreceptor-mediated vasoconstriction in the splanchnic and renal region (Amberson, 1943; Chapman et al., 1975; Nadel, 1980; Rowell, 1974). This vasoconstriction facilitates heat dissipation by shunting more blood from the visceral region to the cutaneous vasculature, thereby increasing cutaneous blood flow and tissue conductance while sustaining normal blood pressure (Ingram & Mount, 1975; Nadel, 1977; Rowell, 1974).

In addition, a heat challenge causes an increase in peripheral venous blood volume which reduces the amount of blood returning to the heart and thus potentially compromises cardiac output. Brengelmann, Johnson, Hermansen, and Rowell (1977) found that cardiac output in humans

was sustained through baroreceptor-mediated cutaneous vasoconstriction which competes with, and may have overridden, the heat-induced cutaneous vasodilation. The vasoconstriction promoted venoconstriction in the superficial veins and a concurrent venodilation in the deep veins. The venodilation, along with contraction of the venous valves, enhances blood return to the heart. The net result was the maintenance of arterial blood pressure and cardiac filling pressure at the expense of promoting hyperthermia. This cutaneous vasoconstriction is the result of the baroreceptor reflexes having precedence over the thermoregulatory reflex. This is only one instance where cutaneous sympathetic vasoconstrictor nerves constitute the efferent arm of the reflexes involving the regulation of both blood pressure and body temperature.

The metabolic component of thermoregulation is comprised of heat production resulting from specific dynamic action of foods, or changes in sympathetic nervous system activity, or both (Christensen & Galbo, 1983; Himms-Hagen, 1967; Stitt, 1978). Thermoneutrality refers to a range of ambient temperatures in which metabolic rate is constant. Metabolic thermoregulation occurs in endotherms when deviations from thermo-neutrality are detected (Poole & Stephenson, 1977). Under such circum-stances there is an increase in oxygen consumption and carbon dioxide production (Christensen & Galbo, 1983; Himms-Hagen, 1967). This increase in metabolism below the thermoneutral zone is attributable to the sympathetic nervous system which releases norepinephrine from nerve endings (Himms-Hagen, 1972; Stitt, 1978) and contributes to metabolism in several ways: Firstly, the sympathetic nervous system is essential for

the mobilization of substrates such as glucose and fatty acids during cold exposure and thereby controls the oxidative metabolism of thermogenic tissues such as muscle and brown adipose tissue. Secondly, the sympathetic nervous system is responsible for the usual circulatory adjustments of vasoconstriction that facilitate heat retention. Alterations in vasomotor tone may affect not only vascular heat exchange but also nutrient supply to thermogenic tissues. The alterations in vasomotor tone and nutrient supply is the result of blocking the release of norepinephrine from the postganglionic sympathetic fibers which are under baroreceptor-mediated control (Molnar, Soltesz, & Mestyan, 1979; Wright, Badger, Samueloff, Toraason, & Dukes-Dobos, 1978).

Once the upper critical limit of thermoneutrality is exceeded, vasodilation occurs in the presence of a sympathetically-induced rise in metabolism (Hart, 1971; Poole & Stephenson, 1977). If the heat challenge approaches 40 ^{o}C in rats, the rise in sympathetic activity leads to the release of norepinephrine and hence causes cutaneous vasoconstriction in addition to an increase in metabolism. The cutaneous vasoconstriction satisfies oxygen demand by maintaining blood flow to the active tissue and muscle (Poole & Stephenson, 1977). However, when combined with the increase in metabolism such alterations may promote lethal hyperthermia (Hart, 1971; Ludbrook, 1983).

When animals are exposed to cold thermal challenges they also increase their metabolic rate through nonshivering thermogenesis. Evidence for the sympathetically-mediated alterations in carbon dioxide production can be found in studies showing that: (a) sympathetically-induced increases in carbon dioxide production can be attenuated by

30% upon α-adrenergic blockade by phentolamine (Polosa, Lioy, & Hanna, 1983) and (b) lowering body temperature to 33-35 °C in goats increased sympathetic nerve discharge by 85% and carbon dioxide production by 30% (Heisey, Adams, Hofman, & Riegle, 1971). Moreover, evidence for the sympathetically-mediated increase in oxygen consumption can be found in studies showing that: (a) the cold-induced increase in oxygen consumption in the curarized rat can be mimicked by the administration of norepinephrine (Molnar et al., 1979); (b) the increase in the capacity for nonshivering thermogenesis during cold acclimation is paralleled by an increase in the capacity for norepinephrine to increase metabolic rate in curarized rats (Vanhoutte & Janssens, 1978); and (c) that nonshivering thermogenesis is retarded by inactivation of the sympathetic nervous system with hexamethonium or propranolol in cold-acclimated, curarized rats (Schonbaum, Johnson, Seller, & Gill, 1966).

Wasserstrum and Herd (1977a) found that squirrel monkeys acutely exposed to 10 °C showed an elevated oxygen consumption twice that recorded at 28 °C along with increased blood pressure. Intravenous infusions of phenylephrine in intact animals in the cold induced further elevations in blood pressure and an immediate reduction in oxygen consumption, shivering and rectal temperature (Wasserstrum & Herd, 1977b). The magnitude of reduction in oxygen consumption was inversely correlated with the increase in blood pressure. They further found that the normal reduction in oxygen consumption and heart rate in response to an increase in blood pressure was substantially attenuated following sinoaortic denervation. They concluded that the increase in blood pressure can inhibit thermoregulatory increases in oxygen consumption normally

produced by cold ambient temperatures and this inhibition, like the concomitant bradycardia, is probably mediated by the baroreceptor reflex.

Thus, it is apparent that both blood pressure and thermoregulation have common neurogenic, metabolic, and vascular processes operating in their control. The manner in which these mechanisms operate in synchrony to control blood pressure and thermoregulation is illustrated in Figure 1.

Statement of the Problem and Hypotheses

It appears that an interaction exists between blood pressure and thermoregulation when an animal is placed in a thermal challenge situation. However, the specific nature of this relationship remains unclear for several reasons. First, few studies have assessed the metabolic and blood pressure consequences of mild thermal challenges in shaved rats. Pelage masks most changes in vasomotor tone brought about by an ambient temperature change. Therefore, shaving the animals may serve to exaggerate the vasomotor responses which may occur during temperature variations. Second, thermal challenges are excellent means for examining the effects of stress in the cardiovascular system. Ambient temperature provides a physical continuum that alters bidirectionally the components of blood pressure regulation. The problem that exists in most literature is that thermal extremes or unidirectional stressors are often employed instead of bidirectional thermal challenges. Thus, most studies assess the consequences of traumatic, nonspecific stressors which seldom clarify the principles of neurogenic control of the cardiovascular system.

This study addresses the hypotheses that lesions to the NTS region eliminate baroreceptor reflex mechanisms that buffer thermoregulatory-induced alterations in blood pressure. When intact, Sham-operated animals are exposed to a graded cold thermal challenge, a small, temperature-dependent increase in blood pressure should result. The small rise should reflect the interaction of cold-induced vasoconstriction and baroreceptor-mediated vasodilation. Because of a reciprocity between vasomotor tone and metabolic means of thermoregulation, such animals should exhibit a large increase in metabolic rate due to nonshivering thermogenesis. When intact, Sham-operated animals are exposed to a progressively warm thermal challenge, a small temperature-dependent decrease in blood pressure should result. The small decline should reflect the interaction of heat-induced vasodilation and baroreceptor-mediated vasoconstriction. Again, the reciprocity between vasomotor tone and metabolic means of thermoregulation should result in a large decrease in metabolic rate.

In contrast to Sham-operated animals, NTS-lesioned animals should exhibit temperature-dependent pressor responsiveness to progressively decreasing test temperatures. Moreover, due to the reciprocity between vasomotor tone and metabolic thermoregulation, NTS animals should exhibit smaller alterations in metabolic rate in a cold environment. On the other hand, the NTS animals should exhibit a temperature-dependent reduction in blood pressure in response to progressively warmer test temperatures. Due to the reciprocity between vasomotor tone and metabolic thermoregulation, the large change in vasomotor tone in NTS animals

should be accompanied by a small decline in metabolic rate. Because central debuffering specifically alters the relative roles of metabolism and vascular mechanisms employed for thermoregulation and does not alter the ability to thermoregulate, one would anticipate no differential change in rectal temperature between the NTS and Sham animals.

Method

Subjects

Sixteen male, Sprague Dawley rats weighing 300-400 g were used. The animals were housed in individual wire-mesh cages with free access to water and food. Room temperature was maintained at 23 $\pm$ 2 ^{o}C and kept on a 12 h light/dark cycle (lights on 0700-1900).

Adaptation Procedure

All animals underwent a 9-day adaptation to a mild physical restraint and food deprivation regimen. On days 1-3 of adaptation the animals were placed in Biodec restrainers for 2 h/day starting at 0700. The restrainer's design avoids heat accumulation by the animal. During the first three days of adaptation the animals had access to food from 1200-0300 h, thus incurring a 9-h food deprivation period. On days 4-6 of adaptation the duration of restraint was increase to 4 h/day, and food was available from 1500-0300 h, thus incurring a 12 h deprivation period. At the end of the restraint period on day 6 the animals were lightly anesthetized with sodium pentobarbital (Nembutal, Allen and Hanburys, 50 mg/Kg), shaved and fitted with an Elizabethan collar. The collar

was secured comfortably to the animal's neck with adhesive tape and was designed to prevent the animal from gaining access to a later implanted aortic catheter. On days 7-9 of adaptation the animals were placed in the restrainers for 8 h/day with access to food limited to 1700-0300 h, thus, increasing food deprivation to 14 h. During restraint on days 7-9 the animals had a rectal probe (YSI 400 probes, Fisher Scientific Co. Ltd., vinyl, 2.4 mm diameter) inserted 4 cm into their rectum. This procedure adapted the animals to the probe placement used during thermal testing. During days 8 and 9 of adaptation the rats' mean systolic blood pressures were assessed indirectly using tail-cuff plethysmography. Throughout the entire adaptation period body weights were monitored daily to ensure stabilization to the food regimen. Following restraint on day 9 the animals were lightly anesthetized with ether and re-shaved.

Indirect blood pressure assessment. Systolic blood pressure was assessed using indirect tail-cuff plethysmography. This method has been validated against direct recordings of carotid blood pressure (Buñag, 1973; Pfeffer, Pfeffer, & Fröhlich, 1971). Measurements were obtained following warming of the tail to 38 $\pm$ 1 ^{o}C. A pulse detector (Buffington Clinical Systems, Cleveland, O.) positioned on the ventral surface of the tail distal to an occlusion cuff detected the return of the arterial pulse following a slow deflation of the cuff. The cuff pressure was determined by a Statham P23 pressure transducer, and pulses were recorded on a Grass polygraph (Model 79D) as full scale pen deflections. Five determinations were made at each blood pressure measurement session, with a 2 min interval between each determination. Basal

systolic blood pressure was established over two recording sessions during the last two days of adaptation. Those animals with mean systolic blood pressures above 135 mm Hg or below 100 mm Hg were discarded from the study. Before and after the session, rectal temperatures were assessed using a probe inserted 4 cm rectally and recorded on a YSI telethermometer (Yellow Springs Instruments Inc., Model 46 TUC). Any animal with an initial rectal temperature above 37.5 ^{o}C or below 35.5 ^{o}C was discarded from the study.

Presurgery Thermal Testing

Following the completion of the 9-day adaptation period the animals' baseline metabolism and metabolic response to test temperatures were assessed. Following a 4-h food deprivation period each animal was placed in a metabolic chamber located inside a temperature-controlled cabinet. The metabolic chamber was a modified glass aquarium with an inside dimension of 36 x 16 x 17 cm. A 45 x 25 x 1.2 cm Plexiglass lid provided a tight seal over the metabolic chamber and contained inlet and outlet air ports, temperature probes, and an arterial catheter interface coupler. Dry air passed through the chamber at a rate of 708.5 ml/min. Expired gases were dried by passage through Drierite and analyzed for oxygen and carbon dioxide content using a Beckman OM-11 Oxygen Analyzer and a Beckman LB-2 Medical Gas Analyzer connected in series. Oxygen and carbon dioxide content were continuously recorded on a dual channel Omniscribe recorder (Fisher Recordall series 5000). Rectal temperature (Tc), tail skin temperature (Tsk), abdominal skin temperature (Tsc), and ambient temperature (Ta) inside the metabolic

chamber were recorded continuously with a YSI telethermometer (Model 46 TUC, Yellow Springs Instruments Inc.) connected to a Grass Model 58 polygraph. In order to assess evaporative heat loss the Drierite tube through which the expired gases passed, was weighed to the nearest .001 g (Sartorius Balance, Model 2604) before and after each temperature for the entire session.

The metabolic chamber was housed in a controlled temperature cabinet maintained at 23 ^{o}C (baseline condition) by a YSI thermistemp temperature controller (Model 63RC). Once the oxygen and carbon dioxide readings and rectal temperature had stabilized (a 3-h period), the ambient temperature was raised to 27 ^{o}C for 1.5 h. The temperature in the metabolic chamber was then lowered to 23 ^{o}C and the animal allowed to stabilize for 1 h. This process was repeated at 31 ^{o} and 35 ^{o}C. During each baseline condition (23 ^{o}C) and test temperature, Tc, Tsk, Tsc, Ta, oxygen consumption (VO_2) and carbon dioxide production (VCO_2) were assessed at 10 min intervals. The total test time was 9.5 h/day/animal. Following testing the animals were returned to their home cages. The next day the same basic protocol was repeated using 19, 15, and 11 ^{o}C as the incremental test temperatures. Daily testing began at 0700 h, with one rat tested per day.

Surgical Procedures

NTS lesions. Subjects were randomly divided into one of two groups; (n = 8/group): the NTS lesioned group (NTS) or the Sham operated group (Sham). Lesioning electrodes consisted of 13 cm Teflon coated tungsten wires (0.17 mm in diameter) from which 0.3-0.5 mm of insulation

was removed to expose their tips. Each electrode was inserted into an L-shaped length of 26 ga hypodemic tubing to facilitate holding in the electrode guide. The exposed tungsten wire extended 0.5 cm beyond the end of the hypodermic tubing. Both the electrode and its support tube were sterilized in a 70% alcohol bath before use. One electrode was used to lesion one animal and was then replaced.

The animals were anesthetized with Nembutal (50 mg/Kg) and given an intramuscular injection of Atropine (1 mg/Kg). They were placed in a Kopf stereotaxic instrument with the tooth bar arranged to bend the head to nose down at an angle of 15^{o}. Each rat's scalp and dorsal neck were shaved and then swabbed successively with 70% alcohol and isotonic saline. A mid-sagital incision was made to expose the occipital plates and foramen magnum at the back of the skull. The overlying muscles were retracted, the alanto-occipital membrane cut, and excess cerebrospinal fluid aspirated with a Gomco vacuum pump (Buffalo, N.Y.). A small, semicircular area, 4-5 mm in diameter was chipped away from the occipital plates with rongeur tips inserted through the foramen magnum. Deeper meninges were nicked at the approximate lesion sites. At this time the tooth bar was adjusted to place the head at an angle of 25^{o} nose down. The cerebellum was retracted to expose the underlying floor of the fourth ventricle (dorsal medulla) at the level of the obex (the apex of the area postrema). The obex was used as the zero reference point for the anterior-posterior (AP) and medial-lateral (ML) placement of the lesions. The dorsal-ventral (DV) placement was made with reference to the dorsal surface of the medulla at the lesion sites. The NTS lesions

were made at the following coordinate from the reference points: AP = +0.2-0.3 mm; ML = ±0.8-0.9 mm; DV = -0.5mm. Lesion parameters were 0.8 mA anodal current for 5 sec with an anal cathode completing the circuit.(Stoelting Co. Lesion Device, Model 58040). Sham-operated rats were prepared in an identical manner surgically including the electrode placement; however, no current was passed through the circuit.

Immediate postoperative care consisted of packing the wound with Gelfoam (Upjohn) soaked in sterile isotonic saline and suturing the overlying tissues with silk suture (Ethicon, size 00). Topical analgesics and anti-bacterial cream was applied to the wound, and an injection of Ethacilin penicillin was given intramuscularly. All NTS lesioned animals were placed in a positive pressure ventilation on a respirator with 100% oxygen for 6-8 h. If an animal displayed signs of respiratory distress it was fitted with a face mask modified from a rubber balloon. The balloon was positioned by placing the lower edge behind the upper incisors and by pulling the upper edge tightly over the rat's snout. The balloon was attached to a cut 20 cc syringe which held a Y-tube connected to polyethylene tubing to the inspiration and expiration posts of a small animal respirator (Narco Bio-systems, V5KG). The rats were respirated at a 1:2 I/E ration at 70±2 cpm with a 6 cc positive pressure volume/stroke. During respiration the rat was placed on a folded surgical padding placed on top of a heating pad. Rectal temperature was monitored hourly and the heating pad adjusted in order to prevent hypothermia. Repeated anesthetic injections equalling one third of the initial dose were administered hourly while respiration

continued. The full dose of Atropine (1 mg/Kg) was administered with each injection of anesthetic. During this period the animal's pharynx was aspirated every 2-3 h to minimize mucous accumulation. Following this 8-h maintenance period the animal was placed in a metabolic chamber and ventilated with 50% oxygen until the next morning when it was removed from the chamber. If the rat could than breath unassisted in atmospheric oxygen, it was returned to the home cage; otherwise it was replaced in the chamber for an additional 6-8 h. Sham-lesioned animals were maintained on the one-third dose of Nembutal every hour for 6-8 h following surgery, but they were not respirated or ventilated in the chamber. At the end of this maintenance period they were returned to their home cages and allowed to recover for a 10-day period. On days 5-7 they were once again restrained for 4 h/day and maintained on a 12 h food deprivation schedule. On days 8-10 they were restrained for 8 h/day and were maintained on a 14 h food deprivation regimen. Body weights were monitored daily and returned to presurgery values within the allowed recovery period.

Aortic catheterization. Once body weights were reestablished and stabilized after 10 days of recovery all animals were implanted with a descending aortic catheter. The catheter had a Teflon tip attached to 45 cm of Tygon tubing (OD - 0.75 cm, ID - 0.15 cm). The connection was made by soaking 1-2 cm of the Tygon in dichloroethane for 4-5 min and inserting the Teflon tip approximately 1 cm into the Tygon tube. The completed catheter was flushed with distilled water and left to dry overnight. The Teflon tip was cut to 1.7 cm with a blunt, tapered end.

Surgery was performed under aseptic conditions and the animals were anesthetized with Nembutal (50 mg/Kg). A 2-3 cm incision was made through the midabdominal region. The intestines were then gently retracted, and that descending aorta approximately 2 cm caudal to the left renal artery was exposed and isolated. The catheter was led subcutaneously to the nape of the neck where it was externalized. The aorta was gently lifted with hemostats to temporarily occlude blood flow, while a small puncture was made with a 27 ga stainless steel hypodermic needle. The catheter was inserted 1.7 cm into the hole, and blood flow through the aorta was reestablished. The catheter was then sutured to surrounding muscles to provide secure anchorage. Abdominal and cutaneous incisions were sutured with surgical silk and topical analgesics and antibacterial cream was applied to the wound. Animals were placed in their home cages and maintained on the food deprivation regimen. The catheter was flushed once daily with 0.25 cc of 100 U/ml heparinized isotonic saline (Sigma Chemical Co., St. Louis M.) Following a 48 h recovery period post-surgery testing began.

Post-Surgery Thermal Testing

Pre- and Post-surgical thermal testing were identical. The animal was restrained and placed in the metabolic chamber inside the controlled-temperature cabinet. The aortic catheter was connected to a Gould Statham pressure transducer (Model P23Gb) with Intramedic polyethylene tubing (PE 100), and blood pressure was continuously recorded on a Grass Model 5B polygraph. The animal's Tc and expired gases were allowed to stabilize for a minimum of 3 h at 23 ^{o}C (baseline condition). The

temperature was then raised to 27 °C for 1.5 h. The temperature in the metabolic chamber was then returned to 23 °C for 1 h. This process was repeated at 31 ° and 35 °C. During each baseline and test temperature, Tc, Tsk, Tsc, Ta, VO_2, VCO_2, and mean arterial blood pressure (MABP) were assessed at 10 min intervals. Following each testing session, which lasted 9.5 h, the animal was returned to its home cage. Evaporative heat loss was assessed by weighing the expired Drierite tube before and after exposure to each baseline and test temperature. The next day the same basic procedure was followed, except that 19, 15, and 11 °C were used as the test temperatures. Testing began at 0700 h following a 4 h food deprivation period.

Blood gas analysis. During post-surgery thermal testing the pH, pO_2, and pCO_2 content of the blood was analyzed. Blood samples were obtained after 3 h stabilization in the metabolic chamber at 23 °C and also immediately following completion of the most extreme test temperature. A 0.2 cc volume of blood was withdrawn directly from the aortic catheter by a heparinized hypodermic syringe. A sample of 200 ul was then collected from the catheter in a Corning microcollecting tube (no. 477476) and inserted into a Corning pH/Blood Gas Analyzer (Model 165) for determination. The 0.2 cc of blood initially collected in the syringe was returned to the animal via its aortic catheter in order to minimize changes in blood volume. The catheter was then flushed with 0.2 cc of heparinized saline and reconnected to the pressure transducer.

Lesion Verification and Histology

After the final test session, the animals were anesthetized with

Nembutal (50 mg/Kg) and a 10 ul jugular catheter (Taflon tubing, 10-15 cm, Stt-30, Small Parts Inc.) was implanted. The left jugular vein was exposed, isolated from surrounding tissue, and punctured with a 27 ga hypodermic needle. The catheter was inserted 5 cm beyond the puncture so that venous blood could be withdrawn. The catheter was then anchored to the surrounding tissue and the wound covered with a gauze pad soaked in sterile isotonic saline. Two bolus injections of phenylephrine (150 ug/Kg) were given with a 5-min interval between injections, while aortic blood pressure and heart rate were recorded on a Grass polygraph (Model 79D). Thirty min following phenylephrine testing baroreceptor functioning was further tested by two sequential bolus injections of acetylcholine (1 mg/Kg) with a 5-min interval between injections. Any NTS-lesioned animal who showed an increase in heart rate greater than 15 bpm in response to acetylcholine or a decrease in heart rate greater than 15 bpm in response to phenylephrine was placed in a Control Lesion group.

The rats were then sacrificed with an overdose of Nembutal and perfused through the heart successively with saline and 10% formalin. Following removal and fixation, the brains were embedded in paraffin and sectioned coronally at 10 um. The sections were stained with Cresyl violet for Nissl substance and counterstained with Luxol fast blue for myelin.

Statistical Analysis. The dependent variables were analyzed using repeated measures ANOVAs. Due to metabolic chamber equilibration time only the last three 10-min recordings for oxygen consumption (VO_2) and

carbon dioxide production (VCO_2) were used during the three 23 ^{o}C baseline conditions. Similarly, during the 90-min test temperatures, VO_2 and VCO_2 data obtained during the last 60-min period were analyzed. No such deletions were made for any other dependent variable.

Results

An overview of the results suggests that metabolic rate tended to decline during the heat challenge sessions but exhibits a trend to increase during the cold challenge sessions. The NTS-lesioning procedure had a general suppressive effect on metabolic rate and responsiveness during heat challenge but had no differential effects during cold challenge. The NTS-lesioning procedure also tended to promote hypotension during the baseline conditions in both heat and cold challenges. The lesions did, however, enhance a hypotensive trend during warm test temperatures and a hypertensive trend during cold test temperatures. Rectal temperature and abdominal and tail skin temperatures exhibited a tendency to increase during heat challenge and to decline during cold challenge sessions. These trends were not altered following lesions to the NTS.

Heat Stress: Baseline Data

All baseline oxygen consumption (VO_2), carbon dioxide production (VCO_2) and respiratory quotient (RQ) data were analyzed by 2 x 3 x 3 (Group x Baseline Condition x 10-min Interval) factorial ANOVAs with repeated measures on the last two factors. Data compiled before and

after surgery were analyzed separately. Following overall significant F ratios, trend analyses were run using orthogonal decomposition. Finally, Newman-Keuls tests provided post-hoc comparisons of group means. Probability levels for all analyses were set at $p < .05$.

Oxygen consumption (VO_2): Presurgery. Random assignment of subjects to treatment groups presurgically did not bias the VO_2 data. That is, there were no presurgical differences in mean VO_2 between subjects assigned to NTS and those assigned to the Sham groups. Mean VO_2 for all rats decreased across baseline conditions, $F(2,28)=44.50$, $p < .01$. Trend analysis showed the decrease to be linear, $F(2,28)=55.98$, $p < .01$. Within baseline conditions, however, mean VO_2 increased during the last three 10-min time intervals, $F(2,28)=7.11$, $p < .01$, with a significant linear trend, $F(2,28)=12.30$, $p < .01$.

Carbon dioxide production (VCO_2): Presurgery. Random assignment of subjects to treatment groups presurgically did not bias VCO_2 data in that there were no differences in mean VCO_2 between subjects assigned to NTS and those assigned to the Sham group. For all rats, VCO_2 decreased across baseline conditions, $F(2,28)=25.01$, $p < .01$, and the decrease was found to be linear, $F(2,28)=36.20$, $p < .01$.

Respiratory quotient (RQ): Presurgery. The presurgical assignment of subjects to treatment groups did not bias RQ data in that there were no differences in mean RQ between subjects assigned to NTS and those assigned to Sham groups. For all rats, RQ increased linearly across baseline conditions, $F(2,28)=5.42$, $p < .05$ and $F(2,28)=7.22$, $p < .05$ for the linear trend.

All baseline rectal temperature (Tb), abdominal skin temperature (Tsc) and tail skin temperature (Tsk) data were analyzed by 2 x 3 x 6 (Group x Baseline Condition $\bar{x}$ 10-min Interval) factorial ANOVAs with repeated measures on the last two factors. Data compiled before and after surgery were analyzed separately. Following overall significant F ratios, trend analyses were run using orthogonal decomposition. Finally, Newman-Keuls tests provided post hoc comparisons of group means. Probability levels for all analyses were set at $p < .05$.

Rectal temperature (Tb): Presurgery. Random assignment of subjects to treatment groups presurgically did not bias the Tb data. That is, there were no presurgical differences in mean Tb between subjects assigned to NTS and those assigned to the Sham group. Mean Tb for all rats increased across baseline conditions, $F(2,28)=9.83$, $p < .01$. Trend analysis showed the increase to be linear, $F(2,28)=13.89$, $p < .01$. Within baseline conditions, however, mean Tb decreased during the six 10-min time intervals, $F(5,70)=11.62$, $p < .01$, with a significant linear trend, $F(5,70)=15.02$, $p < .01$. In addition, post hoc tests of a significant Baseline Condition x 10-min Interval interaction, $F(10,140)=6.34$, $p < .01$, revealed that the tendency for Tb to decline within each baseline condition was significantly greater during the third presentation than during the initial two presentations. It was also revealed that Tb during the second and third presentation tended to decrease toward the initial baseline level.

Abdominal skin temperature (Tsc): Presurgery. Random assignment of subjects to treatment groups presurgically did not bias Tsc data in that

there were no differences in mean Tsc between subjects assigned to NTS and those assigned to the Sham group. Mean Tsc for all subjects increased across baseline conditions, $F(2,28)=19.36$, $p < .01$. Trend analysis showed the increase to be linear, $F(2,28)=26.95$, $p < .01$. Within baseline conditions, however, mean Tsc decreased during the six 10-min intervals, $F(5,70)=11.36$, $p < .01$, with a significant linear trend, $F(5,70)=17.54$, $p < .01$. In addition, post hoc tests of a significant Baseline Condition x 10-min Interval interaction, $F(10,140)=5.21$, $p < .01$, revealed that the trend for Tsc to decline within each baseline condition was significantly greater during the third presentation than during the first two presentations. It was also revealed that Tsc during the second and thirs presentation tended to decreased toward the initial baseline level.

Tail skin temperature (Tsk): Presurgery. The presurgical assignment of subjects to treatment groups did not bias Tsk data in that there were no differences in mean Tsk between subjects assigned to NTS or Sham groups. Mean Tsk for all rats increased linearly across baseline conditions, $F(2,28)=136.02$, $p < .01$ and $F(2,28)=239.35$, $p < .01$ for the linear trend. Within baseline conditions, however, mean Tsk decreased linearly during the six 10-min intervals, $F(5,70)=140.94$, $p < .01$ and $F(5,70)=328.55$, $p < .01$ for the linear trend. Moreover, post hoc tests of a significant Baseline Condition x 10-min Interval interaction, $F(10,140)=73.46$, $p < .01$, revealed that the trend for Tsk to decline within each baseline condition was significantly greater during the third presentation than during the first two presentations.

Evaporative heat loss (EHL) baseline values were analyzed by 2 x 3

(Group x Baseline Condition) factorial ANOVAs with repeated measures on the last factor. Data compiled before and after surgery were analyzed separately. Presurgery baseline EHL revealed no differences in means between subjects assigned to NTS and those assigned to the Sham group. Mean EHL for all subjects increased linearly across baseline conditions, $\underline{F}(2,28)=16.80$, $\underline{p} < .01$ for the linear trend.

Oxygen consumption (VO_2): Postsurgery. As Figure 2 and Table 1 show, NTS lesions suppressed mean VO_2, $\underline{F}(1,14)=5.03$, $\underline{p} < .05$ ($1.49 \pm .07$ vs $1.90 \pm .13$ ml $O_2 \cdot g^{-1} \cdot h$). Mean VO_2 decreased linearly across the baseline conditions, $\underline{F}(2,28)=28.67$, $\underline{p} < .01$ and $\underline{F}(2,28)=50.02$, $\underline{p} < .01$ for the linear trend, as it had in presurgery testing. A significant Treatment x Baseline Condition interaction, $\underline{F}(2,28)=8.57$, $\underline{p} < .01$, however, emphasized that the decline in VO_2 across baseline conditions differed for lesioned and sham rats (Fig. 3). The significant post hoc test revealed that the rate of VO_2 decline was steeper for Sham than for NTS rats. Mean VO_2 increased linearly across the 10-min intervals postsurgically, as they had presurgically, $\underline{F}(2,28)=17.13$, $\underline{p} < .01$ and $\underline{F}(2,28)=21.87$, $\underline{p} < .01$ for the linear trend.

Carbon dioxide production (VCO_2): Postsurgery. As Figure 4 and Table 1 show, the NTS lesions did not affect VCO_2 data since there were no differences in mean VCO_2 between NTS and Sham rats. For all subjects, VCO_2 decreased across baseline conditions, $\underline{F}(2,28)=9.09$, $\underline{p} < .01$ and was found to be linear, $\underline{F}(2,28)=26.47$, $\underline{p} < .01$, as it was presurgically. Within baseline conditions, however, mean VCO_2 increased during the six 10-min intervals, $\underline{F}(2,28)=5.58$, $\underline{p} < .01$ with a significant linear trend,

$F(2,28)=5.78$, p .05.

Direct aortic blood pressure (BP): Postsurgery. Blood pressure data was analyzed by 2 x 3 x 6 (Treatment x Baseline Condition x 10-min Interval) factorial ANOVAs with repeated measures on the last two factors. As Figure 5 and Table 2 show, NTS lesions suppressed mean BP, $F(1,14)=9.30$, $p < .01$ ($104.3 \pm .67$ vs $129.1 \pm .94$ mm Hg). In addition, post hoc tests of a significant Treatment x Baseline Condition interaction, $F(2,28)=3.97$, $p < .05$, revealed that the suppressed BP of the NTS group showed a trend to decline across the baseline conditions when compared to the stable but elevated BP of the Sham animals (Fig. 6).

Rectal temperature (Tb): Postsurgery. As shown in Figure 7 and Table 3, NTS lesions did not alter the Tb data. That is, there were no postsurgical differences in mean Tb between NTS-lesioned and Sham groups. Mean Tb for all subjects increased across baseline conditions, $F(2,28)=13.83$, $p < .01$. Trend analysis showed the increase to be linear, $F(2,28)=19.30$, $p < .01$. Within baseline conditions, however, mean Tb decreased during the six 10-min time intervals, $F(5,70)=36.97$, $p < .01$, with a significant linear trend, $F(5,70)=62.08$, $p < .01$. In addition, post hoc tests of a significant Baseline Condition x 10-min Interval interaction, $F(10,140)=8.00$, $p < .01$, revealed that the tendency for Tb to decline within each baseline condition was significantly greater during the third presentation than during the initial two presentations. It was also revealed that Tb during the second and third presentation tended to decrease toward the initial baseline level.

Tail skin temperature (Tsk): Postsurgery. As shown in Figure 9 and

Table 3, NTS lesions did not alter Tsk data. That is, there were no postsurgical differences in mean Tsk between NTS lesioned and Sham animals. Mean Tsk for all subjects increased linearly across baseline conditions, $F(2,28)=146.37$, $p < .01$ and $F(2,28)=251.01$, $p < .01$ for the linear trend. Within baseline conditions, however, mean Tsk decreased linearly during the six 10-min time intervals, $F(5,70)=138.95$, $p < .01$ and $F(5,70)=156.90$, $p < .01$ for the linear trend. Moreover, post hoc tests of a significant Baseline Condition x 10-min Interval interaction, $F(10,140)=67.98$, $p < .01$, revealed that the tendency for Tsk to decline within each baseline condition was significantly greater during the third presentation than during the initial two presentations. Post hoc tests of a significant Treatment x Baseline Condition x 10-min Interval interaction, $F(10,140)=2.30$, $p < .05$, revealed a trend for the Tsk of NTS animals to decline during all three baseline conditions while for the Sham animals, Tsk declined only during the third baseline presentation and remained stable during the first two presentations.

Evaporative heat loss (EHL): Postsurgery. There were no postsurgical differences in mean EHL between NTS and Sham animals. Mean EHL increased linearly across baseline conditions for all subjects, $F(2,28)=14.38$, $p < .01$ and $F(2,28)=24.42$, $p < .01$ for the linear trend. In addition, post hoc tests done on a significant Treatment x Baseline Condition interaction, $F(2,28)=5.18$, $p < .05$, revealed a steeper rise in EHL for Sham animals than for NTS animals (Fig. 10).

Heat Stress: Test Temperature Data

All test temperature oxygen consumption (VO_2) and carbon dioxide

production (VCO_2) data were analyzed by 2 x 3 x 6 (Group x Test Temperature x 10-min Interval) factorial ANOVAs with repeated measures on the last two factors. Data compiled before and after surgery were analyzed separately. Following overall significant F ratios, trend analyses were run using orthogonal decomposition. Finally, Newman-Keuls tests provided post hoc comparisons of group means. Probability levels for all analyses were set at $p < .05$.

Oxygen consumption (VO_2): Presurgery. Random assignment of subjects to treatment groups presurgically did not bias the VO_2 data. That is, there were no presurgical differences in mean VO_2 between subjects assigned to NTS and those assigned to the Sham groups. Mean VO_2 for all rats decreased across test temperatures, $F(2,28)=14.84$, $p < .01$. Trend analysis showed the decrease to be linear, $F(2,28)=25.70$, $p < .01$. Within test temperatures, however, mean VO_2 increased during the last six 10-min intervals, $F(5,70)=10.62$, $p < .01$, with a significant linear trend, $F(5,70)=15.16$, $p < .01$. In addition, post hoc tests on a significant Test Temperature x 10-min Interval interaction, $F(10,140)=9.14$, $p < .01$, revealed that the increase in VO_2 during the test temperatures occurred only during the most extreme test temperature (35 ^{o}C).

Carbon dioxide production (VCO_2): Presurgery. Random assignment of subjects to treatment groups presurgically did not bias the VCO_2 data in that there were no differences in mean VCO_2 between subjects assigned to NTS and those assigned to the Sham group. Mean VCO_2 for all subjects decreased linearly across test temperatures, $F(2,28)=5.23$, $p < .05$ and $F(2,28)=4.61$, $p < .05$ for the linear trend. Within test temperatures,

however, mean VCO_2 increased during the last six 10-min time intervals, $F(5,70)=5.74$, $p < .01$, with a significant linear trend, $F(5,70)=7.70$, $p < .05$. In addition, post hoc tests on a significant Test Temperature x 10-min Interval interaction, $F(10,140)=9.15$, $p < .01$, revealed that the increase in VCO_2 during the test temperatures occurred only during the most extreme test temperature (35 ^{o}C).

All test temperature rectal temperature (Tb) and abdominal skin temperature (Tsc) and tail skin temperature (Tsk) data were analyzed by 2 x 3 x 9 (Group x Test Temperature x 10-min Interval) factorial ANOVAs with repeated measures on the last two factors. Data compiled before and after durgery were analyzed separately. Following overall significant F ratios, trend analyses were run using orthogonal decomposition. Finally, Newman-Keuls tests provided post hoc comparisons of group means. Probability levels for all analyses were set at $p < .05$.

Rectal temperature (Tb): Presurgery. Random assignment of subjects to treatment groups presurgically did not bias the Tb data. That is, there were no presurgical differences in mean Tb between subjects assigned to NTS and those assigned to the Sham group. Mean Tb for all rats increased across test temperatures, $F(2,28)=17.38$, $p < .01$. Trend analyses showed the increase to be linear, $F(2,28)=24.61$, $p < .01$. Within test temperatures, mean Tb increased during the nine 10-min time intervals, $F(8,112)=59.22$, $p < .01$, with a significant linear trend, $F(8,112)=74.67$, $p < .01$. In addition, post hoc tests of a significant Test Temperature x 10-min Interval interaction, $F(16,224)=24.54$, $p < .01$, revealed that the tendency for Tb to increase within each test temperature was significantly

greater during the 35 °C temperature.than during the 31 and 27 °C temperatures. It was also revealed that Tb during the initial sample at each test temperature was not significantly different across the test temperatures, while during the final sample Tb during 35 °C was greater than that at 31 °C, which was greater than that at 27 °C.

Abdominal skin temperature (Tsc): Presurgery. Random assignment of subjects to treatment groups presurgically did not bias Tsc data in that there were no differences in mean Tsc between subjects assigned to NTS and those assigned to the Sham group. Mean Tsc for all subjects increased across test temperatures, $F(2,28)=46.43$, $p< .01$. Trend analysis showed the increase to be linear, $F(2,28)=61.14$, $p< .01$. Within test temperatures, mean Tsc increased during the nine 10-min intervals, $F(8,112)=64.55$, $p< .01$, with a significant linear trend, $F(8,112)=93.89$, $p< .01$. In addition, post hoc tests of a significant Test Temperature x 10-min Interval interaction, $F(16,224)=27.86$, $p< .01$, revealed that the tendency for Tsc to increase within each test temperature was significantly greater during the 35 °C temperature than during 31 and 27 °C. It was also revealed that Tsc during the initial sample at each test temperature was not significantly different across the test temperatures, while during the final sample Tsc during 35 °C was greater than that at 31 °C, which was greater than that at 27 °C.

Tail skin temperature (Tsk): Presurgery. Random assignment of subjects to treatment groups presurgically did not bias the Tsk data. That is, there were no presurgical differences in mean Tsk between subjects assigned to NTS and those assigned to the Sham group. Mean Tsk for all

subjects increased across test temperatures, $F(2,28)=568.35$, $p < .01$. Trend analysis showed the increase to be linear, $F(2,28)=1034.87$, $p < .01$. Within test temperatures, mean Tsk increased during the nine 10-min intervals, $F(8,112)=365.90$, $p < .01$, with a linear trend, $F(8,112)=711.02$, $p < .01$. In addition, post hoc tests of a significant Test Temperature x 10-min Interval interaction, $F(16,224)=46.28$, $p < .01$, revealed that the tendency for Tsk to increase within each test temperature was significantly greater during the 35 ^{o}C temperature than during 31 and 27 ^{o}C. It was also revealed that Tsk during the initial sample at each test temperature was not significantly different across the test temperatures, while during the final sample Tsk during 35 ^{o}C was greater than at 31 ^{o}C, which was greater than that at 27 ^{o}C.

Evaporative heat loss (EHL) test temperature values were analyzed by 2 x 3 (Group x Test Temperature) factorial ANOVAs with repeated measures on the last factor. Data compiled before and after surgery were analyzed separately. Presurgery test temperature EHL revealed no differences in means between subjects assigned to NTS and those assigned to the Sham group. Mean EHL for all subjects increased linearly across test temperatures, $F(2,28)=9.97$, $p < .01$ and $F(2,28)=28.35$, $p < .01$ for the linear trend.

Oxygen consumption (VO_2): Postsurgery. As Figure 2 and Table 4 show, NTS lesions had no effect on mean VO_2 data since there were no differences in means between NTS and Sham animals. Mean VO_2 decreased linearly across the test temperatures, $F(2,28)=27.90$, $p < .01$ and $F(2,28)=35.60$, $p < .01$ for the linear trend, as it had in presurgery testing.

A significant Treatment x Test Temperature interaction, $F(2,28)=7.63$, $p<.01$, however, emphasized that the decline in VO_2 across test temperatures differed for the lesioned and sham rats (Fig. 11). The post hoc test revealed that the rate of VO_2 decline was steeper for Sham than for NTS rats. In addition, post hoc tests of a Test Temperature x 10-min Interval ineraction, $F(2,28)=4.02$, $p< .01$, revealed that VO_2 tended to remain stable during 27 and 31 ^{o}C but tended to increase during the latter half of the 35 ^{o}C presentation.

Carbon dioxide production (VCO_2): Postsurgery. As Figure 4 and Table 4 show, the NTS lesions did not affect VCO_2 data since there were no differences in mean VCO_2 between NTS and Sham rats. For all subjects, mean VCO_2 decreased across test temperatures, $F(2,28)=9.21$, $p< .01$ and was found to be linear, $F(2,28)=23.44$, $p< .01$. In addition, post hoc tests of a significant Test Temperature x 10-min Interval interaction, $F(10,140)=3.30$, $p< .01$, revealed a trend for VCO_2 to decline during the 27 and 31 ^{o}C presentations while it tended to increase during the 35 ^{o}C presentation.

Direct aortic blood pressure (BP): Postsurgery. Blood pressure data was analyzed by 2 x 3 x 9 (Treatment x Test Temperature x 10-min Interval) factorial ANOVAs with repeated measures on the last two factors. As Figure 5 and Table 5 show, NTS lesions suppressed mean BP, $F(1,14)=5.66$, $p< .05$ (88.7 ± 1.26 vs $122.4\pm.94$ mm Hg). Mean BP for all subjects decreased linearly across the test temperatures, $F(2,28)=5.43$, $p< .05$ and $F(2,28)=6.15$, $p< .05$ for the linear trend. Within test temperatures, mean BP decreased during the nine 10-min intervals, $F(8,112)=3.71$, $p< .01$, with a

significant linear trend, $F(8,112)=8.61$, $p < .05$.

Rectal temperature (Tb): Postsurgery. As shown in Figure 7 and Table 6, NTS lesions did not alter the Tb data. That is, there were no postsurgical differences in mean Tb between NTS-lesioned and Sham groups. Mean Tb for all rats increased across test temperatures, $F(2,28)=15.20$, $p < .01$. Trend analysis showed the increase to be linear, $F(2,28)=22.91$, $p < .01$. Within test temperatures, mean Tb also increased during the nine 10-min time intervals, $F(8,112)=118.79$, $p < .01$, with a significant linear trend, $F(8,112)=163.92$, $p < .01$. In addition, post hoc tests of a Test Temperature x 10-min Interval interaction, $F(16,224)=16.63$, $p < .01$, revealed that the initial Tb value was similar within each test temperature. However, the trend for Tb to increase within each test temperature was greatest during the 35 ^{o}C presentation, was moderate during 31 ^{o}C, and was not significant during the 27 ^{o}C presentation.

Abdominal skin temperature (Tsc): Postsurgery. As shown in Figure 8 and Table 6, NTS lesions did not alter Tsc data since there were no postsurgical differences in mean Tsc between NTS and Sham groups. Mean Tsc for all animals decreased linearly across test temperatures, $F(2,28)=17.56$, $p < .01$ and $F(2,28)=25.38$, $p < .01$ for the linear trend. Within test temperatures, mean Tsc increased linearly during the nine 10-min time intervals, $F(8,112)=22.31$, $p < .01$ and $F(8,112)=115.63$, $p < .01$ for the linear trend. Moreover, post hoc tests done on a significant Test Temperature x 10-min Interval interaction, $F(16,224)=5.78$, $p < .01$, revealed that the initial Tsc value was similar within each test temperature. However, the trend for Tsc to increase within each test temperature

was greatest for 35 °C, was moderate for 31 °C, and was nonsignificant for the 27 °C presentation.

Tail skin temperature (Tsk): Postsurgery. As shown in Figure 9 and Table 6, NTS lesions did not alter Tsk data since there were no postsurgical differences in mean Tsk between NTS and Sham groups. Mean Tsk for all rats decreased linearly across test temperatures, $F(2,28)=204.94$, $p < .01$ and $F(2,28)=284.87$, $p < .01$ for the linear trend. Within test temperatures, mean Tsk increased linearly during the nine 10-min time intervals, $F(8,112)=165.56$, $p < .01$ and $F(8,112)=280.14$, $p < .01$ for the linear trend. Moreover, post hoc tests of a significant Test Temperature x 10-min Interval interaction, $F(16,224)=22.92$, $p < .01$, revealed that the tendency for Tsk to increase within each test temperature was greatest for 35 °C, moderate for 31 °C and relatively small for the 27 °C presentation.

Evaporative heat loss (EHL): Postsurgery. There were no postsurgical differences in mean EHL between NTS and Sham animals. Mean EHL increased linearly across test temperatures, $F(2,28)=43.00$, $p < .01$ and $F(2,28)=82.34$, $p < .01$ for the linear trend.

Blood pH: Postsurgery. Blood gases were analyzed by 2 x 2(Treatment x Temperature) factorial ANOVAs with repeated measures on the last factor. As Table 7 shows, the NTS lesions significantly suppressed blood pH as compared with the Sham animals ($7.30 \pm .001$ vs $7.39 \pm .003$).

Cold Stress: Baseline Condition Data

All baseline oxygen consumption (VO_2), carbon dioxide production (VCO_2) and respiratory quotient (RQ) data were analyzed by 2 x 3 x 3

(Group x Baseline Condition x 10-min Interval) factorial ANOVAs with repeated measures on the last two factors. Data compiled before and after surgery were analyzed separately. Following overall significant F ratios, trend analyses were run using orthogonal decomposition. Finally, Newman-Keuls tests provided post hoc comparisons of group means. Probability levels for all analyses were set at $p < .05$.

No significant presurgical effects were found for VO_2, VCO_2 and RQ data.

All baseline rectal temperature (Tb), abdominal skin temperature (Tsc) and tail skin temperature (Tsk) data were analyzed by 2 x 3 x 6 (Group x Baseline Condition x 10-min Interval) factorial ANOVAs with repeated measures on the last two factors. Data compiled before and after surgery were analyzed separately. Following overall significant F ratios, trend analyses were run using orthogonal decomposition. Finally, Newman-Keuls tests provided post hoc comparisons of group means. Probability levels for all analyses were set at $p < .05$.

Rectal temperature (Tb): Presurgery. Random assignment of subjects to treatment groups presurgically did not bias the Tb data. That is, there were no presurgical differences in mean Tb between subjects assigned to NTS and those assigned to the Sham group. Mean Tb for all rats decreased across baseline conditions, $F(2,28)=8.67$, $p < .01$. Trend analyses showed the decrease to be linear, $F(2,28)=13.04$, $p < .01$. In addition, post hoc tests of a significant Baseline Condition x 10-min Interval interaction, $F(10,140)=2.23$, $p < .05$, revealed that there was a tendency for Tb to increase within only the final baseline condition exposure.

Abdominal skin temperature (Tsc): Presurgery. Random assignment of subjects to treatment groups presurgically did not bias Tsc data in that there were no differences in mean Tsc between subjects assigned to NTS and those assigned to the Sham group. Mean Tsc for all subjects decreased across baseline conditions, $F(2,28)=6.62$, $p < .01$. Trend analyses showed the decrease to be linear, $F(2,28)=8.25$, $p < .05$. Within baseline conditions, however, mean Tsc increased during the six 10-min time intervals, $F(5,70)=17.97$, $p < .01$, with a significant linear trend, $F(5,70)=40.14$, $p < .01$.

Tail skin temperature (Tsk):Presurgery. Random assignment of subjects to treatment groups presurgically did not bias Tsk data in that there were no differences in mean Tsk between subjects assigned to NTS and Sham groups. Mean Tsk for all subjects decreased linearly across baseline conditions, $F(2,28)=399.41$, $p < .01$ and $F(2,28)=754.43$, $p < .01$ for the linear trend. Within baseline conditions, however, mean Tsk increased linearly during the six 10-min time intervals, $F(5,70)=222.26$, $p < .01$ and $F(5,70)=288.21$, $p < .01$. In addition, post hoc tests of a significant Baseline Condition x 10-min Interval interaction, $F(10,140)=133.26$, $p < .01$, revealed that the trend for Tsk to increase within each baseline condition was significantly greater during the third presentations than during the first two presentations.

Oxygen consumption (VO_2): Postsurgery. No effects were significant (Fig. 12).

Carbon dioxide production (VCO_2): Postsurgery. As Figure 13 and Table 1 show, the NTS lesions did not affect VCO_2 data since there were

no differences in mean VCO_2 between NTS and Sham rats. For all subjects, mean VCO_2 increased linearly across baseline conditions $F(2,28)=12.00$, $p < .01$ and $F(2,28)=14.83$, $p < .01$ for the linear trend. Moreover, post hoc tests of a significant Treatment x Baseline Condition interaction, $F(2,28)=5.41$, $p < .05$, revealed that the increase in VCO_2 across baseline conditions occurred only with the Sham animals. Furthermore, the post hoc tests revealed that the mean VCO_2 during the initial baseline condition was similar between NTS and Sham animals (Fig. 14).

Direct aortic blood pressure (BP): Postsurgery. Blood pressure data was analyzed by 2 x 3 x 6 (Treatment x Baseline Condition x 10-min Interval) factorial ANOVAs with repeated measures on the last two factors. As Figure 5 and Table 2 show, NTS lesions suppressed mean BP, $F(1,14)=9.04$, $p < .01$ (86.6±.05 vs 134.1±.64 mm Hg). Mean BP for all rats decreased linearly across baseline conditions, $F(2,28)=5.42$, $p < .05$ and $F(2,28)=6.03$, $p < .05$ for the linear trend. In addition, post hoc tests of a significant Treatment x Baseline Condition interaction, $F(2,28)=3.78$, $p < .05$, revealed that the suppressed BP of the NTS group showed a trend to decline across the baseline conditions when compared to the stable, but elevated BP of the Sham animals. Post hoc tests on a significant Treatment x Baseline Condition x 10-min Interval interaction, $F(10,140)=2.16$, $p < .05$, revealed that the trend for BP to decline during the first two baseline presentations occurred only with the NTS animals. The BP for the Sham animals remained stable but elevated. Moreover, the significant three way interaction suggests that the decline in BP during the first two baseline presentations observed in the significant Baseline Condition x

10-min Interval interaction, $F(10,140)=3.26$, $p < .01$, was due mainly to the NTS animals.

Rectal temperature (Tb): Postsurgery. As Figure 15 and Table 3 show, NTS lesions did not alter the Tb data in that there were no postsurgical differences in mean Tb between NTS and Sham groups. Mean Tb for all subjects decreased across baseline conditions, $F(2,28)=7.37$, $p < .01$, with a significant linear trend, $F(2,28)=7.97$, $p < .05$. Within baseline conditions, however, mean Tb increased linearly during the six 10-min time intervals, $F(5,70)=4.16$, $p < .01$ and $F(2,28)=4.98$, $p < .05$ for the linear trend. In addition, post hoc tests of a significant Baseline Condition x 10-min Interval interaction, $F(10,140)=17.52$, $p < .01$, revealed that the tendency for Tb to increase within each baseline condition was significantly greater during the second and third presentation than during the initial presentation.

Abdominal skin temperature (Tsc): Postsurgery. As shown in Figure 16 and Table 3, NTS lesions did not alter Tsc data since there were no postsurgical differences in mean Tsc following NTS and Sham animals. Mean Tsc for all rats decreased linearly across baseline conditions, $F(2,28)=9.28$, $p < .01$ and $F(2,28)=10.47$, $p < .01$ for the linear trend. Within baseline conditions, however, mean Tsc increased linearly during the six 10-min time intervals, $F(5,70)=12.61$, $p < .01$ and $F(5,70)=30.44$, $p < .01$ for the linear trend. Moreover, post hoc tests of a significant Baseline Condition x 10-min Interval interaction, $F(10,140)=16.17$, $p < .01$, revealed that the tendency for Tsc to increase within each baseline condition was significantly greater during the second and third presentation

than during the initial baseline presentation. It was also revealed that Tsc during the second and third presentation tended to increase toward the initial baseline level.

Tail skin temperature (Tsk): Postsurgery. As illustrated in Figure 17 and Table 3, NTS lesions did not alter Tsk data in that there were no postsurgical differences in mean Tsk between NTS and Sham groups. Mean Tsk for all subjects decreased linearly across baseline conditions, $F(2,28)=124.74$, $p< .01$ and $F(2,28)=189.52$, $p< .01$ for the linear trend. Within baseline conditions, however, mean Tsk increased linearly during the six 10-min time intervals, $F(5,70)=190.40$, $p <.01$ and $F(5,70)=252.38$, $p< .01$ for the linear trend. In addition, post hoc tests of a significant Baseline Condition x 10-min Interval interaction, $F(10,140)=114.40$, $p< .01$, revealed that the tendency for Tsk to increase within each baseline condition was significantly greater during the second and third presentation than during the initial baseline presentation.

Evaporative heat loss (EHL): Postsurgery. There were no postsurgical differences in mean EHL between NTS and Sham animals. Post hoc tests done on a significant Treatment x Baseline Condition interaction, $F(2,28)=4.18$, $p <.05$, revealed steeper rises in EHL for Sham animals than for NTS animals.

Cold Stress: Test Temperature Data

All test temperature oxygen consumption (VO_2) and carbon dioxide production (VCO_2) data were analyzed by 2 x 3 x 6 (Group x Test Temperature x 10-min Interval) factorial ANOVAs with repeated measures on the last two factors. Data compiled before and after surgery were analyzed

separately. Following overall significant F ratios, trend analyses were run using orthogonal decomposition. Finally, Newman-Keuls tests provided post hoc comparisons of group means. Probability levels for all analyses were set at $p < .05$.

Oxygen consumption (VO_2): Presurgery. Random assignment of subjects to treatment groups presurgically did not bias the VO_2 data. That is, there were no presurgical differences in mean VO_2 between subjects assigned to NTS and those assigned to the Sham group. Mean VO_2 for all rats increased linearly across test temperatures, $F(2,28)=11.66$, $p < .01$ and $F(2,28)=14.69$, $p < .01$ for the linear trend. Within test temperatures, mean VO_2 increased linearly during the last six 10-min time intervals, $F(5,70)=23.39$, $p < .01$ and $F(5,70)=37.13$, $p < .01$ for the linear trend. In addition, post hoc tests of a significant Test Temperature x 10-min Interval ineraction, $F(10,140)=2.77$, $p < .01$, revealed that the increase in VO_2 during the test temperatures occurred progressively more during 15 and 11 ^{o}C while remaining stable and suppressed during the 19 ^{o}C test temperature.

Carbon dioxide production (VCO_2): Presurgery. Random assignment of subjects to treatment groups presurgically did not bias the VCO_2 data in that there were no differences in mean VCO_2 between subjects assigned to NTS and those assigned to the Sham group. Mean VCO_2 for all subjects increased linearly across test temperatures, $F(2,28)=22.43$, $p < .01$ and $F(2,28)=30.80$, $p < .01$ for the linear trend. Within test temperatures, mean VCO_2 increased during the last six 10-min time intervals, $F(5,70)=12.86$, $p < .01$, with a significant linear trend, $F(5,70)=16.92$, $p < .01$.

In addition, post hoc tests of a significant Test Temperature x 10-min Interval interaction, $F(10,140)=3.29$, $p < .01$, revealed that the increase in VCO_2 during the test temperatures was greater during 15 and 11 ^{o}C while VCO_2 during 19 ^{o}C remained suppressed and stable.

All test temperature rectal temperature (Tb), abdominal skin temperature (Tsc) and tail skin temperature (Tsk) data were analyzed by 2 x 3 x 9 (Group x Test Temperature x 10-min Interval) factorial ANOVAs with repeated measures on the last two factors. Data compiled before and after surgery were analyzed separately. Following overall significant F ratios, trend analyses were run using orthogonal decomposition. Finally, Newman-Keuls tests provided post hoc comparisons of group means. Probability levels for all analyses were set at $p < .05$.

Rectal temperature (Tb): Presurgery. No significant effects were obtained.

Abdominal skin temperature (Tsc): Presurgery. Random assignment of subjects to treatment groups presurgically did not bias Tsc data since there were no differences in mean Tsc between subjects assigned to NTS and those assigned to the Sham group. Mean Tsc for all rats decreased across test temperatures, $F(2,28)=7.51$, $p < .01$, with a significant linear trend, $F(2,28)=10.07$, $p < .01$. Within test temperatures, mean Tsc decreased during the nine 10-min time intervals, $F(8,112)=13.33$, $p < .01$, with a significant linear trend, $F(8,112)=31.19$, $p < .01$. In addition, post hoc tests of a significant Test Temperature x 10-min Interval interaction, $F(16,224)=3.03$, $p < .01$, revealed that the tendency for Tsc to decrease within each test temperature was greater during the 11 ^{o}C temperature

than during the 15 and 19 °C temperatures. It was also revealed that Tsc during the initial sample at each test temperature was not significantly different across the test temperatures.

Tail skin temperature (Tsk): Presurgery. Random assignment of subjects to treatment groups presurgically did not bias the Tsk data. That is, there were no presurgical differences in mean Tsk between subjects assigned to NTS and to Sham groups. Mean Tsk for all subjects decreased across test temperatures, $F(2,28)=397.42$, $p < .01$, with a significant linear component, $F(2,28)=552.17$, $p < .01$. Within test temperatures, mean Tsk decreased linearly during the nine 10-min time intervals, $F(8,112)=449.45$, $p < .01$ and $F(8,112)=674.45$, $p < .01$.for the linear trend. In addition, post hoc tests of a significant Test Temperature x 10-min Interval interaction, $F(16,224)=130.15$, $p < .01$, revealed that the tendency for Tsk to decrease within each test temperature was greater during the 11 °C temperature than during 15 and 19 °C. It was also revealed that Tsk during the initial sample at each test temperature was not significantly different across the test temperatures, while during the final sample Tsk during 11 °C was less than at 15 °C, which was less than that at 19 °C.

Oxygen consumption (VO_2): Postsurgery. As shown in Figure 12 and Table 4, NTS lesions had no effect on mean VO_2 data in that there were no postsurgical differences in mean between NTS and Sham animals. Mean VO_2 increased linearly across the test temperatures, $F(2,28)=8.99$, $p < .01$ and $F(2,28)=14.56$, $p < .01$ for the linear trend, as it had in presurgery testing. Within test temperatures, mean VO_2 increased linearly

during each test temperature, $F(5,70)=7.44$, $p<.01$ and $F(5,70)=36.60$, $p<.01$ for the linear trend.

Carbon dioxide production (VCO_2): Postsurgery. As Figure 13 and Table 4 show, the NTS lesions did not affect VCO_2 data since there were no differences in mean VCO_2 between NTS and Sham rats. For all subjects, mean VCO_2 increased across test temperatures, $F(2,28)=36.44$, $p<.01$, with a significant linear trend, $F(2,28)=44.08$, $p<.01$. Within test temperatures, mean VCO_2 increased during the six 10-min time intervals, $F(5,70)=13.18$, $p<.01$, with a linear trend, $F(5,70)=15.58$, $p<.01$. Post hoc tests of a significant Treatment x 10-min Interval interaction, $F(5,70)=3.10$, $p<.05$, revealed a steeper increase in VCO_2 for Sham animals than for the suppressed NTS VCO_2 (Fig. 18). In addition, post hoc tests of a significant Test Temperature x 10-min Interval interaction, $F(10, 140)=4.50$, $p<.01$, revealed a trend for VCO_2 to increase steeper during the 11 ^{o}C presentation as compared to 15 and 19 ^{o}C temperatures.

Direct aortic blood pressure (BP): Postsurgery. Blood pressure data were analyzed by 2 x 3 x 9 (Treatment x Test Temperature x 10-min Interval) factorial ANOVAs with repeated measures on the last two factors. As Figure 4 and Table 5 show, NTS lesions did not alter mean BP in that there were no differences in mean BP between NTS and Sham groups. Mean BP increased linearly across the test temperatures, $F(2,28)=28.36$, $p<.01$ and $F(2,28)=38.26$, $p<.01$ for the linear trend. Within test temperatures, mean BP decreased during the nine 10-min time intervals, $F(8,112)=17.70$, $p<.01$, with a significant linear trend, $F(8,112)=43.50$, $p<.01$. Post hoc tests performed on a significant Treatment x Test Temperature

interaction, $F(2,28)=18.43$, $p < .01$, revealed that the trend for BP to increase across test temperatures was greater in the NTS animals than in the Sham group (Fig. 19). Post hoc tests done on a significant Treatment x 10-min Interval interaction, $F(8,112)=8.92$, $p < .01$, revealed a stable BP for the Sham group while for NTS animals BP initially rose and then proceeded to decline during the last three-quarters of the test temperature exposure (Fig. 20). In addition, post hoc tests done on a significant Test Temperature x 10-min Interval interaction, $F(16,224)=9.29$, $p < .01$, revealed that the initial increase in BP during test temperatures was greatest for the 11 ^{o}C temperature, was moderate for 15 ^{o}C and was slight for 19 ^{o}C. Moreover, the rate of decline in BP within the last three-quarters of the test temperature exposure was steepest for 11 ^{o}C, moderate for 15 ^{o}C and did not occur within the 19 ^{o}C presentation.

Rectal temperature (Tb): Postsurgery. As shown in Figure 15 and Table 6, NTS lesions did not alter the Tb data in that there were no postsurgical differences in mean Tb between NTS lesioned and Sham groups. Within test temperatures, mean Tb declined linearly during the nine 10-min time intervals, $F(8,112)=7.12$, $p < .01$ and $F(8,112)=10.94$, $p < .01$ for the linear trend. In addition, post hoc tests performed on a significant Test Temperature x 10-min Interval interaction, $F(16,224)=1.95$, $p < .05$, revealed that the rate of decline in Tb was steeper at 11 ^{o}C than at 15 and 19 ^{o}C. Moreover, it was shown that the initial Tb recorded during the test temperatures were similar across test temperatures.

Abdominal skin temperature (Tsc): Postsurgery. As shown in Figure 16

and Table 6, NTS lesions did not alter Tsc data since there were no postsurgical differences in mean Tsc between NTS and Sham groups. Mean Tsc for all rats decreased linearly across test temperatures, $F(2,28)=10.41$, $p \leq .01$ and $F(2,28)=13.00$, $p < .01$ for the linear trend. Within test temperatures, mean Tsc decreased linearly during the nine 10-min time intervals, $F(8,112)=38.33$, $p < .01$ and $F(8,112)=59.59$, $p < .01$ for the linear trend. In addition, post hoc tests done on a significant Test Temperature x 10-min Interval interaction, $F(16,224)=7.34$, $p < .01$, revealed that the rate of decline in Tsc was greatest during 11 ^{o}C, moderate at 15 ^{o}C and slight during 19 ^{o}C. Furthermore, the initial Tsc values obtained during the test temperatures were found to be similar across the test temperatures.

Tail skin temperature (Tsk): Postsurgery. As shown in Figure 17 and Table 6, NTS lesions did not alter Tsk data in that there were no postsurgical differences in Tsk between NTS and Sham groups. Mean Tsk for all rats decreased linearly across test temperatures, $F(2,28)=163.87$, $p < .01$ and $F(2,28)=264.24$, $p < .01$ for the linear trend. Within test temperatures, mean Tsk decreased linearly during the nine 10-min time intervals, $F(8,112)=334.09$, $p < .01$ and $F(8,112)=5.89$, $p < .05$ for the linear trend. Moreover, post hoc tests done on a significant Test Temperature x 10-min Interval interaction, $F(16,224)=40.46$, $p < .01$, revealed that the rate of decline in Tsk was steepest for 11 ^{o}C, moderate for 15 ^{o}C, and was slight for the 19^{o}C presentation. Moreover, the initial Tsk obtained during each test temperature were similar across test temperatures.

Evaporative heat loss (EHL): Postsurgery. There were no postsurgical differences in mean EHL between NTS and Sham animals. Mean EHL increased linearly across test temperatures, $F(2,28)=4.23$, $p< .05$ and $F(2,28)=5.06$, $p <.05$ for the linear trend.

Baroreflex testing. Results of pharmacological baroreflex testing analysis, using an independent t-test, are presented in Table 8. For the phenylephrine reflex test there was no significant difference, $t(14)=1.65$, $p >.05$ in the change in BP obtained. The NTS animals had a mean change of $76.50\pm.22$ mm Hg and the Sham animals had a mean change of $70.13\pm.52$ mm Hg. The mean change in heart rate between NTS and Sham animals in response to phenylephrine injections was significantly different, $t(14)=4.98$, $p <.01$. The NTS animals had a mean change in heart rate of $-7.13\pm.12$ bpm and the mean change in heart rate for the Sham animals was $-72.06\pm.36$ bpm (Fig. 21). For the acetylcholine reflex test there were no significant differences, $t(14)=1.24$, $p >.05$ in the BP changes between NTS and Sham animals. The NTS animals had a mean change of $-49.00\pm.20$ mm Hg while the Sham animals had a mean change of $-47.69\pm.22$ mm Hg. Upon acetylcholine injection there was a significant difference, $t(14)=4.90$, $p <.01$ in the heart rate changes for NTS and Sham animals. The NTS animals had a mean change in heart rate of $+8.50\pm.10$ bpm while the Sham animals had a mean change of $+85.13\pm.70$ bpm, (Fig. 22).

Body weights. Results of body weight analysis, using an independent t-test are presented in Table 9. Presurgery body weights were not significantly different between NTS and Sham animals, $t(14)=.17$, $p >.05$ and a similar finding was obtained for postsurgery body weights,

$t(14)=1.96$, $p > .05$. NTS presurgery body weights were not significantly different from NTS postsurgery body weights. Similarly, for Sham animals, pre- and postsurgery body weights were not significantly different.

Indirect systolic blood pressure: Presurgery. Presurgery indirect blood pressures were analyzed using an independent t-test. No statistically significant difference between NTS and Sham animals was obtained, $t(14)=.04$, $p > .05$ with the NTS animals having a mean blood pressure of $117.06 \pm .63$ and the Sham animals having a mean blood pressure of $116.88 \pm .95$ mm Hg.

Histology. Brain histologies illustrated in Figure 23 revealed discrete bilateral damage to the nucleus of the solitary tract (NTS) of all NTS-lesioned animals. The larger extent of the lesions produced bilateral damage to the dorso-lateral portion of the medial and spinal vestibular nucleus in the rostral direction, with progressive damage occurring to the solitary tract in the caudal direction. The smallest extent of the lesions induced bilateral damage to the NTS region where the primary baroreceptor afferents make the first synapse in the baroreflex arch (Palkovits & Zaborszky, 1977). In no instance was there damage to the medial portion of the solitary tract, a region where chemoreceptor synapses tend to occur (Cherniak & Longobardo, 1970). Thus, the NTS lesions did not directly affect the centrally located chemoreceptor afferent. Histological examination of the Sham brains revealed no damage to the NTS region or surrounding structures.

Discussion

Several observations argue against the possibility that either sampling biases in assignment of subjects to treatments or the debilitating consequences of deafferentation contributed systematically to the obtained results. First, there were no indications of group differences in either pre- or postsurgical body weights. While this is largely secondary to the food deprivation regimen used throughout the study it does indicate that any sampling error contributed marginally to the assignment of subjects to treatments. This finding also suggests that the 10 day post-operative recovery period was sufficient to restore the body weights of the NTS-lesioned rats. Second, few significant group differences were revealed in pre- or postsurgery rectal, abdominal, or tail skin temperatures. This supports the contention that inadvertent biases in assignment of subjects to treatment groups contributed negligibly to the observed trends. Moreover, the fact that there were no postsurgical group differences suggests that the NTS lesions did not debilitate the maintenance of body temperature. Finally, presurgery indirect systolic blood pressure, oxygen consumption and carbon dioxide production revealed few differences between the animals assigned to the NTS and those assigned to the Sham group. This indicates that sampling errors in the assignment of subjects to treatments contributed minimally to obtained metabolic and blood pressure results.

Several investigators have indicated that the thermoneutral temperature range for a rat is 27 - 31 ^{o}C (Hart, 1971; Poole & Stephenson, 1977). Thus, the possibility exists that in the shaved rat the 23 ^{o}C baseline

used in this study was not "neutral" but constituted a cold thermal challenge. This would be consistent with several observations. First, rectal temperature tended to decline within each baseline presentation, as would be expected if 23 ^{o}C was a cold challenge. Second, along similar lines, abdominal and tail skin temperatures showed a tendency to decline within the baseline conditions. Finally, oxygen consumption and carbon dioxide production tended to increase within the baseline presentations, suggesting that 23 ^{o}C may have constituted a cold exposure. However, there are several lines of evidence obtained in the present study which suggest that the baseline conditions did not constitute a cold exposure. First, temperature acclimation studies by Hammel (1968) and Hammel et al. (1961).reported that an exposure of two weeks was sufficient to acclimate rats to 5 ^{o}C. In this regard the colony room where the rats were housed for two weeks prior to testing, was maintained at a similar temperature as the baseline condition. Accordingly, one could assume that the rats in the present study may have been acclimated to 23 ^{o}C. Cold acclimation is characterized by a suppressed metabolic rate in the cold yet a relatively stable core temperature. If 23 ^{o}C had constituted a cold challenge, an increase in metabolic rate would be expected. Instead, a decline observed in the present study in both oxygen consumption and carbon dioxide production across the three baseline conditions during all test sessions suggests that the animals were acclimated to these baseline conditions. Moreover, if 23 ^{o}C constituted a hypothermic challenge, a steadily declining rectal temperature would be expected. In the present study, however, rectal temperatures were generally stable and tended to exhibit a temperature-

dependency upon exposure to only the most extreme hypo- or hyperthermic challenges. From this it seems that the baseline condition used in the present study may have been slightly below the thermoneutral zone but did not serve as a cold exposure.

The first set of results to be discussed are those resulting from the presurgery heat challenge session. During this test session, baseline rectal temperature (Tb) remained stable at 35 ^{o}C. This relatively low value may be linked to procedural features of this study. For example, it might be an artifact of lower insulation in the shaved rats. Under normal circumstances, pellage provides thermal insulation which helps the animal sustain a normal core temperature (Hart, 1971). Accordingly, ambient temperatures even slightly below the thermoneutral zone may promote hypothermia in the shaved rat. However, the normalcy of the baseline metabolic adjustments and stability of Tb to the test temperatures imply that other factors may be contributing. One possibility is that the relatively short insertion distance (4 cm) of the rectal probe may have been insufficient to detect a true "colonic" temperature. In this regard, the investigator generally observed that Tb changed very little over the course of adaptation. Furthermore, the literature surveyed to date by the investigator has not assessed the rectal temperature of chronically shaved rats. Thus, there is little basis from which to compare the 35 ^{o}C Tb obtained in the present study. Baseline Tb also tended to increase across the three 23 ^{o}C presentations. This may be a residual effect of the preceeding test temperature. In this regard the increase is consistent with Takano, Mohri, and Nagasaka's (1978) finding that colonic temperature of rats returns slowly to

baseline values following heat (35 ^{o}C) exposure. They also demonstrated that the greater the preceeding test temperature, the more time was required to re-establish baseline colonic temperature levels. Thus, the time required to re-establish baseline Tb was dependent on the severity of the preceeding test temperature. Since the duration of the baseline condition remained constant, as the test temperature increased so did the overall Tb during the following baseline condition. Rectal temperature also tended to decrease within the baseline conditions and similarly this may simply reflect a return to initial values following heat exposure.

Since abdominal and tail skin temperature response profiles were similar and both are indicies of regional blood flow, they will be discussed together. As measures of regional blood flow these skin temperatures not only provide an indication of regional vasomotor tone but also is an estimation of the amount of heat dissipated to the environment. Thus, an increase in skin temperature is indicative of decreased vasomotor tone as well as enhanced heat dissipation to the environment (Brengelmann, 1983; Brengelmann et al., 1977). Presurgery baseline skin temperatures tended to increase across the warm session. This may reflect the contribution of those mechanisms that increased baseline Tb across the heat challenge session. This involved accumulation of exogenously acquired or metabolically produced heat. Since the time to re-establish baseline body temperature is temperature-dependent (Takano et al., 1978), as the warm test temperature progressively increases more heat will be retained, thereby elevating the skin temperature recorded during the subsequent baseline condition. Skin temperature also declined within each baseline condition. This is consistent with

Johnson et al.'s (1973) report that regional vasoconstriction in response to temperatures near the lower critical value of the thermoneutral zone typically occurs. The regional vasoconstriction tends to promote heat retention and diminish local skin temperature. Accordingly, the decrease in skin temperature observed prior to the warm test temperatures in the present study may have been vasoconstrictor-induced.

Both oxygen consumption and carbon dioxide production are indicies of an organism's metabolic rate, and therefore will be discussed together. Baseline metabolism decreased across the warm session. This general decline in metabolic rate is consistent with the findings of Ball and Jungas (1965). These investigators found that immobilization induced an initial increase in metabolic rate that gradually dissipated over a 5 h test period. From this, one might assume that the decline in metabolic rate over the baseline conditions within the 9.5 h test period observed in the present study may reflect a continuing, nonspecific adaptation to the physical restraint procedure used in testing. In this regard, eventhough the animals had been pre-adapted to physical restraint there was still apparent some residual temperature-independent metabolic hypersensitivity that occurred early in the testing session. Metabolic rate tended to increase within the warm baseline conditions. This supports Carlisle and Laudenslager's (1978) finding that upon return to a baseline temperature (25 ^{o}C) from a warm exposure, rats only gradually re-established their pre-exposure metabolic rate, and often stabilized at a somewhat higher than normal level. Hence, this increase in metabolic rate obtained within the baseline conditions may reflect the animal's attempt to establish a normal metabolic rate.

In endotherms, evaporative heat loss (EHL) reflects the activity of both respiratory and cutaneous channels of dissipating body heat. In the rat there are few histologically identifiable sweat glands and thus, an alteration in EHL is due mainly to respiratory changes (Kay, 1976). Baseline EHL showed a trend to increase across the warm session. In this regard, Kay (1976) demonstrated a temperature-dependent increase in EHL during heat challenges that enabled the rats to dissipate nearly 16% of their heat production. Thus, the increase in baseline EHL observed in the present study probably serves to dissipate the excess heat accumulated in the warm baseline condition.

Following exposure to the baseline conditions the animals were exposed to warm presurgical test temperatures (27, 31, and 35 ^{o}C) and the results obtained during the test temperatures will now be discussed. Rectal temperature (Tb) showed a tendency to increase across the warm test temperatures. This occurred predominantly during the 35 ^{o}C test temperature with only slight increases during 27 and 31 ^{o}C. The increase might be attributed to a combination of factors including a sympathetically-induced increase in heat production (Ludbrook, 1983), the vascular inability of the animal to offset this metabolic hyperthermia, or simply a passive accumulation of exogenously acquired heat. Although the precise nature of the underlying mechanism remains unclear it is consistent with previous observations. For example, Jacobsen and Squires (1970) demonstrated an increase in core temperature in rats exposed to varying degrees of heat. Moreover, as the severity of heat exposure increased so did the rise in core temperature. Thus, in the present study, as the severity of heat exposure increased so did the resulting

rise in Tb.

Skin temperature also tended to increase across the warm test temperatures, with the largest rise occurring during 35 ^{o}C. Since skin temperature is an index of vasomotor tone (Brengelmann, 1983) such an elevation may reflect prolonged heat-induced vasodilation that, in turn, would serve to enhance heat dissipation to the environment. The increase in skin temperature may also be a result of a metabolically-induced rise in heat production (Ludbrook, 1983) or a passive heat accumulation from the environment.

Metabolic indicies tended to decline across the warm test temperatures. This finding is once again consistent with the report by Ball and Jungas (1965) of a gradual decline in metabolic rate over a 5 h period of physical restraint. Thus, throughout the entire warm session the animals exhibited metabolic indications of a general adaptation to restraint. Despire this trend, metabolic rate tended to increase within the 35 ^{o}C exposure. The usual increase in metabolic rate seen upon heat exposure may be explained through the metabolic costs of increased respiration. Several investigators (e.g.Mead, 1960; Milic-Emili & Petit, 1960) demonstrated in guinea pigs, a 100% increase in respiratory rate upon exposure to warm temperatures or exercise. This increase in respiration was accompanied by a 17% increase in metabolic rate due largely to the oxygen demands of the respiratory muscles. Thus, the typical increase in metabolic rate seen in response to 35 ^{o}C may be due to an increase in respiration. In conjunction with the increase in metabolic rate seen upon exposure to warm test temperatures, EHL tended to increase across

the test temperatures. The increase in EHL may not only serve to dissipate excess body heat but may also contribute to the increase in metabolic rate observed in the test temperatures.

In summary, within the entire presurgical heat challenge session, metabolic rate tended to decline across the session ostensibly due to a general adaptation of the rats to physical restraint. However, metabolic rate exhibited a trend to increase within each baseline and test temperature and thus may be linked to the metabolic costs of increased respiration. In this regard, EHL increased across the warm session and in order to supply the respiratory muscles with increased amounts of oxygen, metabolic rate was enhanced. Moreover, these adjustments apparently occurred in the presence of an increase in rectal and skin temperature. While both of these temperature measurements may have increased due to passive heat accumulation from the environment, the increase in metabolic rate may have enhanced the increase in rectal and skin temperatures. Thus, during the presurgical heat challenge those animals assigned to the NTS group did not differ from those assigned to the Sham group and the response patterns of the dependent variables were consistent throughout the session with the reports of other investigators using similar conditions.

Following testing in the heat challenge session all animals were tested presurgically in a cold challenge session. Once again, within the cold session the animals were presented with a baseline condition and with cold test temperatures. The baseline condition will be discussed first. Rectal temperature (Tb) showed a trend to decline across the

23 °C presentations. This may constitute a residual effect of the preceeding test temperature and thereby is analogous to the findings of Takano et al. (1978). Although their study dealt with warm exposures, a similar temperature-dependent amount of time may be required to establish baseline colonic temperature levels following cold exposures. Since the duration of the baseline condition was constant, as the test temperature decreased, so did the overall Tb during the subsequent 23 °C. Within the baseline condition Tb did tend to increase and this trend was observed only during the last two 23 °C presentations. This may be attributable to passive accumulation of exogenous heat since, as discussed later, baseline metabolic rate remained constant.

Skin temperature provides an estimate of regional vasomotor tone and the amount of heat retained by the body. As such, a decline in skin temperature is indicative of increased vasomotor tone as well as enhanced heat retention by the body (Brengelmann et al., 1977). Baseline skin temperatures tended to decrease across the cold session. This decline may reflect the trend for excess passive heat loss from the body during the preceeding test temperature. Thus, as the cold test temperatures became more severe, progressively more heat was lost and, given a constant duration at the baseline temperature, skin temperature declined accordingly. Skin temperature also increased during each baseline condition. Although Johnson et al. (1973) reported a regional vasoconstriction in response to temperatures near the lower critical value of the thermoneutral zone, this degree of vasoconstriction is less than that observed during moderate or severe cold exposures (Atterhog et al., 1975). Accordingly,

a decline in the degree of vasoconstriction during 23 °C may promote heat dissipation and thus may have facilitated the increase in skin temperature observed in the present study.

Baseline metabolic rate remained constant throughout the baseline condition in the cold session. This suggests that the 23 °C baseline procedure was sufficient to reinstate the prechallenge metabolism following exposure to cold test temperatures. It also suggests that the increase in rectal and skin temperature during baseline conditions is not of metabolic origin. A similar observation was made regarding EHL.

Following exposure to the baseline conditions the animals were exposed to cold presurgical test temperatures (19, 15, and 11 °C) and the results obtained during the test temperatures will now be discussed. Rectal temperature (Tb) remained constant across the session. Such an absence of lability in Tb again suggests that the apparently "hypothermic" Tb recorded during baseline may have constituted a "shell" temperature that was defended regardless of the intensity of the presurgery cold challenges. The constancy in Tb may result from the increase in Tb observed during each baseline condition. The baseline increase tended to re-establish Tb at approximately 34.5 °C by the beginning of each cold test temperature. Moreover, the constancy of Tb within each cold test temperature may result from an increase in metabolic heat production as will be discussed shortly. An increase in heat production will help maintain body temperature relatively constant during cold exposures.

Skin temperatures tended to decline across the cold test temperatures and this reflects a greater contribution of the steeper decreases that

emerged during the 15 and 11 ^{o}C exposures. Again, this is consistent with reports (e.g. Brengelmann, 1983; Mount, 1979; Vanhoutte, 1978) that a cold-induced regional vasoconstriction becomes associated with a decline in local skin temperature, both of which serve to enhance heat retention and thus facilitate the maintenance of normal core temperature. Thus, the decline in local skin temperature in the present study may result from regional vasoconstriction designed to facilitate heat retention in the cold.

Metabolic rate showed a tendency to increase across the test temperatures. Moreover,the elevation in metabolic rate observed during the thermal challenge was temperature-dependent in that the lower ambient temperature elicited a proportionally steeper rise in metabolism. A variety of investigators (Hart, 1971; Himms-Hagen, 1972; Molnar et al., 1979; Vanhoutte & Janssens, 1978; Wasserstrum & Herd, 1977) have reported that endotherms often exhibit a cold-induced,sympathetically-mediated rise in metabolic rate that may generate a 20% increase in heat production. The increase in heat production enables the animal to maintain an adequate core temperature in the presence of progressively colder temperatures. Thus, in the present study, the rise in metabolic rate upon cold exposure may be sympathetically mediated and may serve to maintain baseline body temperature.

To recapitulate, over the entire presurgical cold challenge session, metabolic rate tended to remain constant during baseline conditions and to increase during cold exposures. The increase in metabolism may be sympathetically induced and reflects an increase in heat production.

This metabolic adjustment was apparently sufficient to prevent a decline in rectal temperature during the cold test temperature. Moreover, the decline in skin temperature may have further aided in the maintenance of baseline rectal temperature values through enhanced heat retention.

Histological examination of the lesion site revealed that the extent of the bilateral NTS lesions were consistent with that found by previous investigators (Nathan & Reis, 1977). Their lesions generally included the dorsal nucleus of the vagus, the intercalary nucleus, and the medial cuneate nucleus. In the present study, lesion sites extended from the dorsolateral portion of the medial and spinal vestibular nucleus to the lateral portion of the intermediate third section of the solitary tract. Thus, the electrolytic damage induced in this study was comparable in locus but less extensive than earlier reports. The pharmacological baroreceptor reflex tests were also consistent with previous reports (e.g. Talman et al., 1980; Wasserstrum & Herd, 1977a, 1977b; Buckholtz, 1982). Bolus injections of phenylephrine caused a pressor response without inducing baroreceptor-mediated bradycardia in the NTS-lesioned rats, while Sham animals exhibited both an increase in blood pressure and a reflexive bradycardia. Conversely, bolus injections of acetylcholine in the NTS-lesioned rats caused depressor responses without inducing baroreceptor-mediated tachycardia, while Sham animals demonstrated both a decline in blood pressure and a reflexive tachycardia. Hence, according to histological and pharmacological criteria, the baroreceptors were functionally denervated by lesions to the NTS, while those of the Sham-operated animals remained intact.

Following the lesioning procedure the animals were tested in both heat and cold challenges as was done presurgically. The animals were first exposed to heat challenges comprised of both baseline and test temperatures. The baseline conditions will be discussed first. Baseline rectal temperature tended to increase across the three presentations. This rise in Tb may reflect a similar residual effect of the preceeding test temperature as was postulated presurgically. As Takano et al. (1978) demonstrated, the time required to re-establish baseline colonic temperature levels was dependent on the severity of the preceeding test temperature. Since the duration of the baseline condition remained constant in the present study, as the test temperature increased so did the overall Tb during the subsequent baseline condition. Baseline Tb also tended to decrease during each baseline condition and this may simply reflect a return to initial values following heat exposures.

Baseline skin temperatures tended to increase across the heat session. This is similar to that seen presurgically and may reflect excessive accumulation of exogenously acquired or metabolically produced heat from the preceeding test temperature. Baseline skin temperature also tended to decline during each baseline condition. This decline is parallel to that observed presurgically and, as idscussed earlier, is consistent with Johnson et al. (1973). These investigators found a regional vasoconstriction upon exposure to temperatures near the lower critical value of the thermoneutral range, and this vasoconstriction is designed to promote retention and diminish local skin temperature.

During the heat challenge session baseline metabolism was suppressed

for the NTS animals relative to the Sham control group. This suppression in metabolic rate is consistent with reports by Wasserstrum and Herd (1977b). These investigators observed an overall reduction in metabolism mediated by sinoaortic denervation in monkeys. These investigators found that in an intact animal cold exposure resulted in an elevation of blood pressure and oxygen consumption. When the increase in blood pressure was further enhanced by continuous infusions of phenylephrine the normal increase in metabolic rate during cold exposure was inhibited. The investigators hypothesized that the metabolic inihibition associated with infusions of phenylephrine is due to activation of a reflex originating at the sinoaortic baroreceptors. When the afferents of the baroreceptors were interrupted by surgical denervation both the magnitude of the reduction in metabolic rate and the intensity of the bradycardia in response to blood pressure elevation were markedly diminished. Thus, they concluded that the sinoaortic baroreceptors play a similar role in regulating metabolic responses to ambient temperature as they do in mediating the heart rate response to alterations in blood pressure. Following NTS lesions, the central analogue of peripheral sinoaortic denervation, the rats in the present study also exhibited a suppressed metabolic rate. This finding extends the earlier report of peripheral baroreceptors having a regulatory role over metabolic responses to a centrally located regulatory mechanisms involved in the metabolic response to varying temperatures.

For both NTS and Sham animals, baseline metabolic rate tended to decrease across the warm session and is similar to the response observed

presurgically. This decline is also consistent with Ball and Jungas' (1965) finding and suggests that the decline in metabolic rate across the baseline conditions may reflect a continuing adaptation to physical restraint used in testing. On the other hand, baseline metabolic rate tended to increase within the 23 ^{o}C presentations. This response trend is similar to that observed presurgically and is again in accordance with the gradual re-establishment of baseline metabolism following warm exposures as reported by Carlisle and Laudenslager (1978). Along with the increase in metabolic rate, respiratory dissipation of heat, as assessed by EHL, tended to increase across baseline conditions. This finding is consistent with presurgical results and may explain the rise in metabolic rate within each baseline presentation.

The NTS-lesioned rats exhibits a suppressed baseline mean aortic blood pressure (BP) across the warm session.. This decline in BP may be explained by the observations of Nathan and Reis (1977). They reported that following NTS-lesions in cats, BP stabilized at normotensive levels following a one week post-operative recovery period. Despite the BP being at a normotensive level it still retained a labile responsiveness to environmental stimuli. When these results are viewed in conjunction with those of the present study it appears that the BP of NTS-lesioned rats also tends to gradually diminish with a prolonged recovery period while still retaining its hyperreactivity. Thus, following a 14-day post-surgery period used in this study the BP of the NTS animals during 23 ^{o}C continues to exhibit this hypotensive trend relative to the normotensive controls.

Following exposure to baseline conditions the animals were exposed to warm test temperatures (27, 31, and 35 ^{o}C) and the results obtained during these test temperatures will now be discussed. Postsurgical Tb showed a tendency to increase across the test temperatures. This increase occurred predominantly within the 35 ^{o}C temperature with only moderate increases during 31 and 27 ^{o}C and is similar to that observed presurgically. Accordingly, using the same logic, this increase in Tb may be due to actively and/or passively acquired body heat and supports Ludbrook's (1983) finding that an increase in core temperature in rats occurred upon warm exposure. Therefore, the NTS-lesioning procedure did not disrupt the general increase in Tb seen during a warm temperature.

Skin temperature tended to increase across the test temperatures, with the largest rise occurring during 35 ^{o}C. Since this resembles those adjustments observed presurgically, it may be explained through the same mechanisms discussed earlier. Once again, the NTS-lesioned animals did not show signs of disruption in the reduced vasomotor tone which may be responsible for the increase in skin temperature, suggesting that NTS-lesioned animals retained an appropriate response characteristic to warm temperatures in terms of their circulatory assisted heat transport.

For both NTS and Sham animals, metabolism tended to decline across the warm test temperatures. This decline is similar to that observed presurgically and as such, may be explained through the same mechanisms discussed earlier. Further analysis revealed that the metabolic rate of the NTS animals was relatively stable but suppressed, suggesting that the decline across the test temperatures was due mainly to the

Sham animals. The suppressed metabolic rate for the NTS animals is similar to that observed during the warm baseline conditions and again is consistent with the findings of Wasserstrum and Herd (1977b). These investigators found a suppression in metabolic rate following sinoaortic denervation. Since the NTS-lesions are functionally similar to sinoaortic denervation (Doba & Reis, 1975), a suppression in metabolic rate in the NTS animals would be expected. Contrary to the differences in metabolic rate between NTS and Sham animals, EHL tended to increase across the test temperatures for both NTS and Sham animals. This finding is consistent with presurgical responses and may serve to enhance heat dissipation from the body core to the environment.

For the NTS animals, direct aortic blood pressure (BP) was suppressed within the warm test temperatures as compared to the Sham group. The suppressive effect of debuffering may be due to labile characteristics of the vasomotor response to environmental stimuli. For example, Vanhoutte (1978) and Vanhoutte and Janssens (1978) demonstrated proportional heat-induced cutaneous vasodilation which accompanied a decreased BP. This heat-induced cutaneous vasodilation may serve to enhance heat loss from the body core to the environment (Rowell, 1977) by increasing cutaneous blood flow and thereby enhancing the amount of heat dissipated from the blood to the environment. Moreover, Kirchheim (1976) reported that the degree of the depressor response seen during heat exposure was mediated by the baroreceptor-reflex. During heat exposure there was a tendency for BP to decline,

however, the amplitude of this depressor response was attenuated by baroreceptor-mediated vasoconstriction. Thus, the fact that the Sham animals exhibited only a small decline in BP during the warm test temperatures may be a result of a baroreceptor-mediated vasoconstriction. The NTS-lesioned animals, on the other hand, exhibited a heat-induced vasodilation which was not attenuated by the intact baroreceptors and thus, they had a mean BP of only 88.8 mm Hg. These results imply that the BP of NTS-lesioned animals had a greater responsivity to warm temperatures than did the Sham animals.

The blood gas measurements assessed in the present study (pO_2, pCO_2, pH) indicate the content of oxygen and carbon dioxide as a function of the total amount of gas within the blood. These indicies of gas content are typically indicative of the respiratory state of the animal (Bechbache et al., 1979). As such, an increase in respiration will result in an increase in the partial pressure of oxygen in the blood, a decrease in the partial pressure of carbon dioxide and a concommitant increase in pH. This set of responses constitutes a respiratory alkalosis and is commonly observed following heat exposures. Upon cold exposure, respiratory acidosis, as defined by a decrease in pO_2, pCO_2 and a decrease in pH, is typically observed (Schade, 1982). However, in the present study, there was a reduction in blood pH in in the NTS animals following heat exposures. Since blood pO_2 and pCO_2 were not affected by heat exposure in either NTS or Sham groups, the observed acidosis is believed to be of metabolic origin. However,

exposure to warm ambient temperatures may result in metabolic alkalosis for the following reasons. During warm temperatures there typically occurs vasodilation with a concommitant reduction in sympathetic nervous system activity (Vanhoutte, 1978). The decline in sympathetic activity has been correlated with reduced circulating levels of norepinephrine (Sejersted, Medbo, & Hermansen, 1982), which in turn is associated with metabolic alkalosis (Schade, 1982). In the present study the NTS animals exhibited a steady degree of hypotension during the warm session which, according to Schade (1982), should result in metabolic alkalosis. Thus, the interpretation of the metabolic acidosis observed in response to heat exposures remains unclear. The replicability of the apparent metabolic acidosis during heat challenge in a debuffered rat and its physiological significance requires further investigation.

In summary, metabolic rate was suppressed in the NTS animals during the warm challenge session. The suppression is consistent with findings of Wasserstrum and Herd (1977b) and may result from the functional disruption of the baroreceptor reflex following NTS lesions. Thus, the results of the present study extend the findings of a suppressed metabolic rate following peripheral denervation to that of a central effect following NTS lesions. In addition, the NTS lesioned animals exhibited a suppressed BP during the entire warm challenge session. The reduction in BP may reflect two processes; a) the general hypotensive trend following prolonged recovery from surgery and b) a certain degree of unbuffered heat-induced vasodilation in the NTS animals which lowers

total peripheral resistance and, in turn, BP. The increase in Tb observed in all animals occurred in spite of the increase in both EHL and skin temperature during the warm session. Thus, although both metabolic rate and BP were suppressed in the NTS animals, they exhibited the same rectal and skin temperature response as the Sham group during the warm challenge. These findings suggest that the regulation of body temperature was not disrupted by lesions to the NTS although both BP and metabolism were suppressed.

Following testing in the heat challenge session all animals were tested postsurgically in a cold challenge session. Once again, within the cold session the animals were presented with a baseline condition and cold test temperatures. The baseline condition will be discussed first. Both rectal and skin temperatures tended to decline across the baseline conditions. This resembles the presurgery trend and hence may be explained by the same mechanisms discussed earlier. In short, the decline in temperatures may be a residual effect of the heat loss encountered during the preceeding cold test temperatures. Moreover, the decline in rectal and skin temperatures did not occur differentially between the NTS and Sham animals suggesting that the NTS lesioning procedure did not affect the maintenance of body temperature during baseline conditions.

Baseline metabolic rate showed a trend to increase across the cold session that was attributable solely to the Sham group. The metabolic rate of the NTS animals across the 23 ^{o}C presentations was suppressed but stable. The stability of metabolic rate in the NTS-lesioned animals

is consistent with the findings of Wasserstrum and Herd (1977b) who reported an overall reduction in metabolic rate following denervation in monkeys. These investigators concluded that sinoaortic baroreceptors play a role in mediating the metabolic response to ambient temperature. In the present study, central debuffering had a similar suppressive effect on metabolic rate. This may suggest a modulatory role of the NTS region on metabolism. Baseline EHL tended to remain stable for the NTS group while tending to decrease across the cold session for the Sham animals. This implies that the Sham group's increase in metabolic rate may be due to an increase EHL while for the NTS group both EHL and metabolism tended to remain stable.

Baseline BP was suppressed for the NTS as compared to the Sham animals. This is consistent with the baseline response seen during the warm challenge and as such, may be due to the hypotensive trend observed over a prolonged recovery period following NTS lesions (Nathan & Reis, 1977). Moreover, the magnitude of this baseline hypotensive response increased across the session selectively for the NTS-lesioned rats. In contrast, the Sham group exhibited a stable but elevated BP across the baseline conditions. This steep decline in baseline BP for the debuffered animals may result from a rebound effect. As will be discussed below, the NTS animals exhibited an increase in BP across the cold test temperatures that was proportional to the severity of the cold temperatures. Vanhoutte and Janssens (1978) reported that the degree of rebound in BP values following return to baseline temperatures was proportional to the degree of cold-induced vasoconstriction

immediately before. Accordingly, the results of the present study are consistent with those of Vanhoutte and Janssens (1978) in that, as the degree of cold-induced hypertension became more severe, the degree of BP rebound during the baseline conditions increased. Thus, the NTS-lesioned animals exhibited a progressive decline in BP across the baseline conditions.

Following the baseline conditions the animals were exposed to cold test temperatures. Rectal temperature remained constant across the cold test temperatures. This stability may be the result of an increase in metabolic rate. Increased metabolic rates would enhance heat production and this, in turn, would help maintain body temperature relatively constant during the cold exposures. However, Tb did tend to decline within the 15 and 11 ^{o}C test temperatures more rapidly than during 19 ^{o}C. This decline probably reflects passive heat loss from the body core to the environment.

Skin temperatures tended to decline across the test temperatures. Moreover, the decline within each cold temperature tended to be steeper during the 15 and 11 ^{o}C exposures. This response pattern is similar to that seen presurgically and as such, may be explained through the same mechanisms. It should be noted that the decline in both rectal and skin temperatures did not occur differentially between the NTS and Sham animals, suggesting that the NTS lesioning procedure did not affect the maintenance of body temperature during the cold challenge session.

Postsurgical metabolic rate tended to increase slightly across the test temperatures for the NTS animals, however, their metabolic rate

was suppressed relative to the Sham group. The reduced metabolic rate in the NTS-lesioned animals is in accordance with the findings of Wasserstrum and Herd (1977b) who reported a reduced metabolic rate following sinoaortic denervation in monkeys. Thus, in the present study the NTS lesions, the central analogue to peripheral sinoaortic denervation, had a similar suppressive effect on metabolic rate. This suggests that the NTS region may have a modulatory role on metabolism. On the other hand, the Sham animals exhibited a temperature-dependent increase in metabolic rate within each test temperature. This response pattern is in accordance with that found presurgically and therefore, may be explained by similar mechanisms. Briefly, Himms-Hagen (1972) demonstrated that during cold exposures, metabolic rate may increase by up to 20% and thus may result in a proportional rise in heat production. Thus, the rise in metabolic rate in the present study may be evoked in order to maintain baseline body temperature.

Blood pressure assessments revealed that the NTS rats exhibited a more pronounced trend to increase across the cold test temperatures. In this regard, several investigators (e.g. Chapman et al., 1973; Johnson et al., 1973; Nadel, 1980) demonstrated the occurrence of regional vasoconstriction during cold exposures which they concluded may serve to enhance heat retention in the body. This vasoconstriction is presumably mediated by the peripherla release of norepinephrine at the sympathetic nerve terminals. Thus, the overall rise in BP across the cold session may be the result of a sympathetically-induced vasoconstriction designed to facilitate heat retention. Moreover, this pressor response was

transient in nature yet proportional in magnitude to the severity of the cold challenge. As a result BP tapered off during the last one-half of test temperature exposure and supports the findings of Gurtzenstein, Hilton, Marshall, and Timms (1977). They suggested that following enhanced sympathetic nerve activity the noradrenergic receptors desensitize to norepinephrine. Accordingly a reduced activity level of the sympathetic nerves may account for the gradual decline in BP during the latter part of the cold test temperatures. Similarly, the transient feature may be linked to the enhanced sympathetic responsivity of the NTS animals to environmental stimuli as had been demonstrated by Talman et al. (1980) and Nathan and Reis (1981).

In summary, both NTS and Sham animals exhibited an overall rise in metabolic rate during the cold session. However, NTS animals had a suppressed metabolism during both baseline and test temperatures relative to the Sham group. The reduced baseline BP resulted from a rebound effect of the preceeding test temperature. During the test temperature the NTS animals exhibited a transient but marked increase in BP which probably resulted from enhanced responsivity of the sympathetic nervous system to environmental stimuli. Following the transient increase in BP occurred a decline in BP which may be due to desensitization of the sympathetic nerves following exaggerated activity as suggested by Gurtzenstein et al. (1977). The tendency for rectal and skin temperature to decline across the cold challenge session may be due to passive heat loss to the environment. This passive loss is supported by the increase in both metabolism and BP during cold temperatures. Both

increases would serve to increase body temperature. It thus appears that the enhanced heat production and retention mechanisms were not adequate to maintain the initial baseline rectal and skin temperature levels.

Conclusions

Accordingly, it appears that electrolytic NTS lesions disrupt the integrity of the baroreceptor reflex. This disruption has functional implications for both the maintenance of BP and respiratory gases that occur in response to mild thermal challenges. Specifically, the lesions led to a pronounced lability in aortic blood pressure with depressor episodes occurring during heat challenges and marked temperature-dependent pressor episodes during cold challenges. On the other hand, Sham animals exhibited a relatively stable blood pressure during both heat and cold challenges. The NTS-lesioned rats also had a suppressed metabolic rate during both thermal challenges. Moreover, although the relative contributions to thermoregulation of blood pressure and metabolism were altered following NTS lesions, the efficacy of the thermoregulatory processes was sufficient to maintain a presurgical rectal temperature. The relative suppression in metabolism in the cold of NTS-lesioned animals may have reflected increased vasomotor tone. NTS animals apparently rely less on metabolic parameters yet more on unbuffered hemodynamic responses to control the rate of heat dissipation or retention. Thus, since the means but not the

efficacy of thermoregulation were altered through lesions to the NTS, the notion that both BP and thermoregulation are under neurogenic control of a hypothalamo-bulbar longitudinal system of neurons is supported by the results of this study.

It is well documented that various environmental stimuli can affect the functioning of the cardiovascular system (Weick, Ritter, and Ritter, 1980). The effects of environmental stimuli on the cardiovascular system are buffered by the baroreceptor reflex. This buffering action apparently conceals the manner in which the brain encodes certain environmental events into cardiovascular responses. Through debuffering of the baroreceptor reflex arch one is able to assess the basal response of the cardiovascular system to environmental stress in at least two ways. First, once the cardiovascular system is debuffered one may assess the level of sensitivity of the nervous system to environmental events and how the brain encodes environmental information into physiological events without the presence of protective mechanisms. Second, one may also assess how the organism may learn to respond to environmental events in terms of physiological processes when no buffering mechanisms are available to protect the animal. When an understanding of how an organism responds to the environment without the aid of protective mechanisms is obtained, then a better understanding of how the intact organism is able to respond to the environment may be gained. The understanding of how an organism responds to stress may provide the means by which the organism can minimize the deleterious effects of stress.

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Table 1. Mean (±S.E.M.) oxygen consumption (ml $O_2 \cdot g^{-1} \cdot h$) and carbon dioxide production (ml $CO_2 \cdot g^{-1} \cdot h$) recorded at 10 min intervals across 3-30 min baseline temperature (23 °C) conditions.

		VO_2		VCO_2	
Group(n)	Session	Heat	Cold	Heat	Cold
NTS (8)	pre-surgery	1.88±.11	2.07±.03	1.13±.05	1.15±.03
	post-surgery	1.49±.04+	1.66±.09	1.05±.03	1.09±.01
Sham (8)	pre-surgery	1.92±.14	2.01±.03	1.20±.08	1.25±.02
	post-surgery	1.89±.13+	2.11±.03	1.13±.05	1.27±.06

+ significant to $p < .001$.

Table 2. Mean (±S.E.M.) direct aortic blood pressure (mm Hg) recorded at 10 min intervals across 3-60 min baseline temperature (23 °C) conditions.

Group (n)	Blood Pressure	
	Post-surgery Heat challenge	Post-surgery Cold challenge
NTS (8)	104.3±.67	86.6±.05+
Sham (8)	129.1±.94	134.1±.64+

+ significant to $p < .01$.

Table 3. Mean (±S.E.M.) rectal temperature, abdominal skin temperature and tail skin temperature (^{o}C) recorded at 10 min intervals across 3-60 min baseline temperature (23 ^{o}C) conditions.

			Temperature		
	Group (n)	Session	Rectal	Abdominal skin	Tail skin
Heat Challenge	NTS (8)	pre-surgery	35.4±.11	33.6±.15	27.8±.51
		post-surgery	35.1±.13	34.1±.18	27.7±.44
	Sham (8)	pre-surgery	35.2±.12+	33.9±.12*	27.9±.54
		post-surgery	35.9±.16	34.8±.14	28.5±.47
Cold Challenge	NTS (8)	pre-surgery	34.4±.09	32.7±.25	23.8±.34
		post-surgery	34.7±.11	33.1±.14	25.1±.42
	Sham (8)	pre-surgery	33.9±.09	32.7±.17	23.8±.36
		post-surgery	34.8±.09	33.7±.13	25.2±.40

* significant to $p < .05$

+ significant to $p < .01$

Table 4. Mean (±S.E.M.) oxygen consumption (ml $O_2 \cdot g^{-1} \cdot h$) amd carbon dioxide production (ml $CO_2 \cdot g^{-1} \cdot h$) recorded at 10 min intervals across 3-60 min test temperatures.

		VO_2		VCO_2	
Group(n)	Session	Heat	Cold	Heat	Cold
NTS (8)	pre-surgery	1.70±.39	2.34±1.42	1.00±.40	1.43±.79
	post-surgery	1.41±.84	1.92±1.58	.99±.23	1.27±.46
Sham (8)	pre-surgery	1.62±.72	2.31±.87	1.07±.23	1.55±.54
	post-surgery	1.66±.42	2.35±1.21	1.03±.48	1.58±.61

Table 5. Mean (±S.E.M.) direct aortic blood pressure (mm Hg) recorded at 10 min intervals across 3-90 min test temperatures.

Group (n)	Blood Pressure	
	Heat Challenge Post-Surgery	Cold Challenge Post-Surgery
NTS (8)	88.7±1.26*	149.8±8.34
Sham (8)	122.4 ±.94*	144.3±1.30

* significant to $p < .05$

Table 6. Mean (±S.E.M.) rectal temperature, abdominal skin temperature and tail skin temperature (^{o}C) recorded at 10 min intervals across 3-90 min test temperatures.

			Temperature		
	Group (n)	Session	Rectal	Abdominal skin	Tail skin
Heat Challenge	NTS (8)	pre-surgery	35.6±.15	34.3±.18	30.3±.55
		post-surgery	35.5±.14	34.6±.13	30.3±.50
	Sham (8)	pre-surgery	35.5±.13+	35.6±.17	30.7±.53
		post-surgery	36.4±.16+	35.6±.20	31.4±.53
Cold Challenge	NTS (8)	pre-surgery	34.4±.03	32.3±.09	21.7±.43
		post-surgery	34.6±.09	32.6±.11	22.7±.50
	Sham (8)	pre-surgery	34.2±.04	32.3±.08	21.4±.48
		post-surgery	34.7±.07	35.1±.12	22.7±.50

+ significant to $p < .01$

Table 7. Mean (±S.E.M.) blood gas measurements recorded immediately following 35 °C (heat challenge) and 11 °C (cold challenge) post-surgical test temperatures.

Group (n)	Session	pH	pO_2 mm Hg	pCO_2 mm Hg
NTS (8)	Heat challenge	7.30±.001*	44±1	39±3
	Cold challenge	7.30±.01	92±.2	38±.1
Sham (8)	Heat challenge	7.39±.003*	102±1	39±.4
	Cold challenge	7.34±.004	91±1	39±1

* significant to $p < .05$

Table 8: Mean (±S.E.M.) change in direct aortic blood pressure (mm Hg) and heart rate (bpm) in response to bolus injections of 10 ul phenylephrine and 10 ul acetylcholine.

Pharmacological Agent	Group (n)	Blood Pressure	Heart Rate
Phenylephrine	NTS (8)	+76.5±.22	-7.1±.12+
	Sham (8)	+79.1±.52	-72.1±.36
Acetylcholine	NTS (8)	-49.0±.20	+7.5±.11+
	Sham (8)	-47.7±.22	+85.1±.71

+ significant to $p < .01$

Table 9. Mean (±S.E.M.) body weights (g) for NTS and Sham animals across all thermal challenge.

Group (n)	Session	Heat Challenge	Cold Challenge
NTS (8)	pre-surgery	340.3±15.9	326.7±14.0
	post-surgery	385.5±18.9	376.0±18.1
Sham (8)	pre-surgery	329.9±12.0	323.5±12.3
	post-surgery	340.4±11.1	334.4±11.2

Figure 1. Schematic representation of the relationship between the central and peripheral mechanisms governing blood pressure and thermal regulation. CO = cardiac output, DVN = dorsal vagal nucleus, EHL = evaporative heat loss, HP = heat production, HR = heart rate, NTS = nucleus tractus solitari, PNS = parasympathetic nervous system, PO/AH = preoptic/anterior hypothalamus, pCO_2 = partial pressure of carbon dioxide, pO_2 = partial pressure oxygen, SV = stroke volume, SNS = sympathetic nervous system, TPR = total peripheral resistance, VMC = vasomotor centre, VCO_2 = carbon dioxide production, VO_2 = oxygen consumption.

——→ excitatory influence

— — — inhibitory influence

Fig. 1

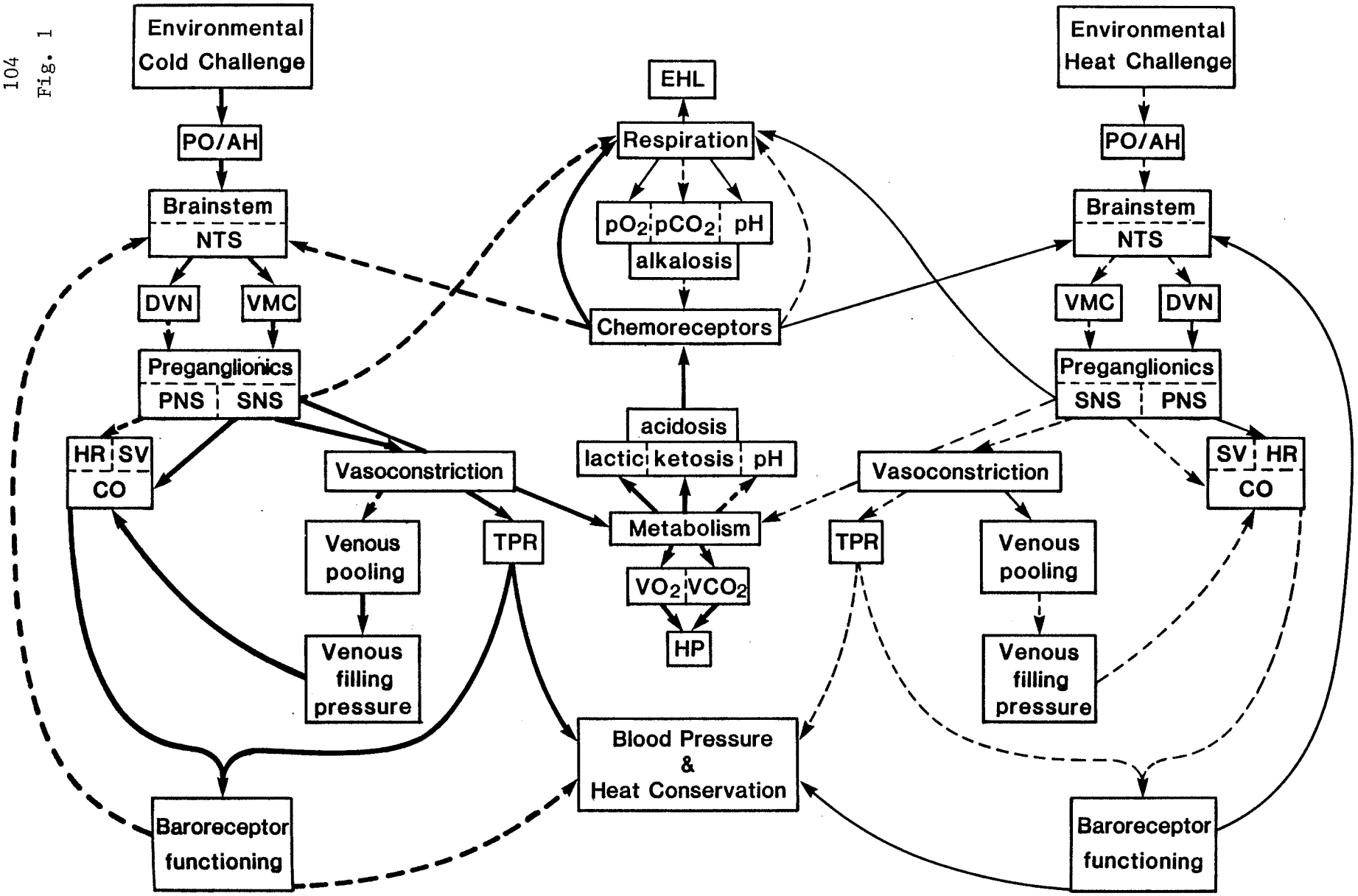

Environmental Cold Challenge
PO/AH
Brainstem
NTS
DVN
VMC
Preganglionics
PNS
SNS
HR
SV
CO
Vasoconstriction
Venous pooling
TPR
Venous filling pressure
Baroreceptor functioning
EHL
Respiration
pO2
pCO2
pH
alkalosis
Chemoreceptors
acidosis
lactic
ketosis
pH
Metabolism
VO2
VCO2
HP
Blood Pressure & Heat Conservation
Environmental Heat Challenge
PO/AH
Brainstem
NTS
VMC
DVN
Preganglionics
SNS
PNS
SV
HR
CO
Vasoconstriction
TPR
Venous pooling
Venous filling pressure
Baroreceptor functioning

Figure 2. Mean (±S.E.M.) oxygen consumption (ml $O_2 \cdot gm^{-1} \cdot h$) for NTS and Sham groups during heat challenges.

Fig. 2

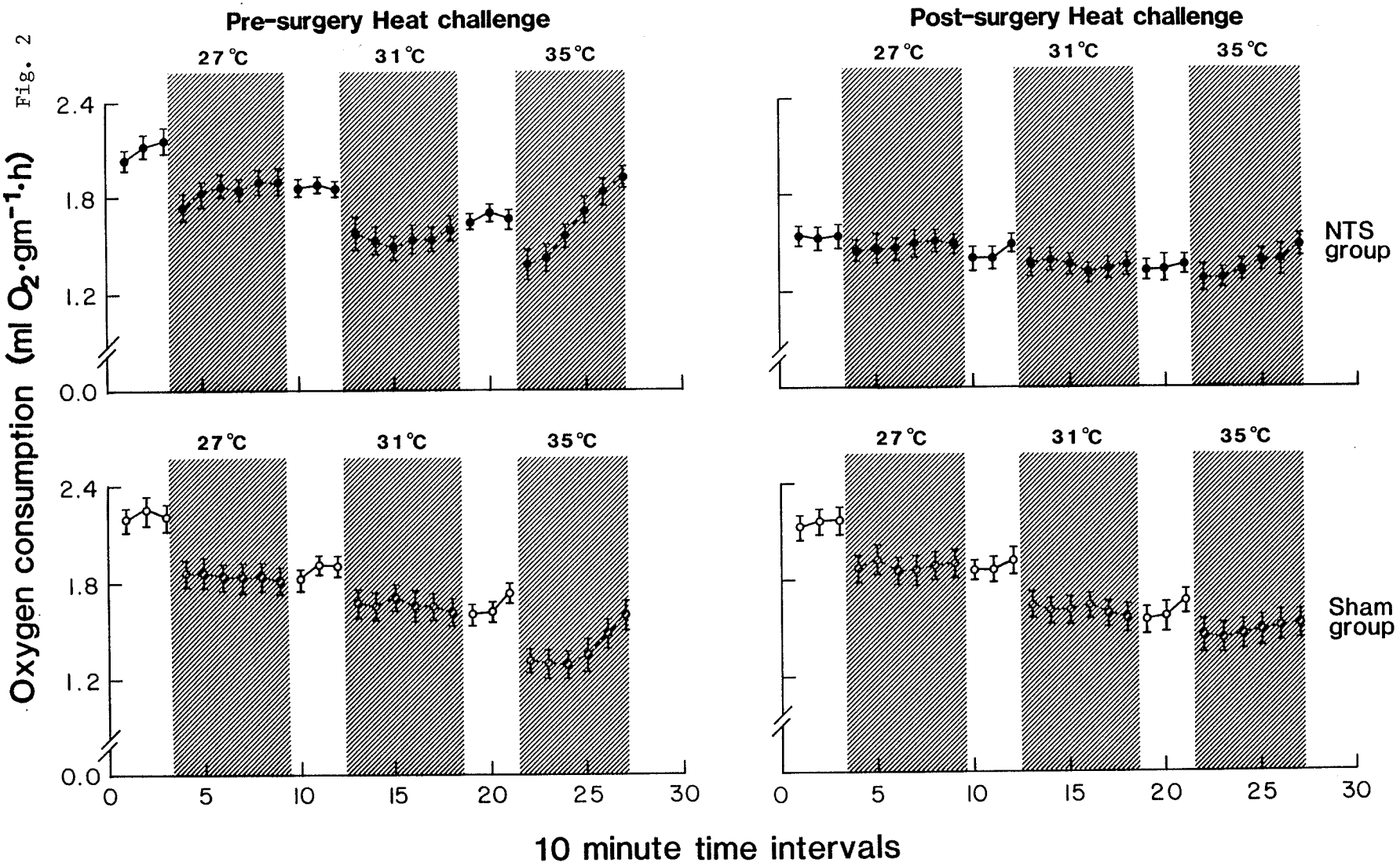

Pre-surgery Heat challenge
Post-surgery Heat challenge
27°C
31°C
35°C
NTS group
Sham group
Oxygen consumption (ml O2·gm-1·h)
2.4
1.8
1.2
0.0
0
5
10
15
20
25
30
10 minute time intervals

Figure 3. Mean (±S.E.M.) oxygen consumption (ml $O_2 \cdot g^{-1} \cdot h$) for NTS and Sham groups across baseline (23 ^{o}C) conditions for postsurgery heat challenge.

Fig. 3

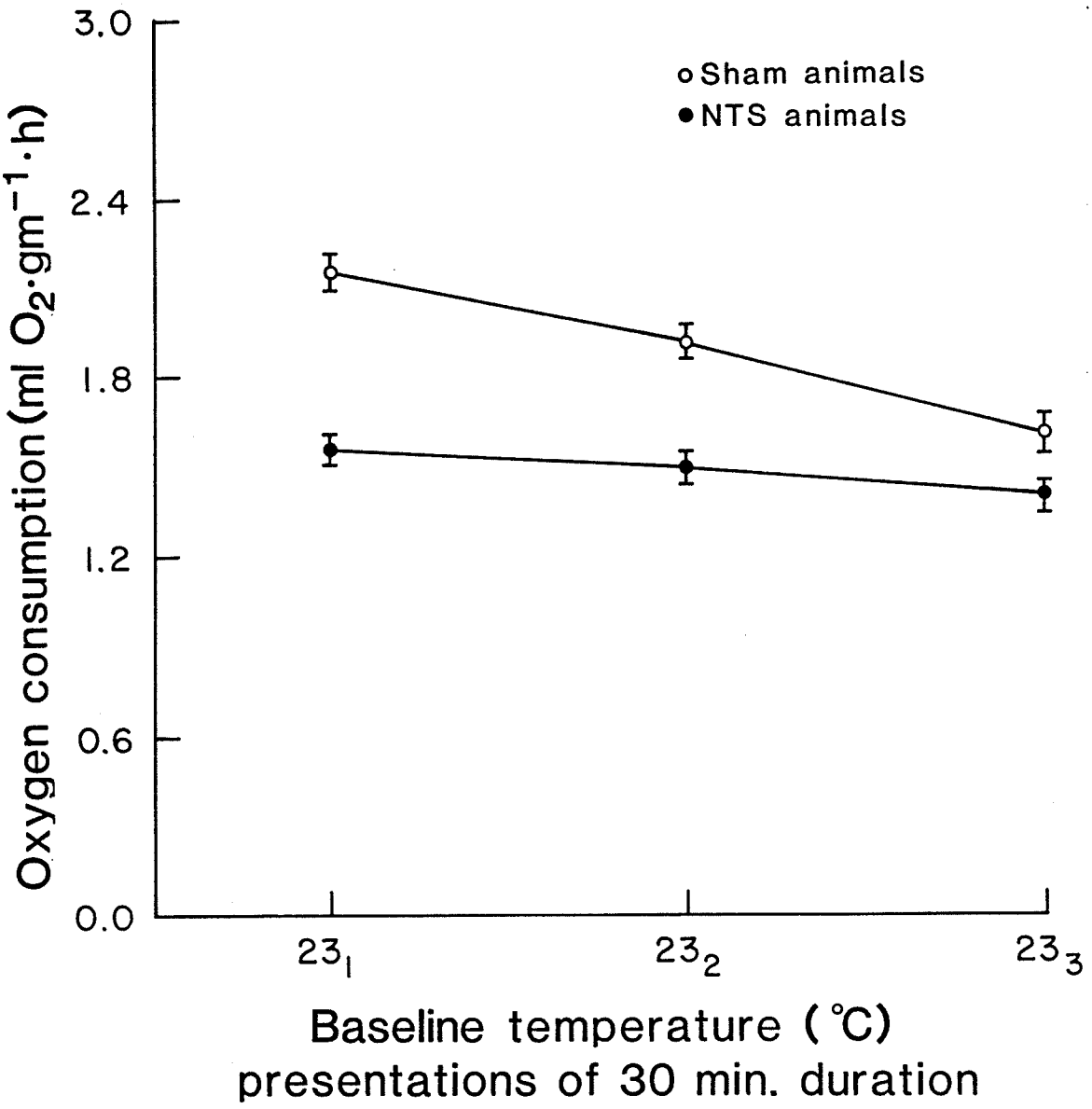

3.0
2.4
1.8
1.2
0.6
0.0
Oxygen consumption (ml $O_2 \cdot gm^{-1} \cdot h$)
o Sham animals
● NTS animals
23_1
23_2
23_3
Baseline temperature (°C)
presentations of 30 min. duration

Figure 4. Mean (±S.E.M.) carbon dioxide production (ml $CO_2 \cdot g^{-1} \cdot h$) for NTS and Sham groups during heat challenges.

Fig. 4

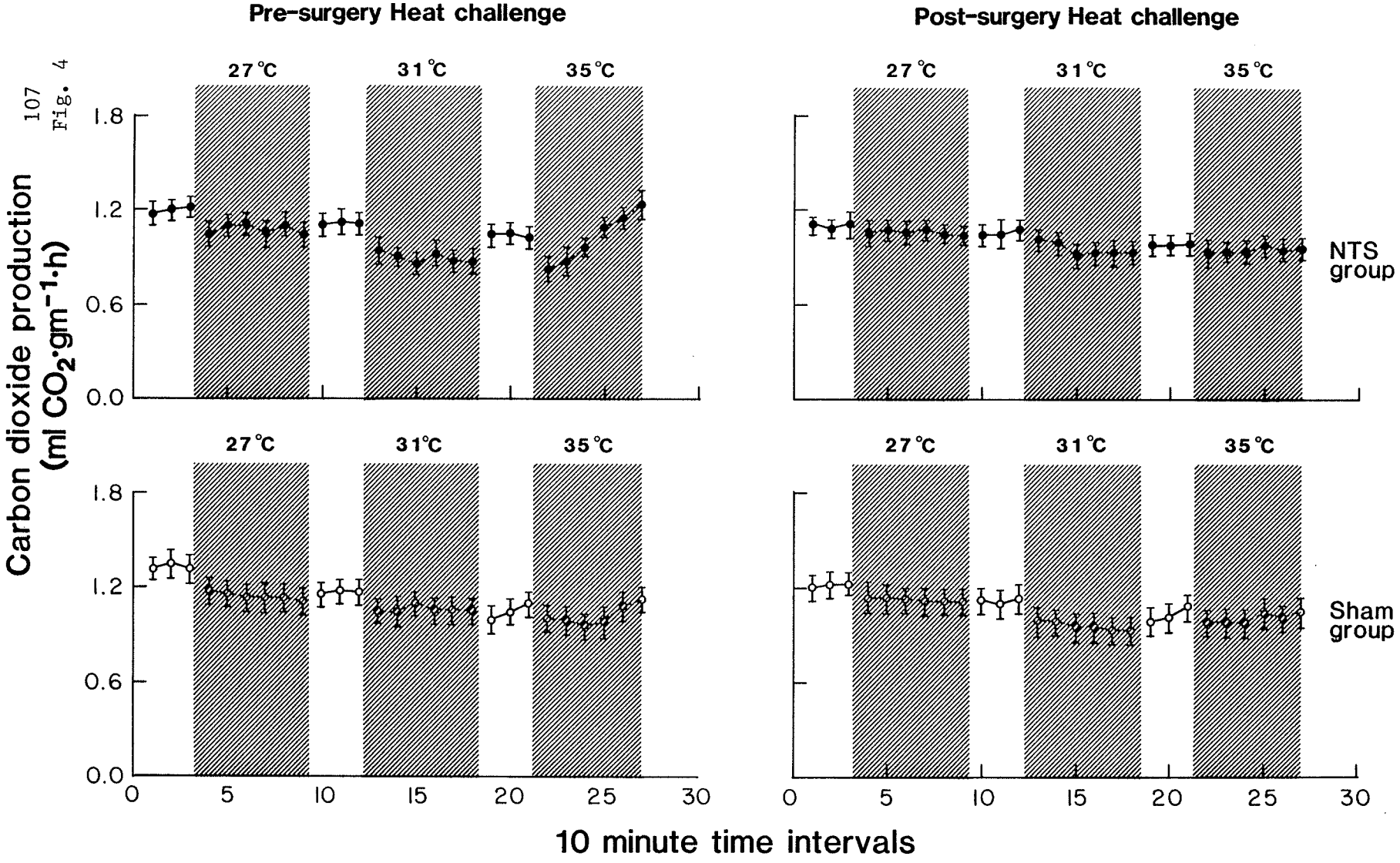

Pre-surgery Heat challenge
Post-surgery Heat challenge
27℃
31℃
35℃
NTS group
Sham group
Carbon dioxide production (ml $CO_2 \cdot gm^{-1} \cdot h$)
1.8
1.2
0.6
0.0
0
5
10
15
20
25
30
10 minute time intervals

Figure 5. Mean (±S.E.M.) direct aortic blood pressure (mm Hg) for NTS and Sham animals during postsurgery heat and cold challenges.

Fig. 5

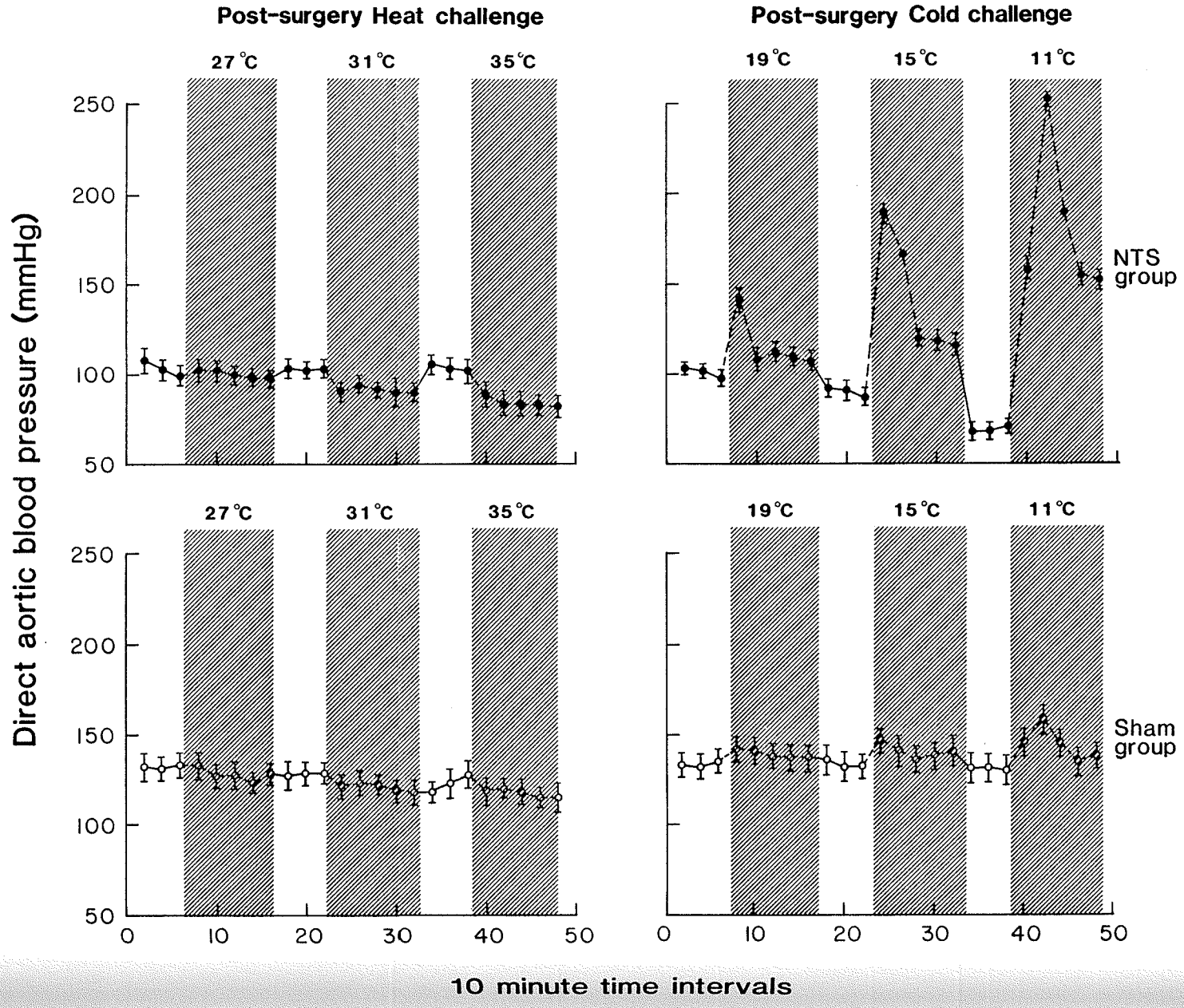

Post-surgery Heat challenge
Post-surgery Cold challenge
27 °C
31 °C
35 °C
19 °C
15 °C
11 °C
NTS group
Sham group
Direct aortic blood pressure (mmHg)
250
200
150
100
50
0
10
20
30
40
50
10 minute time intervals

Figure 6. Mean (±S.E.M.) direct aortic blood pressure (mm Hg) across baseline (23 °C) conditions for NTS and Sham animals during postsurgery cold challenges.

Fig. 6

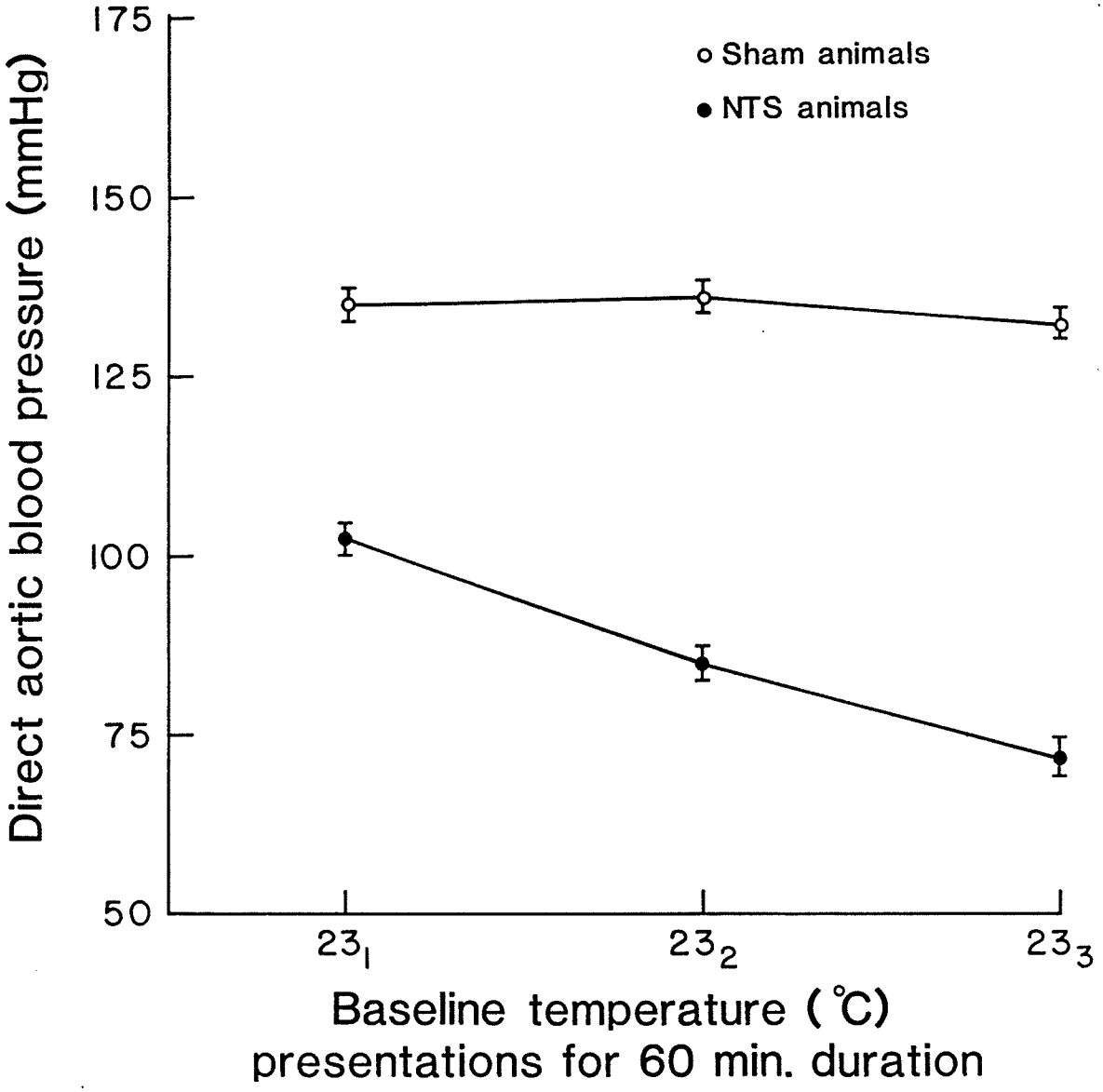

175
150
125
100
75
50
Direct aortic blood pressure (mmHg)
o Sham animals
● NTS animals
23₁
23₂
23₃
Baseline temperature (°C)
presentations for 60 min. duration

Figure 7. Mean (±S.E.M.) rectal temperature (^{o}C) for NTS and Sham groups during heat challenges.

Fig. 7

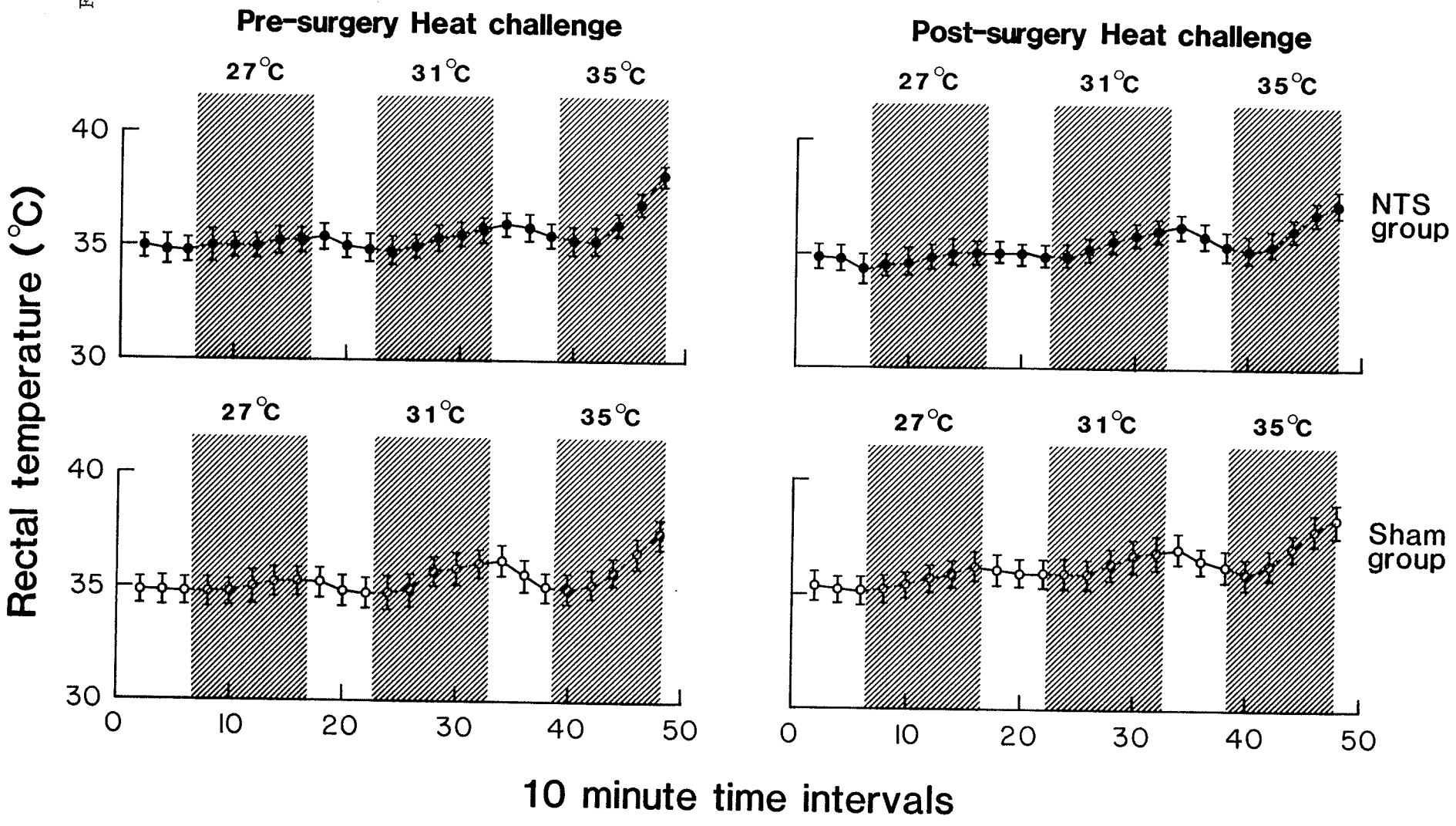

Pre-surgery Heat challenge
Post-surgery Heat challenge
27°C
31°C
35°C
NTS group
Sham group
Rectal temperature (°C)
40
35
30
0
10
20
30
40
50
10 minute time intervals

Figure 8. Mean (±S.E.M.) abdominal skin temperature (^{o}C) for NTS and Sham groups during heat challenges.

Fig. 8

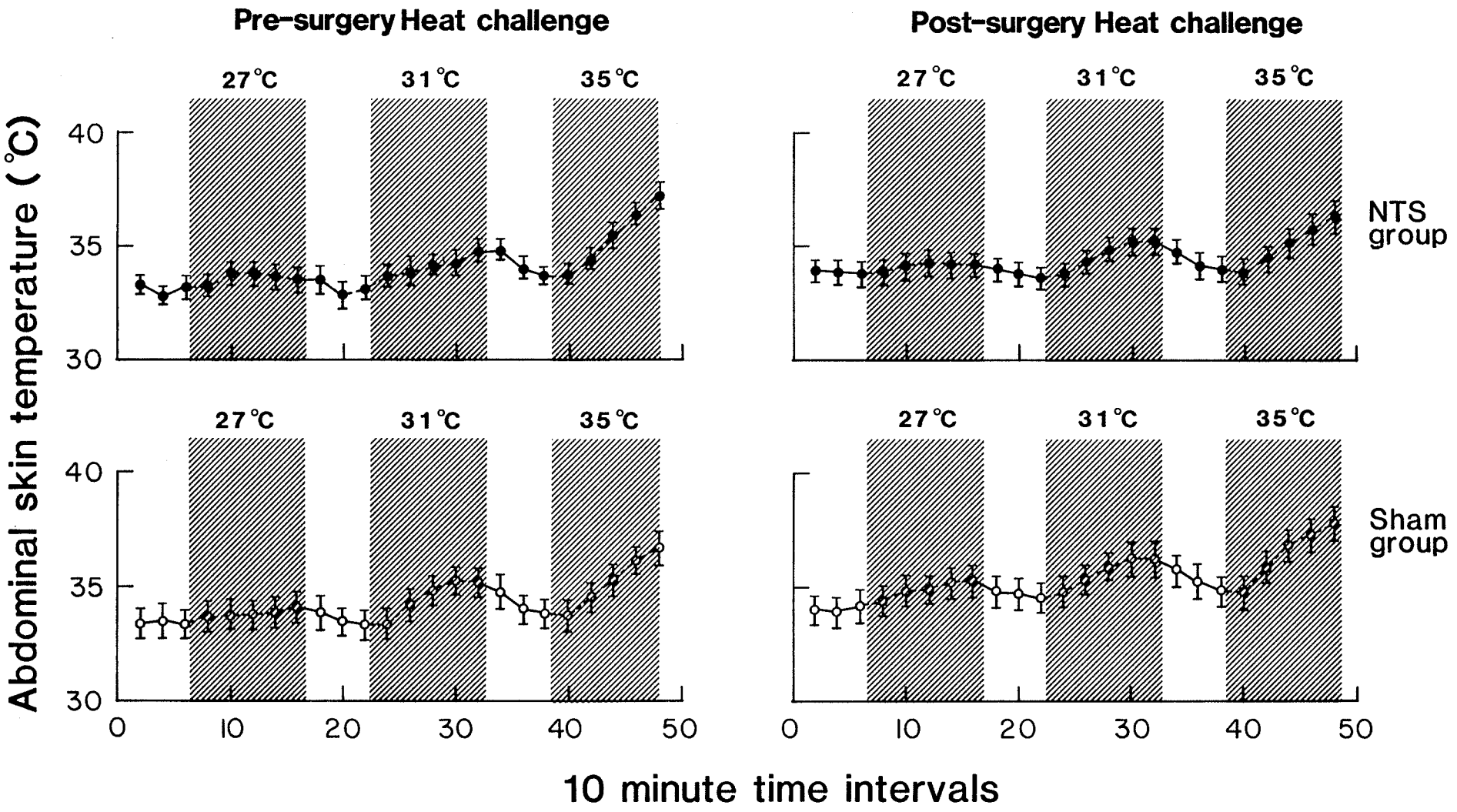

Pre-surgery Heat challenge
Post-surgery Heat challenge
27°C
31°C
35°C
Abdominal skin temperature (°C)
40
35
30
NTS group
Sham group
0
10
20
30
40
50
10 minute time intervals

Figure 9. Mean (±S.E.M.) tail skin temperature (^{o}C) for NTS and Sham groups during heat challenges.

Fig. 9

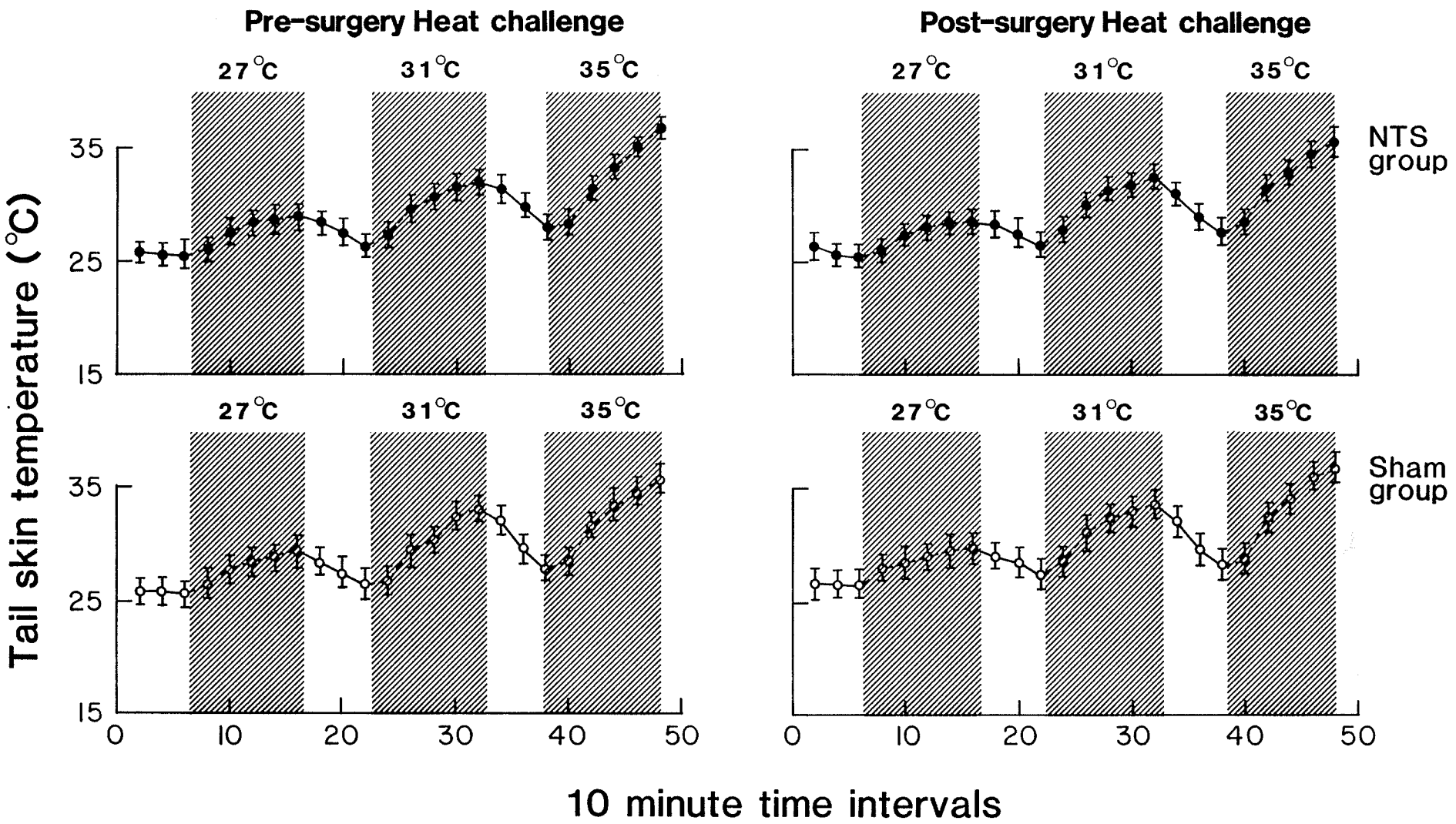

Pre-surgery Heat challenge
Post-surgery Heat challenge
27°C
31°C
35°C
NTS group
Sham group
Tail skin temperature (°C)
35
25
15
0
10
20
30
40
50
10 minute time intervals

Figure 10. Mean (±S.E.M.) evaporative heat loss ($g \cdot h^{-1}$) for NTS and Sham animals during baseline (23 ^{o}C) conditions for heat and cold postsurgery challenges.

Fig. 10

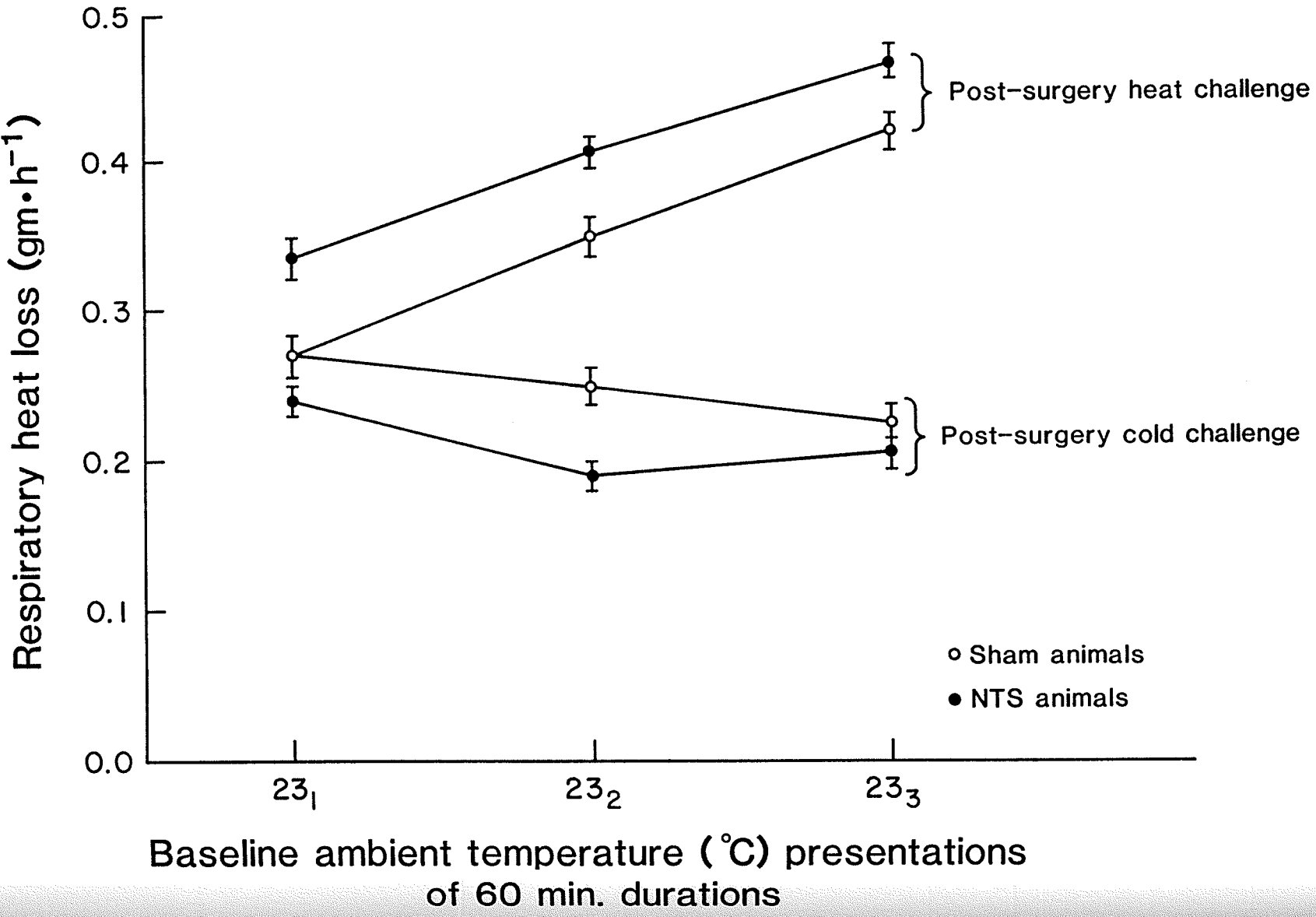

0.5
0.4
0.3
0.2
0.1
0.0
Respiratory heat loss (gm•h⁻¹)
Post-surgery heat challenge
Post-surgery cold challenge
o Sham animals
● NTS animals
23₁
23₂
23₃
Baseline ambient temperature (°C) presentations
of 60 min. durations

Figure 11. Mean (±S.E.M.) oxygen consumption (ml $O_2 \cdot g^{-1} \cdot h$) for NTS and Sham animals across test temperatures during presurgery heat challenge.

Fig. 11

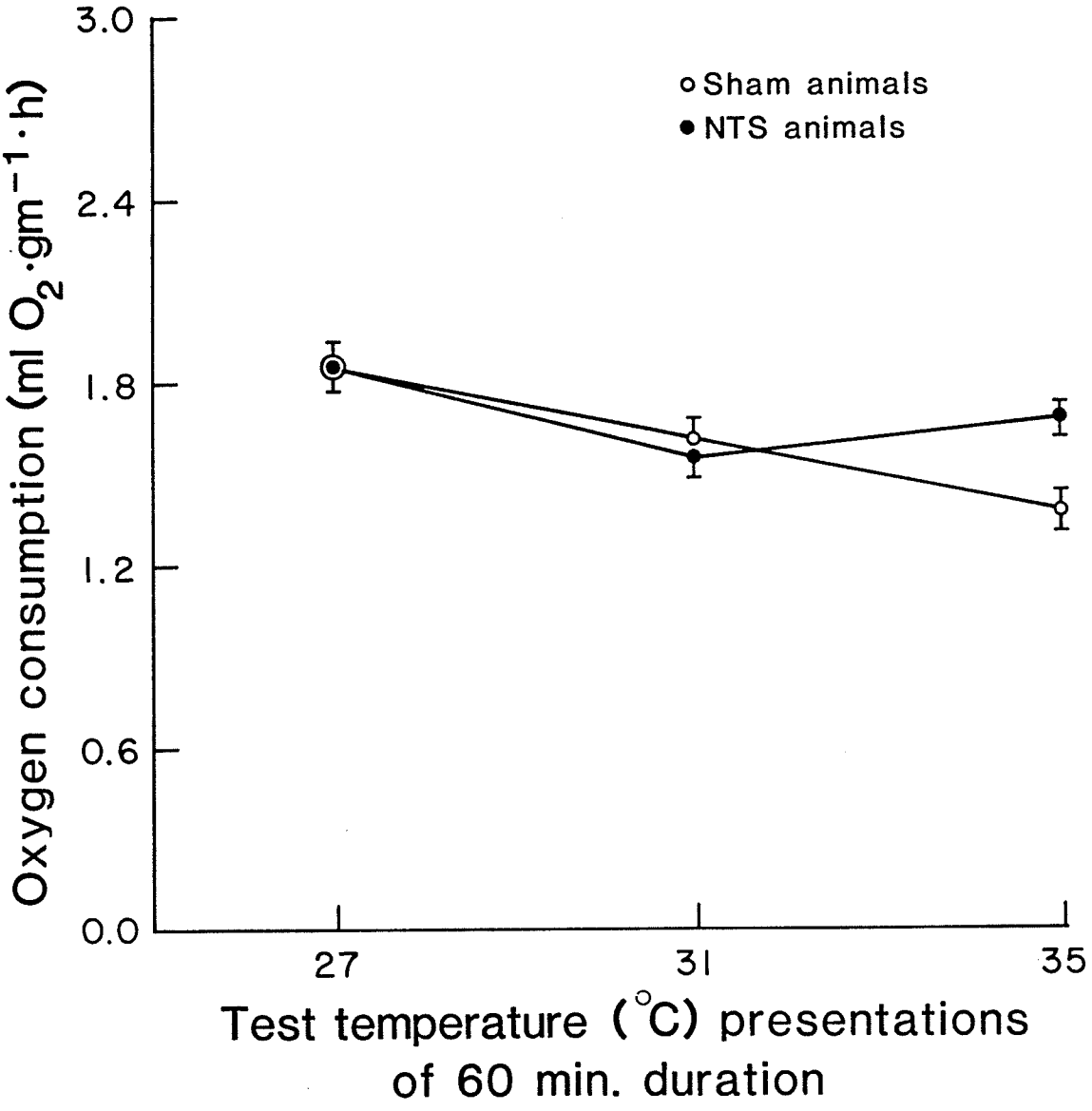

3.0
2.4
1.8
1.2
0.6
0.0
Oxygen consumption (ml $O_2 \cdot gm^{-1} \cdot h$)
Sham animals
NTS animals
27
31
35
Test temperature (°C) presentations
of 60 min. duration

Figure 12. Mean (±S.E.M.) oxygen consumption (ml $O_2 \cdot g^{-1} \cdot h$) for NTS and Sham groups during cold challenges.

Fig. 12

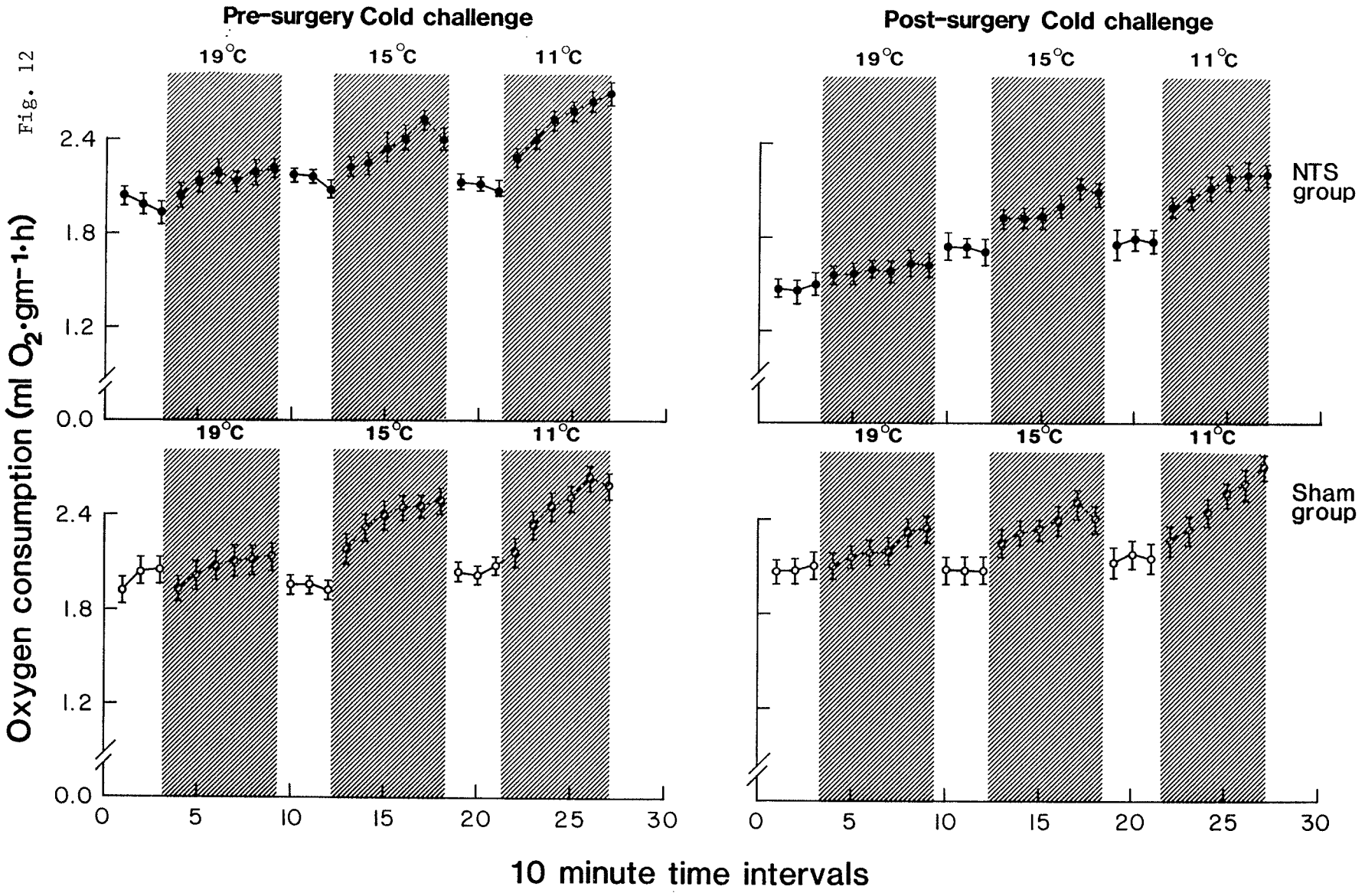

Pre-surgery Cold challenge
Post-surgery Cold challenge
19°C
15°C
11°C
NTS group
Sham group
Oxygen consumption (ml O_2·gm-1·h)
2.4
1.8
1.2
0.0
0
5
10
15
20
25
30
10 minute time intervals

Figure 13. Mean (±S.E.M.) carbon dioxide production (ml $CO_2 \cdot g^{-1} \cdot h$) for NTS and Sham groups during cold challenges.

Fig. 13

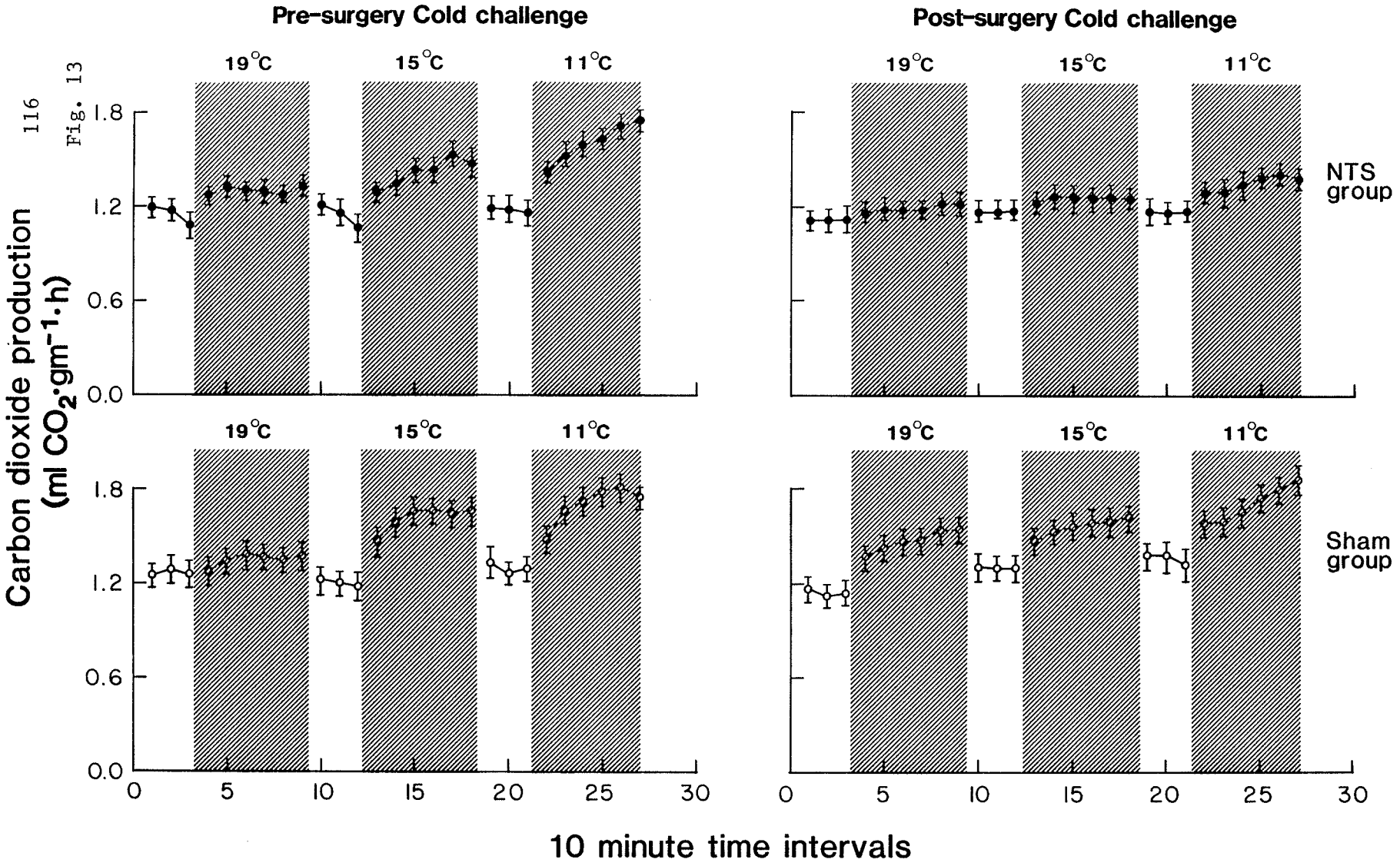

Pre-surgery Cold challenge
Post-surgery Cold challenge
19°C
15°C
11°C
NTS group
Sham group
Carbon dioxide production (ml $CO_2 \cdot gm^{-1} \cdot h$)
0.0
0.6
1.2
1.8
0
5
10
15
20
25
30
10 minute time intervals

Figure 14. Mean (±S.E.M.) carbon dioxide production (ml $CO_2 \cdot g^{-1} \cdot h$) for NTS and Sham animals across baseline (23 °C) conditions during postsurgery cold challenge.

Fig. 14

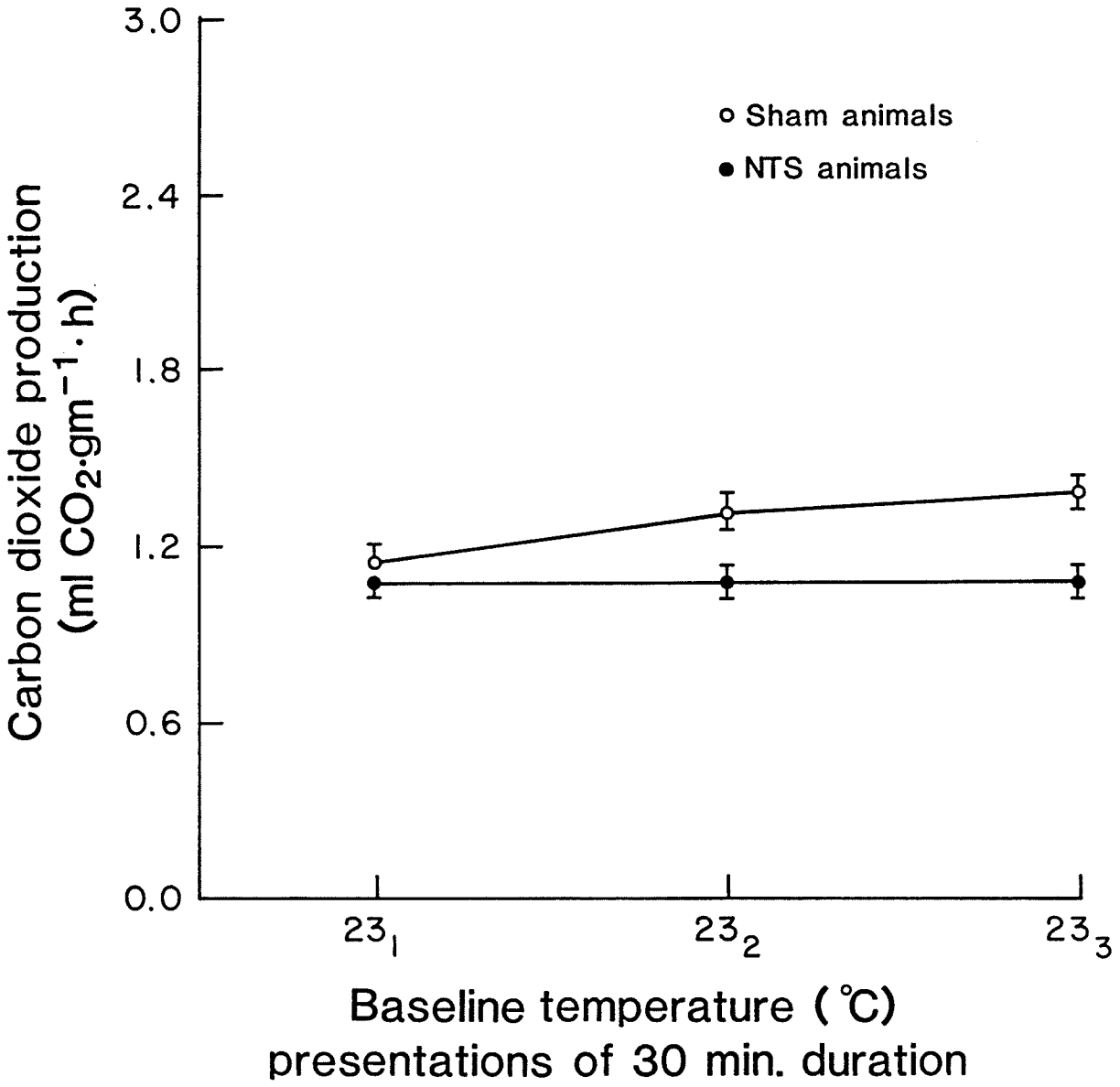

3.0
2.4
1.8
1.2
0.6
0.0
Carbon dioxide production
(ml $CO_2 \cdot gm^{-1} \cdot h$)
o Sham animals
• NTS animals
23_1
23_2
23_3
Baseline temperature (°C)
presentations of 30 min. duration

Figure 15. Mean (±S.E.M.) rectal temperature (^{o}C) for NTS and Sham groups during cold challenges.

Fig. 15

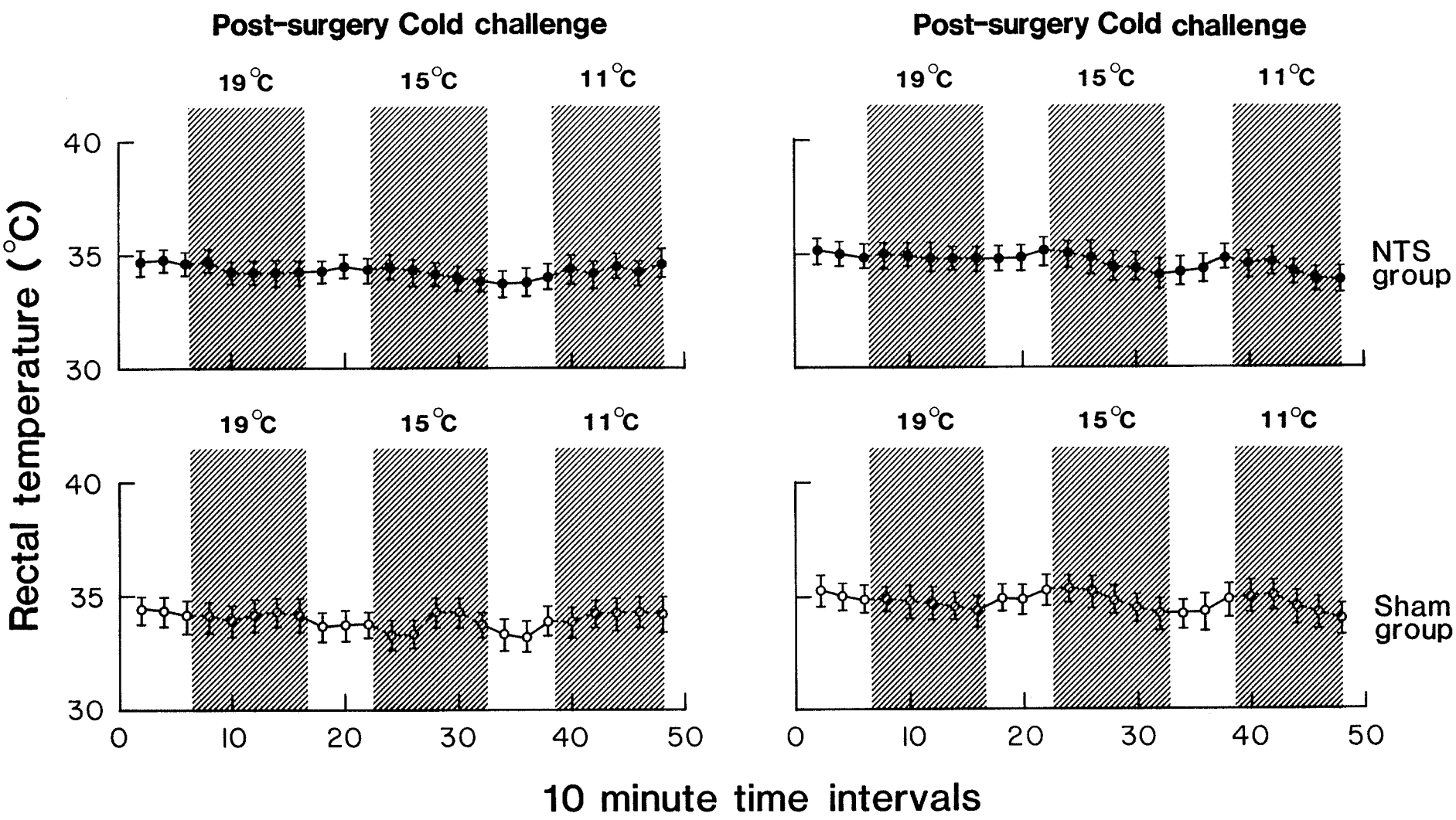

Post-surgery Cold challenge
Post-surgery Cold challenge
19°C
15°C
11°C
NTS group
Sham group
Rectal temperature (°C)
40
35
30
0
10
20
30
40
50
10 minute time intervals

Figure 16. Mean (±S.E.M.) abdominal skin temperature (^{o}C) for NTS and Sham groups during cold challenges.

Fig. 16

Pre-surgery Cold challenge
Post-surgery Cold challenge
19°C
15°C
11°C
Abdominal skin temperature (°C)
40
35
30
NTS group
Sham group
0
10
20
30
40
50
10 minute time intervals

Figure 17. Mean (±S.E.M.) tail skin temperature (^{o}C) for NTS and Sham groups during cold challenges.

Fig. 17

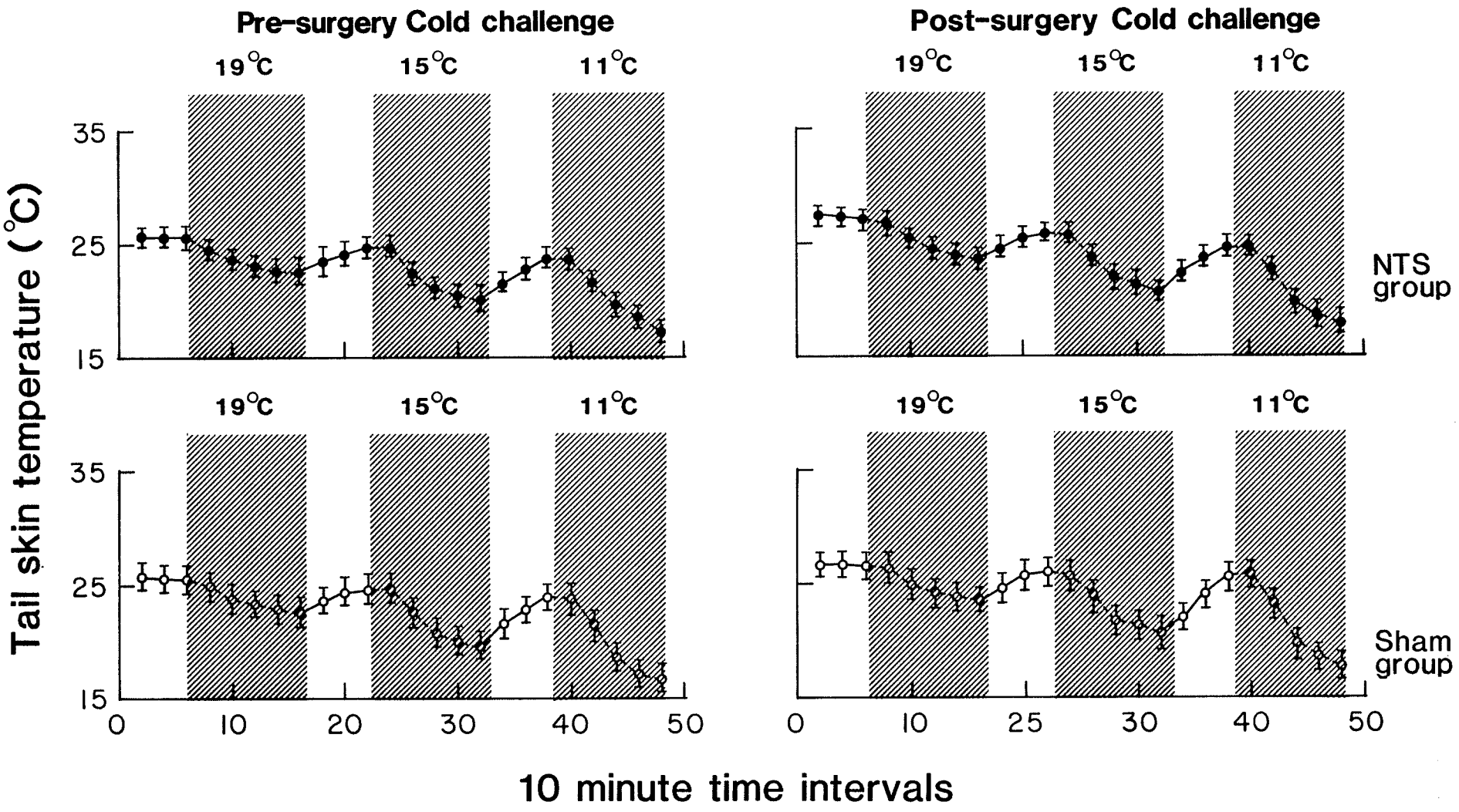

Pre-surgery Cold challenge
Post-surgery Cold challenge
19°C
15°C
11°C
Tail skin temperature (°C)
35
25
15
NTS group
Sham group
0
10
20
30
40
50
10 minute time intervals

Figure 18. Mean (±S.E.M.) carbon dioxide production (ml $CO_2 \cdot g^{-1} \cdot h$) for NTS and Sham animals across test temperatures during postsurgery cold challenge.

Fig. 18

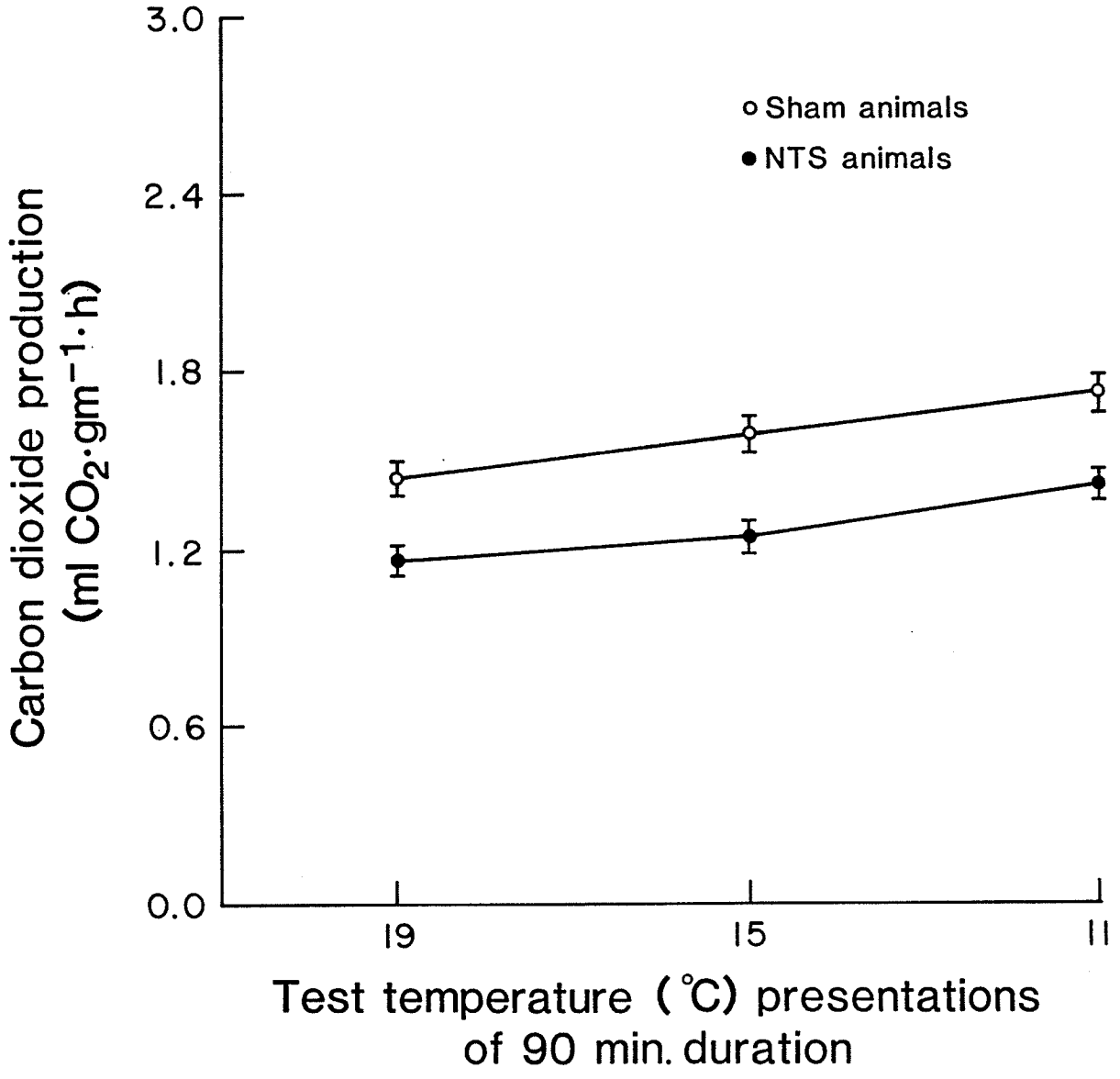

3.0
2.4
1.8
1.2
0.6
0.0
Carbon dioxide production
(ml $CO_2 \cdot gm^{-1} \cdot h$)
o Sham animals
● NTS animals
19
15
11
Test temperature (°C) presentations
of 90 min. duration

Figure 19. Mean (±S.E.M.) direct aortic blood pressure (mm Hg) across test temperatures for NTS and Sham animals during post-surgery cold challenge.

Fig. 19

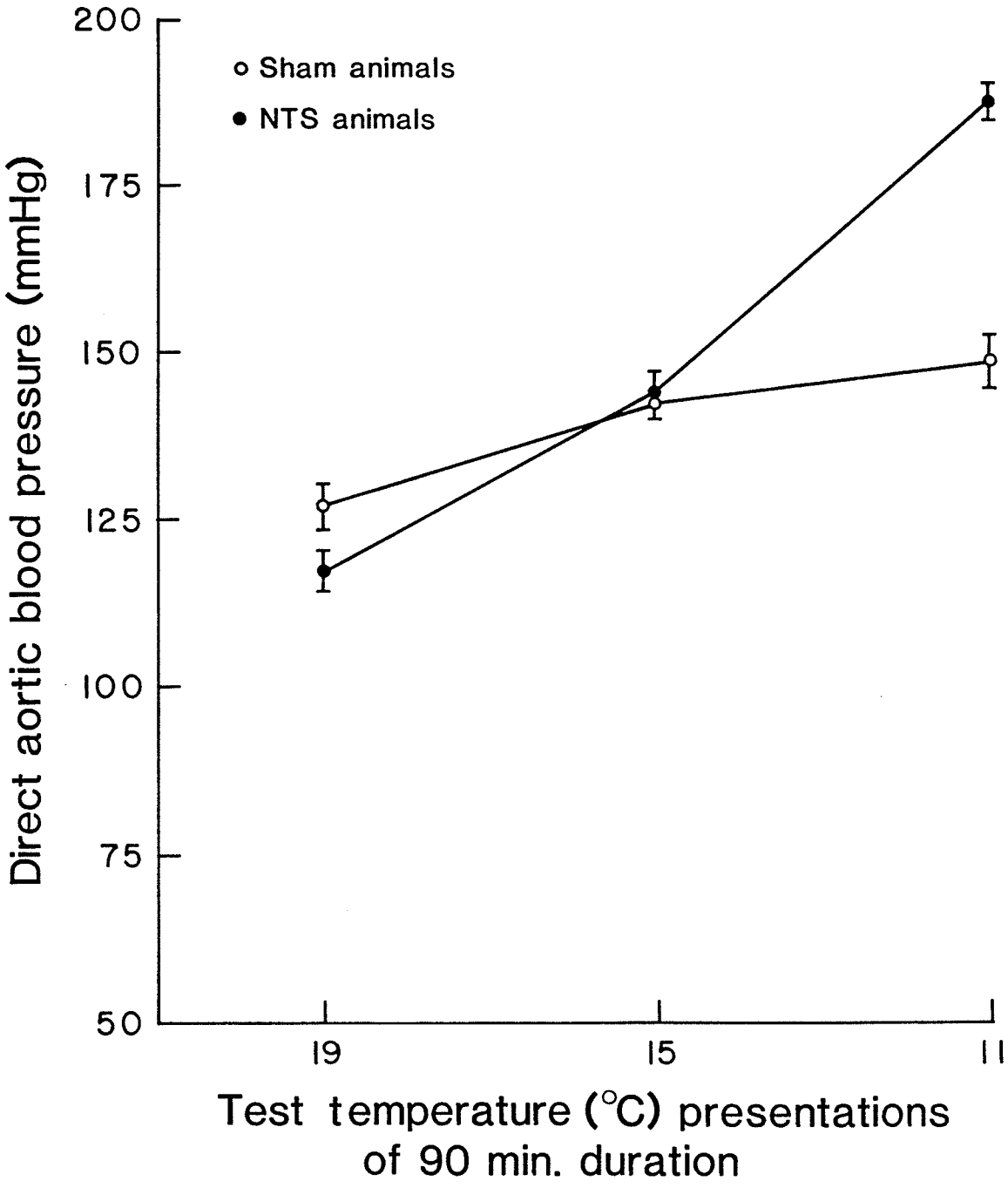

200
175
150
125
100
75
50
Direct aortic blood pressure (mmHg)
Sham animals
NTS animals
19
15
11
Test temperature (°C) presentations
of 90 min. duration

Figure 20. Mean (±S.E.M.) direct aortic blood pressure (mm Hg) for NTS and Sham animals across 10 min trial intervals during test temperatures in post-surgery cold challenge.

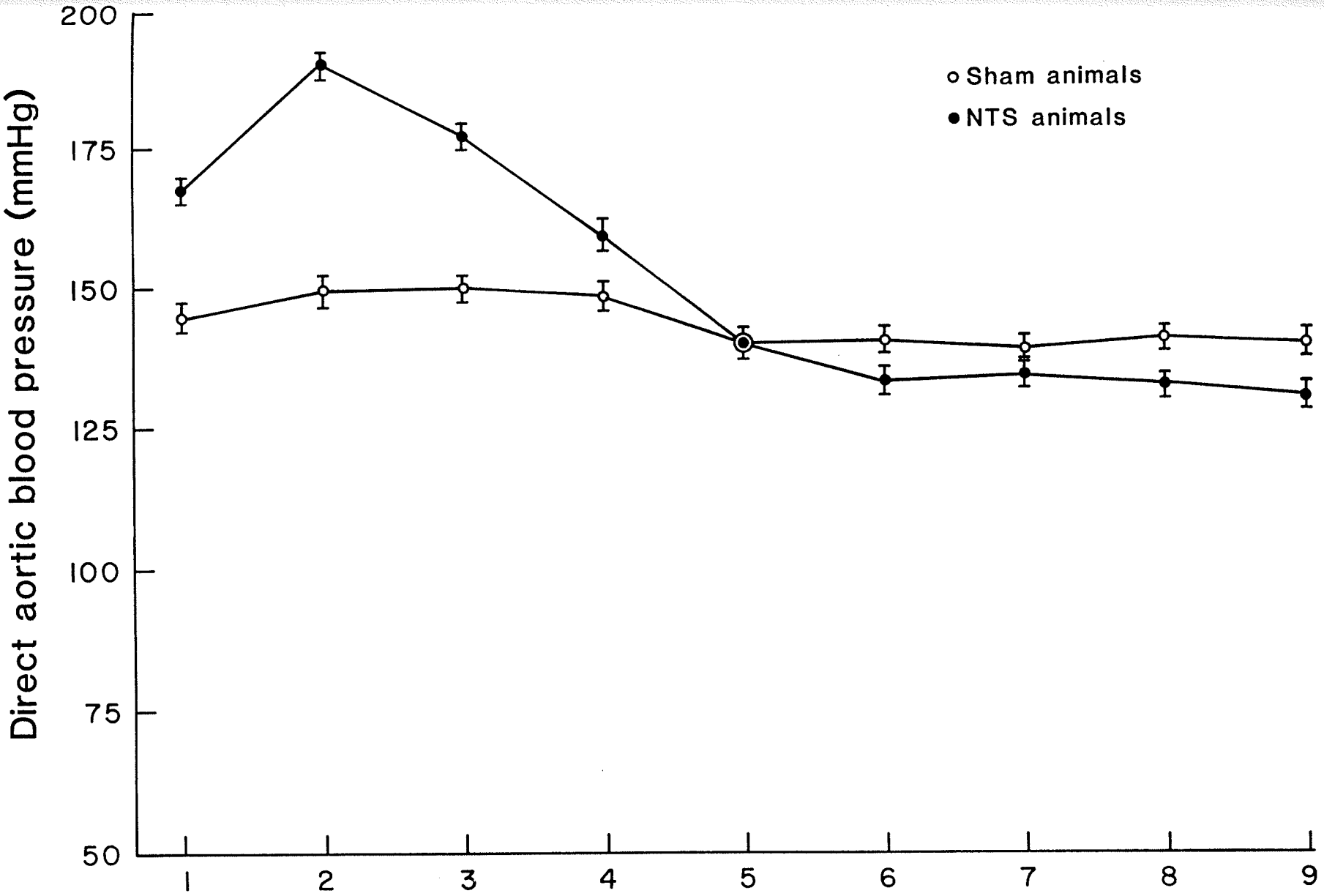

200
175
150
125
100
75
50
Direct aortic blood pressure (mmHg)
Sham animals
NTS animals
1
2
3
4
5
6
7
8
9
Trial intervals of 10 min. duration

Fig. 20

Figure 21. Mean direct aortic blood pressure (mm Hg) and heart rate (bpm) response to a bolus injection of phenylephrine (150 mg/Kg) in NTS-lesioned and Sham-operated animals.

Fig. 21

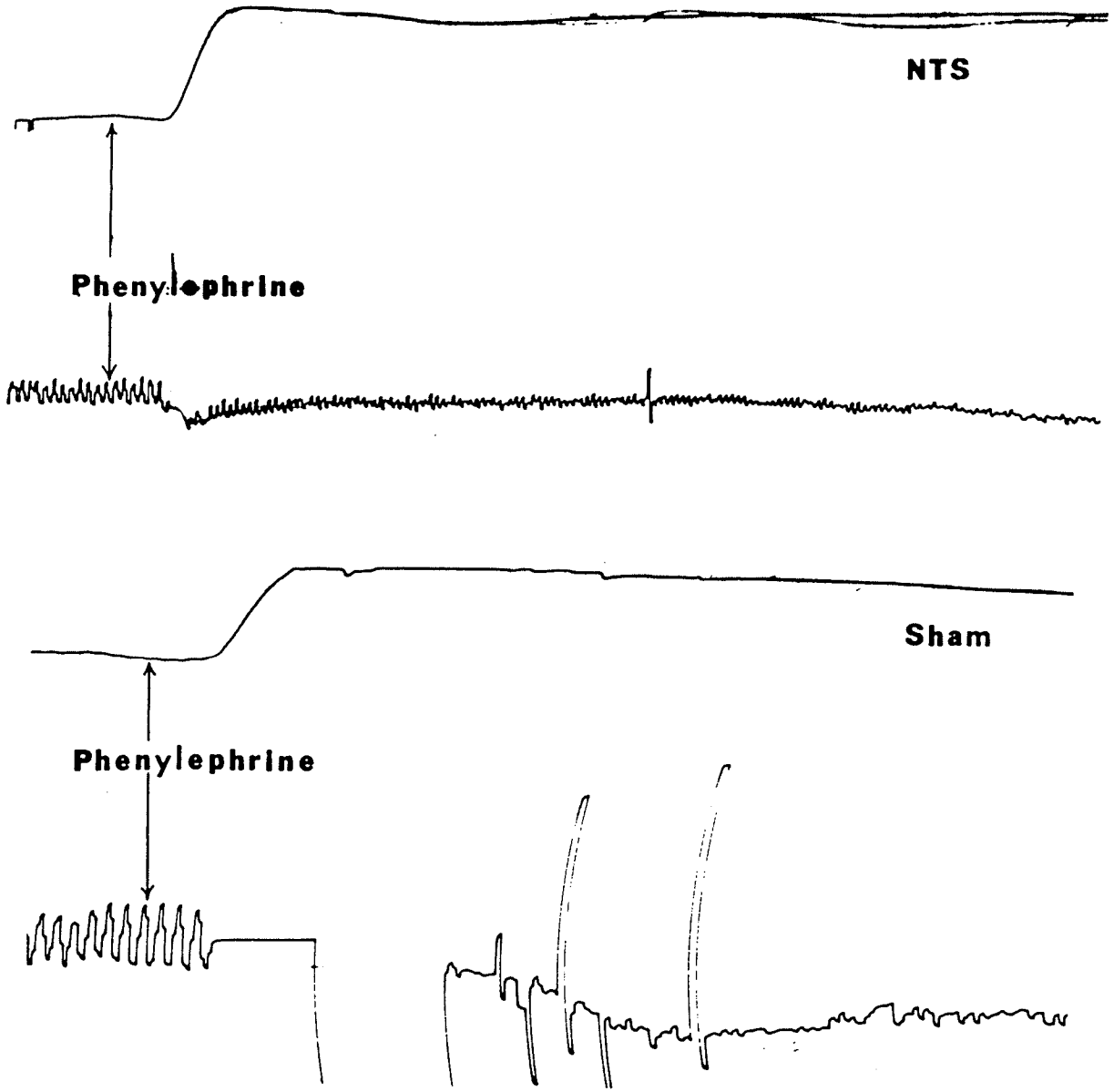


Figure 22. Mean direct aortic blood pressure (mm Hg) and heart rate (bpm) response to a bolus injection of acetylcholine (1 mg/Kg) in NTS-lesioned and Sham-operated animals.

Fig. 22

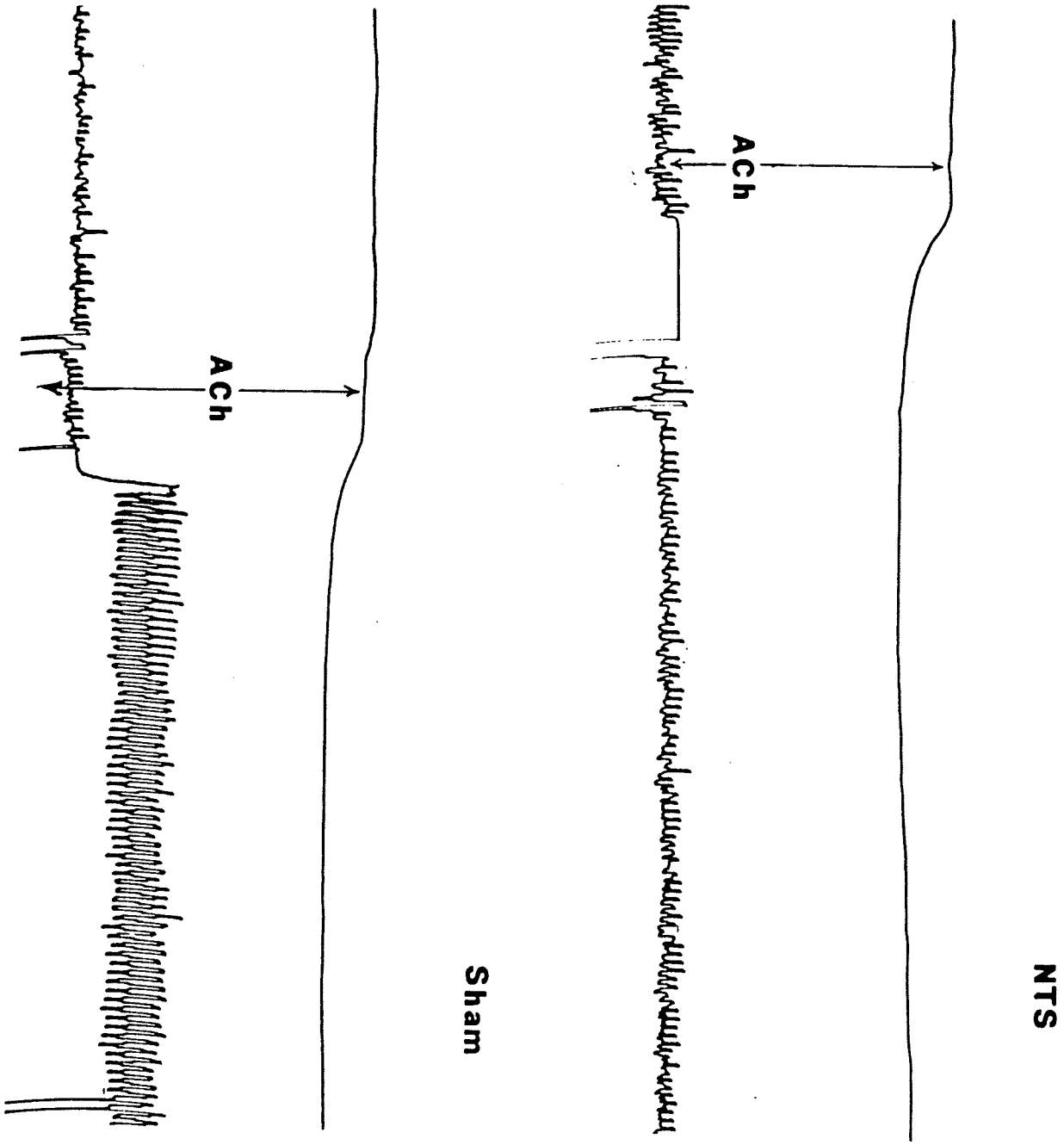
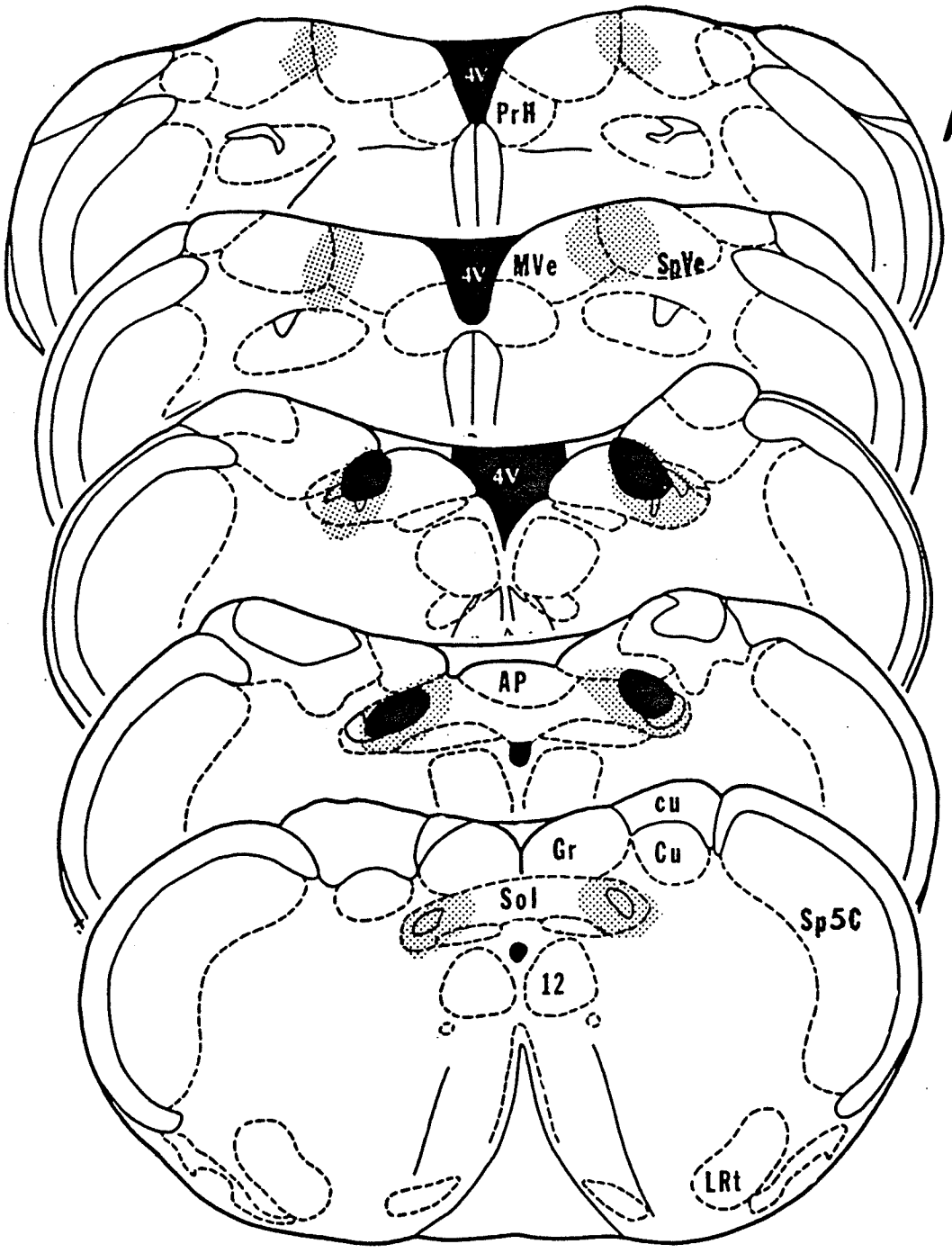


Figure 23. Representation of the largest (cross-hatched) and smallest (shaded) lesion damage in the NTS-lesioned group. Plates obtained coronally from the interaural axis (Paxinos & Watson, 1982). Cu = cuneate nucleus, cu = cuneate fasciculus, 12 = hypoglossal nucleus, Gr = gracile nucleus, Sol = nucleus solitary tract, LRt = lateral reticular nucleus, Sp5C = nucleus spinal tract trigeminal nerve caudal, AP = area postrema, MVe = medial vestibular nucleus, SpVe = spinal vestibular nucleus, PrH = prepositus hypoglossal nucleus.

Fig. 23



Appendix 1

Table 1

ANOVA's of Pre-Surgery Baseline Conditions (23°C) during Heat Challenge for NTS and Sham Data

Dependent Variable	Source of Variance	df	Mean Sq. Error	Error	F
Oxygen Consumption	Group	1,14	0.05	2.11	0.02
	Temperature (Temp.)	2,28	3.24	0.07	44.50***
	Trial	2,28	0.07	0.01	7.11**
	Group x Temp.	2,28	0.05	0.07	0.72
	Group x Trial	2,28	0.01	0.01	0.56
	Temp. x Trial	2,28	0.01	0.01	1.05
	Group x Temp. x Trial	4,56	0.02	0.01	2.14
Carbon Dioxide Production	Group	1,14	0.18	0.60	0.30
	Temperature (Temp.)	2,28	0.82	0.03	25.01***
	Trial	2,28	0.01	0.004	2.17
	Group x Temp.	2,28	0.04	0.03	1.37
	Group x Trial	2,28	0.001	0.004	0.00
	Temp. x Trial	4,56	0.001	0.01	0.29
	Group x Temp. x Trial	4,56	0.01	0.01	1.65
Respiratory Quotient	Group	1,14	0.001	0.01	0.11
	Temperature (Temp.)	2,28	0.004	0.001	5.42*
	Trial	2,28	0.001	0.001	0.59
	Group x Temp.	2,28	0.001	0.001	1.55
	Group x Trial	2,28	0.001	0.001	2.16
	Temp. x Trial	4,56	0.001	0.001	1.14
	Group x Temp. x Trial	4,56	0.001	0.001	1.66
Rectal Temperature	Group	1,14	2.88	6.70	0.43
	Temperature (Temp.)	2,28	23.93	2.43	9.83***
	Trial	5,70	1.88	0.16	11.62***
	Group x Temp.	2,28	0.63	2.43	0.01

Table 1 (Continued)

Dependent Variable	Source of Variance	df	Mean Sq. Error	Error	F
Rectal Temperature	Group x Trial	5,70	0.04	0.16	0.22
	Temp. x Trial	10,140	0.41	0.64	6.34***
	Group x Temp. x Trial	10,140	0.13	0.06	2.01*
Abdominal Skin Temperature	Group	1,14	4.35	8.51	0.51
	Temperature (Temp.)	2,28	28.29	1.46	19.36***
	Trial	5,70	3.05	0.27	11.36***
	Group x Temp.	2,28	1.54	1.46	1.05
	Group x Temp.	5,70	0.15	0.27	0.54
	Temp. x Trial	10,140	1.28	0.25	5.21***
	Group x Temp. x Trial	10,140	0.22	0.25	0.88
Tail Skin Temperature	Group	1,14	1.29	24.09	0.05
	Temperature (Temp.)	2,28	505.98	3.72	136.02***
	Trial	5,70	29.56	0.28	140.94***
	Group x Temp.	2,28	0.35	3.72	0.09
	Group x Trial	5,70	0.63	0.28	2.24
	Temp. x Trial	10,140	12.59	0.17	73.46***
	Group x Temp. x Trial	10,140	0.17	0.17	0.97
Evaporative Heat Loss	Group	1,14	0.001	0.02	0.03
	Temp.	2,28	0.08	0.001	16.80***
	Group x Temp.	2,28	0.001	0.001	1.26

*p < .05, **p. < .01., ***p < .001

Table 2

ANOVA's of Post-Surgery Baseline Conditions (23°C) during Heat Challenge for NTS and Sham Data

Dependent Variable	Source of Variance	df	Mean Sq. Error	Error	F
Oxygen Consumption	Group	1,14	4.95	1.18	5.03*
	Temperature (Temp.)	2,28	1.36	0.07	44.50***
	Trial	2,28	0.09	0.01	17.13***
	Group x Temp.	2,28	0.41	0.05	8.57**
	Group x Trial	2,28	0.001	0.01	0.40
	Temp. x Trial	4,56	0.001	0.001	1.43
	Group x Temp. x Trial	4,56	.007	0.001	3.09*
Carbon Dioxide Production	Group	1,14	0.18	0.35	0.67
	Temperature (Temp.)	2,28	0.27	0.03	9.09***
	Trial	2,28	0.13	0.00	5.58**
	Group x Temp.	2,28	0.31	0.30	1.04
	Group x Trial	2,28	0.00	0.004	0.57
	Temp. x Trial	4,56	0.004	0.004	1.34
	Group x Temp. x Trial	4,56	0.004	0.004	1.27
Respiratory Quotient	Group	1,14	0.001	0.07	0.07
	Temperature (Temp.)	2,28	0.001	0.001	1.98
	Trial	2,28	0.001	0.001	1.07
	Group x Temp.	2,28	0.001	0.001	0.27
	Group x Trial	2,28	0.001	0.001	3.48*
	Temp. x Trial	4,56	0.001	0.001	1.19
	Group x Temp. x Trial	4,56	0.001	0.001	2.73*
Blood Pressure	Group	1,14	44277.92	13422.63	9.30**
	Temperature (Temp.)	2,28	512.28	379.07	1.35

Table 2 (Continued)

Dependent Variable	Source of Variance	df	Mean Sq. Error	Error	F
Blood Pressure	Trial	5,70	51.97	55.55	0.94
	Group x Temp.	2,28	365.84	379.07	0.97
	Group x Trial	5,70	99.47	55.55	1.79
	Temp. x Trial	10,140	33.23	39.82	0.83
	Group x Temp. x Trial	10,140	44.32	39.92	1.11
Rectal Temperature	Group	1,14	47.61	20.92	2 28
	Temperature (Temp.)	2,28	41.95	3.03	13.83***
	Trial	5,70	1.83	0.05	36.97***
	Group x Temp.	2,28	1.15	3.03	0.38
	Group x Trial	5,70	0.08	0.05	1.66
	Temp. x Trial	10,140	0.47	0.06	8.00***
	Group x Temp. x Trial	10,140	0.04	0.06	0.08
Abdominal Skin Temperature	Group	1,14	34.38	17.91	1.92
	Temperature (Temp.)	2,28	27.68	1.44	19.21***
	Trial	5,70	3.37	0.04	94.85****
	Group x Temp.	2,28	2.73	1.44	1.89
	Group x Trial	5,70	0.03	0.04	0.97
	Temp. x Trial	10,140	0.88	0.08	10.55***
	Group x Temp. x Trial	10,140	0.02	0.08	0.29
Tail Skin Temperature	Group	1,14	45.36	27.68	1.64
	Temperature (Temp.)	2,28	341.53	2.33	146.37***
	Trial	5,70	41.32	0.30	138.95***
	Group x Temp.	2,28	0.07	2.33	0.28
	Group x Trial	5,70	0.07	0.30	0.22

Table 2 (Continued)

Dependent Variable	Source of Variance	df	Mean Sq. Error	Error	F
Tail Skin Temperature	Temp. x Trial	10,140	12.68	0.19	67.98***
	Group x Temp. x Trial	10,140	0.43	0.19	2.30*
Evaporative Heat Loss	Group	1,14	0.04	0.02	2.23
	Temp.	2,28	0.05	0.001	14.38***
	Group x Temp.	2,28	0.02	0.001	5.18*

*p < .05, **p < .01, ***p < .001

Table 3

ANOVA'S of Pre-Surgery Baseline Conditions ($23^{o}C$) during Heat Challenge for NTS and Sham Data.

Dependent Variable	Source of Variance	df	Mean Sq. Error	Error	F
Oxygen Consumption	Group	1,14	0.16	0.09	0.05
	Temperature (Temp.)	2,28	0.06	0.14	0.40
	Trial	2,28	0.13	0.02	0.80
	Group x Temp.	2,28	0.06	0.14	0.43
	Group x Trial	2,28	0.03	0.02	1.83
	Temp. x Trial	4,56	0.007	0.007	0.07
	Group x Temp. x Trial	4,56	0.01	0.007	1.31
Carbon Dioxide Production	Group	1,14	0.38	0.88	0.43
	Temperature (Temp.)	2,28	0.23	0.04	0.64
	Trial	2,28	0.03	0.01	3.01
	Group x Temp.	2,28	0.007	0.04	0.02
	Group x Trial	2,28	0.02	0.01	2.04
	Temp. x Trial	4,56	0.01	0.007	1.95
	Group x Temp. x Trial	4,56	0.001	0.007	0.02
Respiratory Quotient	Group	1,14	1.45	1.26	1.15
	Temperature (Temp.)	2,28	1.29	1.29	1.00
	Trial	2,28	0.001	0.001	1.32
	Group x Temp.	2,28	1.30	1.29	1.00
	Group x Trial	2,28	0.001	0.001	0.10
	Temp. x Trial	4,56	0.001	0.001	0.97
	Group x Temp. x Trial	4,56	0.001	0.001	0.86
Rectal Temperature	Group	1,14	13.13	6.34	2.07
	Temperature (Temp.)	2,28	17.51	2.02	8.67**

Table 3 (Continued)

Dependent Variable	Source of Variance	df	Mean Sq. Error	Error	F
Rectal Temperature	Trial	5,70	0.12	0.08	1.59
	Group x Temp.	2,28	0.60	2.02	0.30
	Group x Trial	5,70	0.09	0.08	1.19
	Temp. x Trial	10,140	0.24	0.12	2.23*
	Group x Temp. x Trial	10,140	0.06	0.12	0.06
Abdominal Skin Temperature	Group	1,14	0.001	12.10	0.001
	Temperature (Temp.)	2,28	9.44	1.43	6.62**
	Trial	5,70	2.12	0.12	17.97***
	Group x Temp.	2,28	0.14	1.43	0.10
	Group x Trial	5,70	0.24	0.12	2.02
	Temp x Trial	10,140	0.24	0.14	1.69
	Group x Temp. x Trial	10,140	0.09	0.14	0.07
Tail Skin Temperature	Group	1,14	0.03	21.22	0.001
	Temperature (Temp.)	2,28	222.61	0.56	399.41***
	Trial	5,70	18.74	0.08	22.26***
	Group x Temp.	2,28	0.85	0.56	1.52
	Group x Trial	5,70	0.02	0.08	0.02
	Group x Temp. x Trial	10,140	6.36	0.05	133.27***
Evaporative Heat Loss	Group	1,14	0.02	0.03	0.83
	Temp.	2,28	0.001	0.001	1.87
	Group x Temp.	2,28	0.001	0.001	1.48

*p < .05, **p < .01, ***p < .001

Table 4

ANOVA'S of Post-Surgery Baseline Conditions (23°C) during Cold Challenge for NTS and Sham Data.

Dependent Variable	Source of Variance	df	Mean Sq. Error	Error	F
Oxygen Consumption	Group	1,14	7.01	4.50	1.56
	Temperature (Temp.)	2,28	0.52	0.32	1.68
	Trial	2,28	0.004	0.004	1.07
	Groux x Temp.	2,28	0.25	0.32	0.82
	Group x Trial	2,28	0.00	0.004	0.16
	Temp. x Trial	4,56	0.004	0.007	0.94
	Group x Temp. x Trial	4,56	0.001	0.04	0.10
Carbon Dioxide Production	Group	1,14	1.2	0.73	1.64
	Temperature (Temp.)	2,28	0.24	0.02	12.00***
	Trial	2,28	0.001	0.001	0.16
	Group x Temp.	2,28	0.11	0.02	5.41*
	Group x Trial	2,28	0.001	0.001	0.23
	Temp. x Trial	4,56	0.001	0.001	1.67
	Group x Temp. x Trial	4,56	0.001	0.001	0.65
Respiratory Quotient	Group	1,14	0.001	0.02	0.04
	Temperature (Temp.)	2,28	1.29	1.29	1.66
	Trial	2,28	0.001	0.001	2.02
	Group x Temp.	2,28	0.001	0.001	3.45*
	Group x Trial	2,28	0.001	0.001	1.03
	Temp. x Trial	4,56	0.001	0.001	1.48
	Group x Temp. x Trial	4,56	0.001	0.001	1.47

Table 4 (Continued)

Dependent Variance	Source of Variance	df	Mean Sq. Error	Error	F
Blood Pressure	Group	1,14	162449.99	17961.01	9.04**
	Temperature (Temp.)	2,28	659.50	1216.20	5.42*
	Trial	5,70	20.04	24.73	0.81
	Group x Temp.	2,28	4592.51	2126.20	3.78*
	Group x Trial	5,70	12.26	24.73	0.50
	Temp. x Trial	10,140	71.03	21.80	3.26***
	Group x Temp. x Trial	10,140	47.16	21.80	2.16*
Rectal Temperature	Group	1,14	0.37	40.50	0.01
	Temperature (Temp.)	2,28	18.87	2.56	7.37**
	Trial	5,70	0.30	0.07	4.16**
	Group x Temp.	2,28	0.56	2.56	0.22
	Group x Trial	5,70	0.09	0.07	1.33
	Temp. x Trial	10,140	0.57	0.03	17.52***
	Group x Temp. x Trial	10,140	0.05	0.03	1.53
Abdominal Skin Temperature	Group	1,14	27.69	41.71	0.66
	Temperature (Temp.)	2,28	17.43	1.88	9.28***
	Trial	5,70	0.94	0.08	12.61***
	Group x Temp.	2,28	0.03	1.88	0.16
	Group x Trial	5,70	0.02	0.08	0.30
	Temp. x Trial	10,140	0.76	0.05	16.17***
	Group x Temp. x Trial	10,140	0.10	0.05	2.17*
Tail Skin Temperature	Group	1,14	0.06	20.02	0.00
	Temperature (Temp.)	2,28	303.72	2.44	124.74***
	Trial	5,70	23.33	0.12	190.40***

Table 4 (Continued)

Dependent Variable	Source of Variance	df	Mean Sq. Error	Error	F
Tail Skin Temperature	Group x Temp.	2,28	1.40	2.44	0.57
	Group x Trial	5,70	0.15	0.12	1.24
	Temp. x Trial	10,140	9.20	0.08	114.40***
	Group x Temp. x Trial	10,140	1.17	0.08	2.01*
Evaporative Heat Loss	Group	1,14	0.02	0.04	0.38
	Temp.	2,28	0.001	0.001	1.02
	Group x Temp.	2,28	0.02	0.001	4.18*

*p < .05, **p < .01, ***p < .001

Table 5

ANOVA's of Pre-Surgery Test Temperatures during Heat Challenge for NTS and Sham Data

Dependent Variable	Source of Variance	df	Mean Sq. Error	Error	F
Oxygen Consumption	Group	1,14	0.18	5.25	0.03
	Temperature (Temp.)	2,28	2.96	0.2	14.84***
	Trial	5,70	0.19	0.02	10.62***
	Group x Temp.	2,28	0.80	0.20	4.99*
	Group x Trial	5,70	0.06	0.02	3.65**
	Temp. x Trial	10,140	0.14	0.01	9.14***
	Group x Temp. x Trial	10,140	0.02	0.01	1.36
Carbon Dioxide Production	Group	1,14	0.32	0.47	0.68
	Temperature (Temp.)	2,28	0.45	0.09	5.23*
	Trial	5,70	0.06	0.01	5.74***
	Group x Temp.	2,28	0.22	0.09	2.56
	Group x Trial	5,70	0.18	0.01	1.46
	Temp. x Trial	10,140	0.10	0.01	9.15***
	Group x Temp. x Trial	10,140	0.01	0.01	1.26
Respiratory Quotient	Group	1,14	0.001	0.01	0.02
	Temperature (Temp.)	2,28	0.004	0.007	0.26
	Trial	5,70	0.001	0.001	0.84
	Group x Temp.	2,28	0.14	0.007	1.98
	Group x Trial	5,70	0.001	0.001	0.99
	Temp x Trial	10,140	0.001	0.001	0.80
	Group x Temp. x Trial	10,140	0.001	0.001	1.46

Table 5 (Continued)

Dependent Variable	Source of Variance	df	Mean Sq. Error	Error	F
Rectal Temperature	Group	1,14	0.98	7.67	0.13
	Temperature (Temp.)	2,28	38.01	2.19	17.38***
	Trial	8,112	13.32	0.23	59.22***
	Group x Temp.	2,28	2.52	2.19	1.15
	Group x Trial	8,112	0.11	0.23	0.05
	Temp. x Trial	16,224	3.34	0.14	24.54***
	Group x Temp. x Trial	16,224	0.16	0.14	1.17
Abdominal Skin Temperature	Group	1,14	3.33	10.45	0.32
	Temperature (Temp.)	2,28	89.49	1.93	46.43***
	Trial	8,112	15.72	0.24	64.55***
	Group x Temp.	2,28	4.24	1.93	2.20
	Group x Trial	8,112	0.05	0.24	0.20
	Temp. x Trial	16,224	4.87	0.18	27.86***
	Group x Temp. x Trial	16,224	0.46	0.18	2.62***
Tail Skin Temperature	Group	1,14	3.59	34.85	0.10
	Temperature (Temp.)	2,28	842.75	1.48	568.35***
	Trial	8,112	167.38	0.46	365.90***
	Group x Temp.	2,28	2.37	1.48	1.60
	Group x Trial	8,112	0.04	0.46	0.12
	Temp. x Trial	16,224	13.53	0.29	46.28***
	Group x Temp. x Trial	16,224	1.38	0.29	4.72***
Evaporative Heat Loss	Group	1,14	0.001	0.02	0.26
	Temp.	2,28	0.06	0.01	9.97***
	Group x Temp.	2,28	0.01	0.01	1.53

*p < .05, **p < .01, ***p < .001

Table 6

ANOVA's of Post-Surgery Test Temperatures during Heat Challenge for NTS and Sham Data.

Dependent Variable	Source Variance	df	Mean Sq. Error	Error	F
Oxygen Consumption	Group	1,14	4.75	2.94	1.61
	Temperature (Temp.)	2,28	1.72	0.06	27.90***
	Trial	5,70	0.02	0.01	1.45
	Group x Temp.	2,28	0.47	0.06	7.63**
	Group x Trial	5,70	0.01	0.01	0.73
	Temp. x Trial	10,140	0.03	0.007	4.02***
	Group x Temp. x Trial	10,140	0.007	0.006	1.27
Carbon Dioxide Production	Group	1,14	0.12	0.86	0.14
	Temperature (Temp.)	2,28	0.51	0.05	9.21***
	Trial	5,70	0.004	0.004	1.29
	Group x Temp.	2,28	0.03	0.05	0.59
	Group x Trial	5,70	0.001	0.004	0.33
	Temp. x Trial	10,140	0.01	0.004	3.30***
	Group x Temp. x Trial	10,140	0.004	0.004	0.81
Respiratory Quotient	Group	1,14	0.001	0.01	0.05
	Temperature (Temp.)	2,28	0.001	0.004	0.044
	Trial	5,70	.004	0.001	2.36*
	Group x Temp.	2,28	0.001	0.03	0.11
	Group x Trial	5,70	0.001	0.001	0.99
	Temp. x Trial	10,140	0.001	0.001	0.83
	Group x Temp. x Trial	10,140	0.001	0.001	1.77
Blood Pressure	Group	1,14	1222.44	21607.08	5.66*
	Temperature (Temp.)	2,28	54.24	998.80	5.43*

Table 6 (Continued)

Dependent Variable	Source of Variance	df	Mean Sq. Error	Error	F
Blood Pressure	Trial	8,11	191.12	40.59	4.71***
	Group x Temp.	2,28	300.88	998.80	0.30
	Group x Trial	8,112	14.54	40.59	0.36
	Temp. x Trial	16,224	22.30	26.99	0.83
	Group x Temp. x Trial	16,224	24.38	26.99	0.90
Rectal Temperature	Group	1,14	82.16	38.66	2.13
	Temperature (Temp.)	2,28	64.54	4.25	15.20***
	Trial	8,112	13.14	0.11	118.79***
	Group x Temp.	2,28	0.50	4.25	0.12
	Group x Trial	8,112	0.21	0.11	1.93
	Temp x Trial	16,224	1.49	0.09	16.63***
	Group x Temp. x Trial	16,224	0.05	0.09	0.55
Abdominal Skin Temperature	Group	1,14	95.77	28.00	8.42
	Temperature (Temp.)	2,28	67.86	3.86	17.56***
	Trial	8,112	14.04	0.63	22.31***
	Group x Temp.	2,28	8.91	3.86	2.31
	Group x Trial	8,112	0.37	0.63	0.59
	Temp. x Trial	16,224	2.88	0.50	5.78***
	Group x Temp. Trial	16,224	0.55	0.50	1.11
Tail Skin Temperature	Group	1,14	119.28	47.83	2.49
	Temperature (Temp.)	2,28	820.91	4.01	204.94***
	Trial	8,112	147.72	0.89	165.56***
	Group x Temp.	2,28	0.67	4.01	0.02
	Group x Trial	8,112	0.37	0.89	0.42
	Temp. x Trial	16,224	11.46	0.50	22.92***

Table 6 (Continued)

Dependent Variable	Source of Variance	df	Mean Sq. Error	Error	F
Tail Skin Temperature	Group x Temp. x Trial	16,224	0.41	0.50	0.83
Evaporative Heat Loss	Group	1,14	0.03	0.02	1.80
	Temperature (Temp.)	2,28	0.08	0.00	43.00***
	Group x Temp.	2,28	0.001	0.001	0.20
Arterial pH	Group	1,14	0.001	0.001	5.39*
Arterial pO_2	Group	1,14	0.001	0.000	0.53
Arterial pCO_2	Group	1,14	0.001	0.001	0.001

*p < .05, **p < .01, ***p < .001

Table 7

ANOVA'S of Post-Surgical Test Temperatures during Cold Challenge for NTS and Sham Data.

Dependent Variable	Source of Variance	df	Mean Sq. Error	Error	F
Oxygen Consumption	Group	1,14	0.09	8.06	0.01
	Temperature (Temp.)	2,28	4.09	0.35	11.66***
	Trial	5,70	0.67	0.03	23.39***
	Group x Temp.	2,28	0.06	0.35	0.17
	Group x Trial	5,70	0.01	0.03	0.46
	Temp. x Trial	10,140	0.06	0.02	2.77**
	Group x Temp. x Trial	10,140	0.007	0.02	0.04
Carbon Dioxide	Group	1,14	1.01	2.06	0.49
	Temperature (Temp.)	2,28	2.56	0.12	22.43***
	Trial	5,70	0.24	0.02	12.86***
	Group x Temp.	2,28	0.13	0.12	1.13
	Group x Trial	5,70	0.01	0.02	0.54
	Temp. x Trial	10,140	0.04	0.01	3.29***
	Group x Temp. x Trial	10,140	0.007	0.01	0.62
Respiratory Quotient	Group	1,14	0.004	0.004	0.68
	Temperature (Temp.)	2,28	0.001	0.001	1.39
	Trial	5,70	0.001	0.001	1.32
	Group x Temp.	2,28	0.001	0.001	1.16
	Group x Trial	5,70	0.001	0.001	0.33
	Temp x Trial	10,140	0.001	0.001	1.77
	Group x Temp. x Trial	10,140	0.001	0.001	0.98
Rectal Temperature	Group	1,14	4.98	12.07	0.41
	Temperature (Temp.)	2,28	0.60	1.99	0.30

Table 7 (Continued)

Dependent Variable	Source of Variance	df	Mean Sq. Error	Error	F
Rectal Temperature	Trial	8,112	0.22	0.18	1.12
	Group x Temp.	2,28	0.01	1.99	0.00
	Group x Trial	8,112	0.70	0.18	3.85***
	Temp. x Trial	16,224	0.17	0.15	1.08
	Group x Temp. x Trial	16,224	0.14	0.15	0.90
Abdominal Skin Temperature	Group	1,14	1.71	17.91	0.10
	Temperature (Temp.)	2,28	13.87	1.85	7.51**
	Trial	8,112	3.96	0.30	13.33***
	Group x Temp.	2,28	0.20	1.85	0.11
	Group x Trial	8,112	0.61	0.30	2.05*
	Temp. x Trial	16,224	0.63	0.21	3.03***
	Group x Temp. x Trial	16,224	0.13	0.21	0.62
Tail Skin Temperature	Group	1,14	8.45	30.83	0.27
	Temperature (Temp.)	2,28	501.20	1.26	397.42***
	Trial	8,112	135.01	0.30	449.45***
	Group x Temp.	2,28	4.51	1.26	3.57*
	Group x Trial	8,112	0.30	0.30	1.01
	Temp. x Trial	16,224	12.71	0.10	130.15***
	Group x Temp. x Trial	16,224	0.17	0.10	1.73*
Evaporative Heat Loss	Group	1,14	0.01	0.03	0.44
	Temp.	2,28	0.02	0.01	1.97
	Group x Temp.	2,28	0.01	0.01	1.35

*p < .05, **p < .01, ***p < .001

Table 8

ANOVA'S of Post-Surgical Test Temperature during Cold Challenge for NTS and Sham Data.

Dependent Variable	Source of Variance	df	Mean Sq. Error	Error	F
Oxygen Consumption	Group	1,14	13.32	11.40	1.17
	Temperature (Temp.)	2,28	4.80	0.53	8.99***
	Trial	5,70	0.35	0.05	7.44***
	Group x Temp.	2,28	0.63	0.53	1.18
	Group x Trial	5,70	0.06	0.05	1.35
	Temp. x Trial	10,140	0.07	0.06	1.26
	Group x Temp. x Trial	10,140	0.09	0.06	1.68
Carbon Dioxide Production	Group	1,14	7.32	2.09	3.50
	Temperature (Temp.)	2,28	1.08	0.03	36.44***
	Trial	5,70	1.24	0.01	13.18***
	Group x Temp.	2,28	0.06	0.03	1.95
	Group x Trial	5,70	0.03	0.01	3.10*
	Temp. x Trial	10,140	0.01	0.004	4.50***
	Group x Temp. x Trial	10,140	0.004	0.004	1.09
Respiratory Quotient	Group	1,14	0.004	0.04	0.11
	Temperature (Temp.)	2,28	0.004	0.001	1.41
	Trial	5,70	0.001	0.001	0.37
	Group x Temp.	2,28	0.004	0.001	1.71
	Group x Trial	5,70	0.001	0.001	0.64
	Temp. x Trial	10,140	0.001	0.001	0.46
	Group x Temp. x Trial	10,140	0.001	0.001	1.53
Blood Pressure	Group	1,14	3256.00	26532.08	0.12
	Temperature	2,28	57280.47	28.36***	

Table 8 (Continued)

Dependent Variable	Source of Variance	df	Mean Sq. Error	Error	F
Blood Pressure	Trial	8,112	9917.30	560.28	17.70***
	Group x Temp.	2,28	37728.50	2019.47	18.43***
	Group x Trial	8,112	4996.95	560.28	8.92***
	Temp. x Trial	16,224	3717.51	400.29	0.29***
	Group x Temp. x Trial	16,224	2015.11	400.29	5.03***
Rectal Temperature	Group	1,14	0.66	90.73	0.01
	Temperature (Temp.)	2,28	6.58	6.47	1.02
	Trial	8,112	5.21	0.73	7.12***
	Group x Temp.	2,28	3.84	6.47	0.59
	Group x Trial	8,112	0.31	0.73	0.42
	Temp. x Trial	16,224	0.75	0.39	1.95*
	Group x Temp. x Trial	16,224	0.18	0.39	0.47
Abdominal Skin Temperature	Group	1,14	18.96	78.02	0.24
	Temperature (Temp.)	2,28	29.92	2.87	10.41***
	Trial	8,112	8.14	0.21	38.33***
	Group x Temp.	2,28	0.69	2.87	0.24
	Group x Trial	8,112	0.40	0.21	1.86
	Temp. x Trial	16,224	0.71	0.10	7.34***
	Group x Temp. x Trial	16,224	0.10	0.10	1.01
Tail Skin Temperature	Group	1,14	0.07	35.25	0.00
	Temperature (Temp.)	2,28	596.62	3.64	163.87***
	Trial	8,112	165.57	0.50	334.09***
	Group x Temp.	2,28	2.83	3.64	0.78
	Group x Trial	8,112	0.51	0.50	1.03
	Temp. x Trial	16,224	14.64	0.36	40.46
	Group x Temp. x Trial	16,224	0.40	0.36	1.10

Table 8 (Continued)

Dependent Variable	Source of Variance	df	Mean Sq. Error	Error	F
Evaporative Heat Loss	Group	1,14	0.02	0.02	0.94
	Temp.	2,28	0.01	0.001	4.23
	Group x Temp.	2,28	0.001	0.001	0.83
Arterial pH	Group	1,14	0.001	0.001	3.42
Arterial pO_2	Group	1,14	0.001	0.001	0.20
Arterial pCO_2	Group	1,14	0.001	0.001	0.43

*p < .05, **p < .01, ***p < .001