Symposium Report

Human investigations into the exercise pressor reflex

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During exercise, neural input from skeletal muscles reflexly maintains or elevates blood pressure (BP) despite a maybe fivefold increase in vascular conductance. This exercise pressor reflex is illustrated by similar heart rate (HR) and BP responses to electrically induced and voluntary exercise. The importance of the exercise pressor reflex for tight cardiovascular regulation during dynamic exercise is supported by studies using pharmacological blockade of lower limb muscle afferent nerves. These experiments show attenuation of the increase in BP and cardiac output when exercise is performed with attenuated neural feedback. Additionally, there is no BP response to electrically induced exercise with paralysing epidural anaesthesia or when similar exercise is evoked in paraplegic patients. Furthermore, BP decreases when electrically induced exercise is carried out in tetraplegic patients. The lack of an increase in BP during exercise with paralysed legs manifests, although electrical stimulation of muscles enhances lactate release and reduces muscle glycogen. Thus, the exercise pressor reflex enhances sympathetic activity and maintains perfusion pressure by restraining abdominal blood flow, while brain, skin and muscle blood flow may also become affected because the reflex ‘resets’ arterial baroreceptor modulation of vascular conductance, making BP the primarily regulated cardiovascular variable during exercise.

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During exercise, neural input from skeletal muscles elevates blood pressure (BP) despite a maybe fivefold increase in vascular conductance. How BP is increased during exercise was addressed by Alam & Smirk (1937) when they demonstrated that muscle ischaemia enhances the BP response to hand-grip exercise and that BP remains elevated for as long as the forearm is kept ischaemic after exercise. Likewise, if thigh cuffs are inflated prior to the end of a bicycle task, postexercise BP remains similar to that observed during the cycling trial (Rowell et al. 1976) and muscle ischaemia elevates (muscle) sympathetic nerve activity (Mark et al. 1985). Conversely, influence from the CNS (‘central command’) has only a small role in sympathetic activation during exercise (Victor et al. 1989). Alam & Smirk (1938a) also found that forearm or foot postexercise muscle ischaemia cannot maintain an elevated heart rate (HR). Maybe withdrawal of vagal tone on the heart is terminated after exercise (O’Leary, 1993); however, in humans the exercise HR is not preserved during postexercise muscle ischaemia with parasympathetic blockade (Fischer et al. 2010), supporting a sympathetic contribution to the elevated HR during exercise. Apparently, muscle pressure (Williamson et al. 1994; Gallagher et al. 2001) and metabolites trapped within muscle, perhaps represented by a combination of protons, ATP and lactate (Light et al. 2008), or ischaemia itself, triggers a signal to the CNS and raises BP. Likewise, the exercise pressor reflex stimulates ventilation with concurrent chemoreflex activation (Lykidis et al. 2010; Bruce & White, 2011). The reflex nature of the BP-raising effect of ischaemia was proved when Alam & Smirk (1938b) investigated a Brown-Séquard patient. On the leg devoid of sensation, the BP-raising effect of muscle ischaemia was lost, whereas it was intact on the contralateral leg.

This review addresses the influence of the exercise pressor reflex on the cardiovascular regulation during whole-body exercise. Although we consider that the influence of the exercise pressor reflex for cardiovascular control during exercise implicates a ‘resetting’ of the
arterial baroreceptors, we refer the reader to a more detailed review of the role of the arterial baroreceptors for cardiovascular regulation during exercise (Fadel & Raven, 2012). For the importance of the exercise pressor reflex in cardiovascular regulation during static leg exercise see Mitchell et al. (1989) and for review Waldrup et al. (1996). The focus here is on how the exercise pressor reflex has been evaluated in humans with the use of sensory blockade by spinal application of the morphine analogue fentanyl or by epidural anaesthesia. In addition, the cardiovascular responses to electrically induced exercise in paraplegic and tetraplegic patients are presented as a clinical equivalent to the experimental studies carried out in healthy subjects and because any difference in cardiovascular control between tetraplegic and paraplegic patients was considered to illustrate the importance of controlled abdominal blood flow during exercise.

### Exercise pressor reflex

At the onset of exercise, mechanical and chemical stimuli associated with muscle contractions activate receptors on both thinly myelinated (group III) and unmyelinated nerve fibres (group IV) located within skeletal muscle. This activation triggers an increase in the discharge frequency of these thin fibre muscle afferents which relate exercise-induced intramuscular changes, via the lumbar dorsal horn of the spinal cord, to the CNS (Kaufman, 2012). The CNS in turn raise ventilation and circulation. Stated differently, these sensory neurons, the so-called ‘ergoreceptors’, are the afferent arm of the exercise pressor reflex, which is integrated via neural circuits in the nucleus tractus solitarii and the ventrolateral medulla to control, e.g. HR and BP (Kaufman, 2012).

### Neural control of the circulation during exercise

Evaluation of neural control of the circulation during exercise has focused on whether a given increase in HR and BP can be explained by the exercise pressor reflex or whether the increase is driven by central command. The role of central command has been investigated by the use of partial neuromuscular blockade to cause muscle weakness (e.g. Asmussen et al. 1965; Leonard et al. 1985). In these conditions, an increase in central motor drive is needed to maintain a given external workload, and enhanced central influence on cardiovascular control is expected.

Investigations into the role of the exercise pressor reflex have often used one of the following approaches: (a) assessment of whether responses to leg exercise are replicated during electrically evoked exercise, characterized by the absence of central motor drive; and (b) whether the responses are affected following pharmacological attenuation of neural feedback from the legs to the CNS.

### Electrically evoked exercise

Krogh & Lindhard (1913) found that HR increases even before the onset of exercise, arguing for a central contribution to the regulation of the cardiovascular system during exercise. In addition, the exercise pressor reflex cannot explain the immediate increase in HR, because during electrically induced exercise there is a 1 s delay in the HR increase when compared with voluntary exercise (Krogh & Lindhard, 1917; Iwamoto et al. 1987; Fig. 1). Only when direct depolarization of the thin afferents is produced, by use of very wide electrical stimulus pulse widths, is the HR response immediate (Hollander & Bauman, 1975). Yet, during electrically induced exercise, the HR reaches the same level as during voluntary exercise (Asmussen et al. 1943), suggesting that the exercise pressor reflex dominates control of the circulation. Conversely, that is not the case at the very onset of exercise, when central command (Williamson et al. 1996), probably mediated via the insula area of the brain (Williamson et al. 1997; Novak et al. 1999), appears to be the dominant determinant of the circulation.

### Epidural anaesthesia and spinal blockade during voluntary exercise

Hornbein et al. (1969) used epidural anaesthesia in humans to evaluate control of ventilation during exercise, while Freund et al. (1979) addressed the circulatory control. Unfortunately, however, Freund et al. (1979) included only four subjects and the results were not consistent. The effect of epidural anaesthesia depends on the potency of the chosen drug and on the part of the body that becomes affected by the block, i.e. on the site of administration and the volume administered. To address the role of sensory input for control of the circulation during exercise, it is important that the level of analgesia extents only to the umbilicus and thereby preserves sympathetic influence on leg (Rørdam et al. 1993) and abdominal blood flow. Although lumbar epidural anaesthesia may lower leg noradrenaline spillover from the legs during exercise by 40%, the exercise-induced reduction in hepatosplachnic flow is preserved or enhanced (Kjær et al. 1999). It is important that local anaesthetics also affect neural transmission of efferent nerves (i.e. peripheral motor nerve), as evidenced by the often massive loss in voluntary muscle activation, and therefore muscle strength, in muscles at or distal to the application site. As a consequence of this temporary muscle ‘weakening’, subjects are, in order to maintain a given external workload, required to increase central...
motor drive to overcome this drug-induced ‘side-effect’. However, augmented central command is associated with strong ‘feedforward’ influences, which cause increases in cardiovascular and ventilatory responses during exercise (Waldrup et al. 1996) as demonstrated in studies involving curare-induced partial neuromuscular blockade (Ochwat et al. 1959; Asmussen et al. 1965; Galbo et al. 1987). Thus, partial afferent blockade using local anaesthetics creates a condition of reduced neural feedback in the face of increased feedforward. With this in mind, the resultant net effect on ventilatory and/or circulatory responses during exercise with partly blocked feedback via local anaesthetics depends upon the degree to which the increase in central motor command/feedforward response balances the reduced feedback from the working limb muscles (Amann et al. 2010).

As unmyelinated and lightly myelinated nerve fibres are most sensitive to local anaesthetic agents and represent the afferent arm of the exercise pressor reflex (Kaufman, 2012), light epidural anaesthesia was considered to block cardiovascular responses to exercise. Recently, during a 5 km cycling time trial with light lumbar epidural anaesthesia (0.5% lidocaine; Amann et al. 2008) and during constant-load cycling exercise (1% lidocaine; Friedman et al. 1993), HR and BP were found to remain unaffected. This could falsely be interpreted as a lack of effect of muscle afferents on the pressor response during exercise; however, the findings need to be interpreted with extreme caution. It is critical to note that, in the case of the time-trial exercise (Amann et al. 2008), HR and BP were, during the race with afferent blockade, nearly identical compared with control exercise, despite the substantially lower power output (due to the impact of lidocaine on muscle strength) and therefore metabolic and cardiovascular demand. Consequently, HR and BP were increased out of proportion to the real demand. This indicates that the increased central motor drive, subsequent to the blockade of the inhibitory effects of group III/IV muscle afferents on central motor drive (see Amann, 2011 for review), was powerful enough not only to compensate for the missing afferent feedback (i.e. attenuated exercise pressor reflex), but even to increase the circulatory response during exercise further. In the case of the constant-load exercise with lidocaine (Friedman et al. 1993), the lidocaine-evoked increase in central motor drive necessary to maintain the given external workload was strong enough to compensate for the missing feedback, with the net effect of unchanged HR and BP during the exercise. Although these studies, if interpreted with caution, do offer an indirect indication of the role of muscle afferents for the exercise pressor reflex, the associated drug-induced increase in central motor drive masks the cardiovascular consequences associated with blocked afferent feedback. Alternatively, a low level of epidural anaesthesia is insufficient to block the signal from the muscles that influences cardiovascular control during exercise, as indicated by the lack of an effect on the BP response to postexercise muscle ischaemia (Friedman et al. 1993).

To attenuate the BP response to cycling exercise via epidural anaesthesia, the drug needs to be more potent, as with the use of 0.25% bupivacaine, but not affect the HR response (Fernandes et al. 1990). Thus, the drug-induced

Figure 1. Heart rate (HR) at the onset of an electrically evoked leg contraction (top panel) and a voluntary contraction (bottom panel) with (open circles) and without neuromuscular blockade by tubocurarine (filled circles; Iwamoto et al. 1987)

With electrically induced exercise, the HR response is delayed one heartbeat relative to the onset of exercise, and the response becomes affected when the muscle is weakened by partial neuromuscular blockade. Conversely, neuromuscular blockade has no effect on the HR response to the onset of voluntary exercise, indicating an influence from the CNS.
need for an increase in central motor drive can maintain
the normal increase in HR but it cannot maintain the
normal increase in BP, and reduced feedback to the CNS is
supported by a less elevated BP during postexercise muscle
ischaemia. Even when an attempt is made to enhance
the exercise pressor reflex by carrying out the exercise
during hypoxia (administration of 11.5 or 7.8% oxygen),
BP is attenuated with this level of epidural anaesthesia,
although the increase in cardiac output and leg blood
flow is preserved (Kjær et al. 1999). The effect of epidural
anaesthesia on the HR and BP responses to exercise is
reflected in how the arterial baroreceptors are ‘reset’. Thus
there is practically no change in the HR response
to manipulation of carotid transmural pressure during
exercise with epidural anaesthesia, while the BP response
to such manipulation of carotid transmural pressure is
greatly attenuated (Fig. 2; Gallagher et al. 2001; Smith et al.
2003; Fadel & Raven, 2012 for review).

The effect of epidural anaesthesia (0.25% bupivacaine;
analgesia below T10–T12 and a 25% reduction in muscle
strength) on the BP response to exercise takes place,
although regional anaesthesia does not consistently affect
plasma concentrations of lactate, free fatty acids, glycerol,
catecholamines, growth hormone, ACTH, cortisol, insulin
or renin activity (Kjær et al. 1989, 1999). Also, the
muscle concentrations of metabolites, including ATP,
phosphocreatine and lactate, as well as citrate, malate
and fumarate, are unaffected by the block, as is glucose
production and disappearance and lactate release from
and glucose uptake in the legs. Thus, the muscles maintain
metabolic homeostasis during exercise with epidural
anaesthesia.

The confounding effect associated with the use of
local anaesthetics, namely the drug-induced impact on
motor function and the resulting necessary compensatory
increase in central motor drive, was recently circumvented
in a series of studies using lumbar intrathecal fentanyl
(Amann et al. 2010, 2011a,b). Fentanyl is a selective
μ-opioid receptor agonist, which blocks the central
projection of group III and IV muscle afferents without
affecting the force-generating capacity of skeletal muscle
(Amann et al. 2009). In other words, fentanyl creates a
condition of reduced group III/IV-mediated afferent feed-
back combined with an unchanged feedforward/central
command (Amann et al. 2009). If certain precautions are
taken, a direct effect of fentanyl, i.e. activation of medullary
opioid receptors secondary to a cephalad migration, on
ventilation and circulation can be avoided. However,
importantly, this needs to be tested on an individual basis
(Amann et al. 2010).

The first of these three studies revealed the importance
of continuous group III/IV muscle afferent feedback in the
precise regulation of the ventilatory and cardiovascular
response during constant-load leg cycling exercise
(Amann et al. 2010). In the absence of the central
projection of lower limb muscle afferents during cycling
exercise, the cardioventilatory response was, compared
with placebo conditions, substantially attenuated during
various intensities ranging from about 25 to over 90%
of the subjects’ maximal oxygen uptake. Specifically,
HR and BP were between 6–8 and 8–13%, respectively,
lower when the identical exercise was performed with
blocked group III/IV muscle afferents. Likewise, minute
ventilation was up to 17% lower during exercise with
blocked lower limb muscle afferents. These experiments
clearly documented the essential contribution of thin
fibre muscle afferents to the production of normal
exercise hyperpnoea and normal pressor and tachycardiac
responses to whole-body human endurance exercise across
different intensities (Amann et al. 2010).

The second study then focused on the influence of
group III/IV muscle afferents on the regulation of leg
blood flow during dynamic single-leg knee-extension

Figure 2. Carotid baroreflex control of HR and mean arterial
pressure (MAP) at rest and during exercise with or without
epidural anaesthesia
Reflex responses in HR and MAP elicited by rapid pulse train
perturbations to the carotid sinus baroreceptors. Arrow indicates the
directional effect of epidural anaesthesia on baroreflex resetting
compared with control exercise (Smith et al. 2003). Abbreviations:
ECSP, estimated carotid sinus pressure.
exercise across a range of intensities (Amann et al. 2011b). Apart from confirming earlier findings, this study also demonstrated the significant effect of muscle afferents on the regulation of cardiac output. Compared with control exercise, stroke volume and HR were about 13 and 6%, respectively, lower during the exercise with fentanyl blockade, and this resulted in a 19–22% lower cardiac output (Fig. 3). Furthermore, femoral arterial blood flow at identical workloads was about 15% lower with blocked versus intact group III/IV muscle afferents (Fig. 4). This study, based on exercise of only a single leg muscle (and thus a small muscle mass), confirmed the earlier findings obtained during bicycle exercise (i.e. large muscle mass) and emphasized the importance of continuous afferent feedback in regulating the ventilatory and circulatory response during exercise.

The last of these three human studies not only confirmed the substantial effect of group III/IV muscle afferents on the cardioventilatory and pressor responses, but also focused on the associated impact on the development of peripheral locomotor muscle fatigue during exercise (Amann et al. 2011a). The rationale for these experiments arose from earlier findings documenting that the development of peripheral muscle fatigue is highly sensitive to its $O_2$ delivery (Amann & Calbet, 2008). As already shown in the two earlier studies (Amann et al. 2010, 2011b), when group III/IV muscle afferent feedback was blocked via lumbar intrathecal fentanyl during high-intensity, constant-load cycling exercise, pulmonary ventilation and circulation were substantially attenuated. However, important, but not necessarily surprising, in this last study was the finding that locomotor muscle fatigability (i.e. peripheral fatigue) is vastly exacerbated when exercise is performed with blocked group III/IV muscle afferent feedback. Peripheral muscle fatigue in these experiments was measured via changes in quadriceps twitch force (evoked by supramaximal magnetic femoral nerve stimulation) from pre- to postexercise. Specifically, the rate of development of quadriceps fatigue during constant-load leg cycling ($\sim 318$ W) was, compared with control conditions, about 70% steeper when the exercise was performed with blocked group III/IV muscle afferents. These findings clearly emphasize the crucial contribution of the ventilatory and pressor responses in determining an individual’s ability to resist, or minimize, the development of peripheral muscle fatigue during exercise.

**Epidural anaesthesia during electrically induced exercise**

The BP response to exercise is eliminated only when epidural anaesthesia induces motor paralysis via 0.5% bupivacaine, and that is the case both during one- and two-legged knee-extensor exercise (Fig. 5; Strange et al. 1993) and (with 2% lidocaine) during cycling exercise (Kjaer et al. 1994). Accordingly, afferent fibres are not blocked as an all-or-none phenomenon (Strichart & Coumo, 1988), and a given sensory ‘quality’ may be transmitted after regional

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**Figure 3.** Cardiac output, heart rate and stroke volume at rest and during the final minute of single-leg knee-extensor exercise at three submaximal work rates (3 min at each workload)

The exercise was either performed in control conditions (control) or while group III/IV muscle afferent feedback was temporarily blocked via lumbar intrathecal fentanyl. The $P$ values indicate the overall main effect of fentanyl. *$P < 0.05$ versus control; †$P < 0.05$ versus 15 W. $n = 9$. From Amann et al. (2011b).
anaesthesia, provided that it is exposed to vast temporal and/or spatial summation and such integration, in turn, is affected by morphine, which, like fentanyl, binds to μ-opioid receptors (Friedman et al. 1993; for review see Brennum, 1996).

In summary, the use of epidural anaesthesia for evaluation of cardiovascular control during exercise indicates that the exercise pressor reflex does not affect leg blood flow or muscle metabolism. However, the finding that an intense level of the block is needed to eliminate the BP response to exercise suggests that neural input from the working muscles undergoes vast integration, and the importance of such integration is confirmed by the attenuated cardiovascular response to exercise following intrathecal administration of fentanyl, including attenuated cardiac output and leg blood flow.

**Paraplegic patients**

The importance of the muscle pressor reflex for cardiovascular regulation during exercise is confirmed by electrically induced exercise in paraplegic and tetraplegic patients (Dela et al. 2003). For these patients, the leg muscles need to be trained for months to be able to accomplish a reasonable amount of work. Following such training, electrically induced exercise is associated with a reduced BP response in paraplegic individuals (Fig. 6), and these findings thus confirm the experiments in intact humans using electrically induced exercise during paralysing lumbar epidural anaesthesia. Nevertheless, the HR response to such exercise is enhanced in the paraplegic subjects. During electrically induced exercise in paraplegic subjects, the HR response to exercise is, however, eliminated when thigh cuffs are applied (Kjær et al. 1999), demonstrating that blood-borne factors, as for example the elevation in blood temperature, can influence the HR response to exercise, as suggested already by Mansfeld (1890).

The lack of a BP response to electrically induced exercise with lumbar epidural anaesthesia in normal volunteers (2% lidocaine; Kjær et al. 1996) and in individuals with spinal cord injury (Kjær et al. 2001a, b) takes place despite the fact that the metabolic and hormonal responses are enhanced, which probably reflects a different involvement of slow- and fast-twitch muscle fibres compared with voluntary exercise. While muscle recruitment during progressive voluntary exercise follows the ‘size principle’ (Gollnick et al. 1974), indicating that fast-twitch muscle fibres are recruited only during
intense exercise, electrically stimulated exercise is likely to depend mainly on engagement of fast-twitch muscle fibres because they are innervated by the largest motor nerve fibres and in individuals with spinal injury, only fast-twitch muscle fibres remain (Grimby et al. 1976). Thus, the evoked exercise, compared with the same exercise workload performed voluntarily, results in enhanced blood lactate and potassium levels and a decrease in muscle glycogen (Kjaer et al. 1996). Also, the increases in plasma adrenaline, growth hormone, ACTH and cortisol are high during the evoked exercise compared with voluntary exercise carried out at the same workload. Conversely, an attenuated increase in hepatic glucose production and a small increase in glycerol at lower free fatty acid and β-hydroxybutyrate levels during electrically induced exercise suggest that feedback from the muscles influences substrate mobilization.

**Tetraplegic patients**

In contrast to paraplegic patients, tetraplegic individuals are unable to control abdominal blood flow, are more likely to suffer from orthostatic intolerance and are also affected by lack of sympathetic influence on the heart. When seated upright and experiencing passive cyclical leg movement (Fig. 6), Dela et al. (2003) found that these patients had increased BP, presumably due to increased central blood volume and thereby preload when the muscle pump was passively activated, and HR, therefore, decreases. However, on the introduction of electrically induced exercise, BP fell, which illustrates, as suggested by Krogh (1912), that a restraint on abdominal blood flow is required to establish an adequate rise in cardiac output when muscle vascular conductance is enhanced. Also, in the tetraplegic individuals HR increases markedly during exercise, albeit the increase is not so large as in paraplegic subjects, perhaps reflecting lack of sympathetic influence on the heart.

The mechanism(s) governing the increase in muscle blood flow seen during evoked exercise in these patients, for whom there is no sensory input to the CNS, may relate to their dependence on fast-twitch muscle fibres to conduct the exercise (Grimby et al. 1976) and consequently an enhancement of the need for blood flow (Krstrup et al. 2008). In fact, the increase in plasma calcitonin gene-related peptide, which has unique vasodilatory properties, is larger during exercise in spinal cord-injured patients than in control subjects, and the peptide is extracted by the legs (Kjaer et al. 2001b).

**The exercise pressor reflex and cardiovascular regulation during exercise**

Exercise with a small muscle group carries a larger blood flow than when the same muscle group is working in concert with other muscle groups (Secher & Volianitis, 2006 for review). Thus, flow to exercising muscles is affected when other muscle groups are working intensively. For example, Sato et al. (1992) found reduced calf blood

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Figure 5. Mean arterial pressure, heart rate, cardiac output and systemic vascular conductance during voluntary dynamic exercise (open circles; n = 9), electrically induced exercise (inverted filled triangles) and with paralysing epidural anaesthesia (0.5% bupivacaine; filled squares)

Work rates were 10–30 W performed with one-leg extension and 2 × 20 W performed with two legs. Values are means ± SEM (Strange et al. 1993). There was no increase in blood pressure during electrically induced exercise with epidural anaesthesia.
flow when lower leg exercise is combined with intense forearm exercise, and the reduction in flow appeared to be caused by a marked increase in muscle sympathetic nerve activity.

As considered by Alam & Smirk (1937), it may be that sensory influence from skeletal muscles working at an intensity that affects their oxygenation serves to raise perfusion pressure, but the trick is that such an attempt to stabilize blood flow to one muscle group takes place at the expense of blood flow to other working skeletal muscles, and the resulting reduction in their oxygenation, in turn, further stimulates sympathetic activity and thereby limits flow to the ‘primary’ working group. Likewise, when the ability to increase cardiac output during exercise is limited in, e.g. patients with type II diabetes and in patients with cardiac failure, the increase in leg blood flow is limited, while the BP response to exercise is maintained or increased. Conversely, when the ability to increase cardiac output during exercise is enhanced by digitalis in heart failure patients, their leg blood flow is also increased and the exercise pressor reflex is attenuated because the increase is BP is smaller (Schmidt et al. 1985). As illustrated by administration of a β-adrenergic blocking agent, a limited increase in cardiac output during exercise restricts blood flow to the legs by vasoconstriction in response to sympathetic activation, as indicated by enhanced leg noradrenalin spill-over (Pawelczyk et al. 1992).

A limited ability to increase cardiac output during exercise also affects the increase in cerebral perfusion,

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Figure 6. Heart rate (top panel) and MAP responses to electrically induced cycling in patients suffering from paraplegia (Para; \( n = 4 \)), tetraplegia (Tetra; \( n = 6 \)) and voluntary exercise in control subjects (Control; \( n = 6 \)).

For 3 min before exercise, the legs were passively rotated, with the feet attached to the pedals (Pass). Values are means ± SEM. (From Dela et al. 2003 with permission.)
as demonstrated both in cardiac patients (Hellstöm et al. 1996; Ide et al. 1999) and by administration of a $\beta$-adrenergic blocking agent to healthy subjects (Ide et al. 1999). Also, for control of brain blood flow, sympathetic activity seems important, as illustrated by a normal increase in cerebral perfusion following a stelate block when exercise is carried out with $\beta$-adrenergic blockade (Ide et al. 1998). Furthermore, a limited ability to increase cardiac output affects skin blood flow (Cui et al. 2005), leaving heart failure patients vulnerable to heat stress. Taken together, the muscle pressor reflex affects the BP that the arterial baroreceptors are set to control through modulation of vascular conductance (Collins et al. 2001; Ogoh et al. 2003) and that seems to affect even tissues with as a high metabolic rate as the brain and working skeletal muscles.

In conclusion, as illustrated with sensory blockade, the exercise pressor reflex is required to increase BP during exercise by resetting the BP that the arterial baroreceptors control in face of the several-fold enhanced total vascular conductance elicited by the enormous increase in muscle blood flow. Both elevated muscle pressure and the metabolic disturbance appear to trigger sympathetic activation during exercise, and reduction in abdominal blood flow is the primary provider of blood to support cardiac output for adequate muscle blood flow and, as body temperature increases, also skin perfusion. Nevertheless, during whole-body exercise, the challenge on BP is such that the increases in muscle, skin and even cerebral blood flow may become affected. In contrast, as revealed by sensory nerve blockade, the exercise pressor reflex cannot account entirely for the increase in HR during exercise, and both the increase in body temperature and influence from central command appear to play a significant role for HR regulation during exercise.

Since the initial observations by Smirk and Alam (1937) 75 years ago, numerous human and animal studies have investigated what is now referred to as the exercise pressor reflex. Most of these investigations certainly helped to advance our understanding of this phenomenon; however, all of them were characterized by one or more critical limitation(s). Given the fact that the exercise pressor reflex is a highly interwoven mechanism spanning multiple organ systems in the exercising human/animal, each intervention designed to manipulate this complex system resulted in a more or less significant consequence for the interpretability of its outcome. Even those investigations with only a minimal impact on the complexity of the pressor reflex cannot depict its true importance, or relative contribution, to the pressor response during exercise, because the emergence of redundant control mechanisms is able to compensate, at least in part, for one or more manipulated variables. Nevertheless, the combination of various human and animal studies clearly supports a crucial role of the exercise pressor reflex in achieving adequate cardiovascular responses during exercise. These provide the basis for optimal blood/O$_2$ supply for the working muscles and thereby maximize an individual’s endurance capacity.

**References**


