Altered Regional Blood Flow Responses to Submaximal Exercise in Older Rats

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Abstract

Maximal aerobic capacity and the ability to sustain submaximal (submax) exercise (EX) declines with advancing age. Whether altered muscle blood flow (BF) plays a mechanistic role in these effects remains to be resolved. The present investigation determined the effects of aging on the hemodynamic and regional BF response to submax EX in rats. Heart rate (HR), mean arterial pressure (MAP), and BF to different organs (kidneys, splanchnic organs, and 28 hindlimb muscles) were determined at rest (R) and during submax treadmill EX (20 m/min, 5% grade) with radiolabeled microspheres in young (Y; 6-8 month old, 339±8 g, n=9) and old (O; 27-29 month old, 504±18 g, n=7) Fischer 344 x Brown Norway rats. Results demonstrated that HR, MAP, and BF to the pancreas, small and large intestine, and total hindlimb musculature were similar between Y and O rats at rest. BF to the kidneys, spleen, and stomach were 33%, 60%, and 43% lower in O compared to Y rats. BF to the total hindlimb musculature increased (P<0.05) during EX and was similar for both Y and O rats (Y: 16±3 to 124±7 vs O: 20±3 to 137±12 ml/min/100g, respectively). However, in O vs. Y rats BF was reduced in 6 (highly oxidative) and elevated in 8 (highly glycolytic) of the 28 individual hindquarter muscles or muscle parts examined (P<0.05). During EX, BF to the spleen and stomach decreased (P<0.05) from R in Y rats whereas BF decreased in the kidneys, pancreas, spleen, stomach, as well as the small and large intestines of O rats. In conclusion, these data demonstrate that, despite similar increases in total hindlimb blood flow in Y and O rats during submaximal exercise, there is a profound blood flow redistribution from highly oxidative to highly glycolytic muscles.

Keywords: skeletal muscle, splanchnic, blood flow, radiolabeled microspheres, aging
Introduction

The capacity to achieve and sustain a given oxygen uptake ($\text{VO}_2$) is dependent upon the coordinated function of the cardiovascular system to supply blood (and therefore $\text{O}_2$) to the exercising muscle fibers and the ability of the capillary bed to facilitate $\text{O}_2$ extraction. It is well established that exercise tolerance (at submaximal and maximal levels) and maximal oxygen uptake ($\text{VO}_{2\text{max}}$) decrease with advancing age (6,8,11,15,20,24,28,46,49). However, the effects of aging on cardiac output ($Q$), the distribution of $Q$ among and within peripheral tissues and muscle $\text{O}_2$ extraction remain contentious (16,20,25,26,32,40).

There is abundant evidence that aging reduces maximal heart rate ($HR_{\text{max}}$) and maximal $Q$ ($Q_{\text{max}}$) in animals and humans (6,8,11,15,20,24,28,46,49). In marked contrast to these findings, a recent carefully controlled longitudinal study conducted over 30 years reported that the reduced $HR_{\text{max}}$ was coupled with an elevated stroke volume (SV) such that $Q_{\text{max}}$ was unchanged (40). Consequently, the reduced $\text{VO}_{2\text{max}}$ resulted from a decreased ability to increase peripheral $\text{O}_2$ extraction appropriately with advancing age. This latter investigation in combination with the age-related changes in arterial vasocontrol (41,42), arterial and capillary rarefaction (41,51) and capillary hemodynamics (51,60) suggest that aging may alter the $Q$ distribution between and within exercising muscles and thus the $\text{O}_2$ extraction profile.

Other than in laboratory testing or occasional short bursts of activity, aged individuals rarely operate at work rates that elicit $\text{VO}_{2\text{max}}$. Daily activities such as walking, climbing stairs or cycling are performed at a given absolute submaximal level. Thus, it may be argued that understanding the effects of aging on the muscle blood flow response to an exercise intensity that elicits a submaximal $\text{VO}_2$ is particularly germane to understanding the physiological function and dysfunction that attends the aging process. The elegant investigations of Armstrong and Laughlin (3) used radiolabeled microsphere technology to demonstrate that exercise training redistributed blood flow within and between muscles and muscle fiber types during submaximal exercise. Specifically, a training program that increased exercise tolerance caused a preferential redistribution of blood flow away from low oxidative (fast-twitch glycolytic [FG]) towards highly
oxidative (slow-twitch oxidative [SO] and fast-twitch oxidative glycolytic [FOG]) muscles and muscle fibers. To date, the effect of aging on the distribution of submaximal exercise blood flow among different organs and within individual locomotory muscles comprising the spectrum of muscle fiber types has not been determined.

Based upon this latter investigation (3), we utilized young (Y) and old (O) rats to test the hypothesis that aging which reduces exercise tolerance would have the opposite effect to exercise training i.e., aging would redistribute blood flow from highly oxidative to low oxidative muscle and muscle fibers. Moreover, because altered vasomotor control within the kidneys and organs of the splanchnic region has the potential to alter the exercise induced redistribution of cardiac output and thus muscle blood flow, we tested the secondary hypothesis that blood flow to the kidneys and organs of the splanchnic region would be reduced to a greater extent in O than Y animals. This response in visceral tissue has been demonstrated under different conditions during exercise in dogs (21) and rats (32).
Methods

Animal selection and care. Seven Y adult (6-8 months old) and nine O (27-29 months old) Fischer 344 X Brown Norway (F344/BN) were used in this study. These rats were specifically selected for this investigation as they represent Y and O (senescent) rats according to the life span for the F344/BN strain (33). In addition, the F344/BN rat has the distinct advantage over the F344 rat because, it does not develop many of the age-related pathologies that proliferate in their highly inbred F344 cousin (10,36). Rats were maintained on a 12:12 hour light-dark cycle and received food and water ad libitum. All experiments were conducted under the guidelines established by the National Institutes of Health and Kansas State University's Institutional Animal Care and Use Committee.

All rats were familiarized with running on a motor-driven treadmill. During the period of familiarization (2-3 weeks), rats exercised for 5-10 min day⁻¹ at a speed of 20 m min⁻¹ and 10% grade.

Surgical procedures and experimental protocol. After it was established that all rats were proficient runners, each animal was weighed and anesthetized with 5% halothane. While being maintained on a 2% halothane-oxygen mixture, one catheter (PE-10 connected to PE-50) was placed in the ascending aorta via the right carotid artery and another in the caudal (tail) artery, as previously described (45). Both catheters were tunneled subcutaneously to the dorsal aspect of the cervical region and exteriorized through a puncture wound in the skin. After the closure of incisions, anesthesia was terminated and the animal was given ≥2 hours to recover. This period of recovery was selected because previous studies by Flaim et al. (17) showed that cardiac or circulatory dynamics, regional blood flow, arterial blood gases, and acid-base status are stable in the awake unrestrained rat 1-6 hours after halothane anesthesia.

Subsequent to the recovery period, the final experimental protocol was initiated. Each rat was then placed on the treadmill, and after a period of stabilization (~3 hours after instrumentation), the tail artery catheter was connected to a 1-ml plastic syringe that was connected to a Harvard infusion/withdrawal pump (model 907). Exercise was initiated, and the speed of the treadmill was increased progressively during the next 30 seconds to a speed of 20
m min⁻¹ (5% grade). The rat was then required to exercise steadily for another 3 minutes. After 3.5 minutes of total exercise time, blood withdrawal from the tail artery catheter was initiated at a rate of 0.25 ml min⁻¹. Simultaneously, arterial blood pressure was measured via the carotid artery catheter. After 4 minutes of total exercise time, the carotid artery catheter was disconnected from the pressure transducer and 0.5-0.6 X 10⁶ microspheres with a 15 µm diameter (isotopes used were ⁴⁶Sc, ⁸⁵Sr, ¹¹³Sn, or ¹⁴¹Ce, in random order; New England Nuclear Research Products, Boston, MA) were injected into the aortic arch to determine regional blood flow. Approximately 30 seconds after the injection, blood withdrawal from the tail artery catheter was stopped, exercise was terminated. After a 60-min recovery period, hemodynamic parameters were measured as the rats sat quietly on the treadmill. A second microsphere infusion was then performed with the same procedures as described above. This sampling strategy minimizes the potential for blood loss to affect the exercise response and facilitates “resting” measurements that do not reflect the pre-exercise anticipatory response (2).

Upon completion of the study, each animal was given an overdose of pentobarbital (>50 mg kg⁻¹, i.a.). The thorax was opened, and placement of the carotid artery catheter into the aortic arch was confirmed by anatomical dissection. The kidneys, visceral organs and muscles of both hindlimbs were identified and removed by a skilled research technician to ensure uniformity of the dissection process. The muscles examined in this investigation included: ankle extensors: soleus (S), plantaris (P) red portion of the gastrocnemius (Gₗ), white portion of the gastrocnemius (Gₘ), middle portion of the gastrocnemius (Gₜ), tibialis posterior (TP), flexor digitorum longus (FDL), flexor hallucis longus (FHL); ankle flexors: red portion of the tibialis anterior (TAₗ), white portion of the tibialis anterior (TAₘ), extensor digitorum longus (EDL), peroneals (Per); knee extensors: vastus intermedius (VI), vastus medialis (VM), red portion of the vastus lateralis (VLₗ), white portion of the vastus lateralis (VLₘ), middle portion of the vastus lateralis (VLₜ), red portion of the rectus femoris (RFₗ), white portion of the rectus femoris (RFₘ); knee flexors: anterior portion of the biceps femoris (BF₉), posterior portion of the biceps femoris (BF₉), semitendinosus (ST), red portion of the semimembranosus (SMₗ), white portion of the semimembranosus (SMₘ); thigh
adductors: adductor longus (AL), adductor magnus & brevis (AMB), gracilis (GR), pectineus (Pec). All tissues were blotted, weighed, and placed immediately into counting vials.

The radioactivity of each tissue was determined on a gamma scintillation counter (Packard Auto Gamma Spectrometer, model 5230, Downers Grove, IL). Taking into account for the cross-talk fraction between isotopes, blood flows to each tissue were determined using the reference sample method (45) and expressed as milliliters per minute per 100 grams of tissue. Adequate mixing of the microspheres was verified for each injection by demonstrating a <15% difference between blood flow to the right and left kidneys and/or to the right and left hindlimb musculature.

Statistical analysis. All values are expressed as mean±SE. Results were analyzed with a two-way ANOVA with a repeated measures design (ANOVA-R). When a significant F-ratio was demonstrated by the ANOVA-R, a Student-Newman-Kuels post-hoc test was performed to determine differences between mean values. In addition, unpaired t-tests were performed on results between groups where deemed appropriate. Statistical significant was set at P< 0.05.
Results

Old rats had a significantly greater body weight compared to their younger counterparts (O: 504±18 vs Y: 339±8 g; P<0.05). In addition, total hindquarter muscle mass was significantly greater for the O rats when compared to the Y (18.31±0.54 vs 15.35±0.36 g, P<0.05) as were 17 of the 20 individual whole muscles examined. The only exceptions found were the gastocnemius, vastus medialis, and peroneal muscles, in which the muscle weights were similar in Y and O rats.

Heart rate and MAP measured at rest were not different between Y and O rats (Table 1). During exercise, HR increased in both groups, but the HR measured in the O rats was significantly less that that measured in the Y rats. MAP increased from resting values in the Y rats, but remained similar to resting levels in the O rats. Although the Y rats demonstrated an increase in MAP with exercise, the O did not. MAP was not different between the two groups during the submaximal exercise regimen.

Blood flow measured at rest to the total hindlimb musculature and to all of the individual muscles or muscle parts investigated (with the exception of the plantaris) was not different between the O and Y rats (Figure 1 and Table 2). During exercise, blood flow to the total hindlimb musculature increased to a similar degree in both the O and Y rats (Figure 1). Moreover, exercising blood flow increased to a similar degree in 14 of the 28 individual muscles or muscle parts examined (Table 3). However, in 6 of the 28 individual muscles or muscle parts examined (S, P, G_R, T_AR, VI, VL_R; Figure 2A) that normally contain a majority of slow-twitch (SO) and fast-twitch oxidative glycolytic (FOG) types of fibers (range from 59±3 to 100% FOG, ref. 5) blood flow increased during exercise to a lesser degree in the O rats when compared to their Y counterparts. In contrast, in 8 of the 28 individual muscles or muscle parts examined (G_W, TP, VL_W, BF_A, AMB, GR, SM_W, SM_R; Figure 2B) that normally contain a majority of fast-twitch glycolytic (FG) types of fibers (range from 50±5 to 97±3% FG, ref. 5) blood flow increased during exercise to a greater degree in the O rats when compared to the Y.

Blood flow to the kidneys at rest was significantly less in the O rats when compared to their Y counterparts (Figure 3A). During exercise, blood flow to the kidneys was significantly reduced in the O but not Y rats when compared to resting values (Figures 3B). Consequently,
blood flow to the kidneys during submaximal exercise was significantly less in the O rats when compared to their Y counterparts (Figure 3B).

Similar to that found in the kidneys, blood flow at rest was significantly reduced in both the stomach and spleen of O rats when compared to Y (Figures 3A). During exercise, blood flow was reduced in the stomach, small and large intestines, pancreas, and spleen for the O rats when compared to resting values. In contrast, blood flow was only reduced in the stomach and spleen for the Y rats (Figure 3B). Again, similar to that found in the kidneys, blood flow was reduced in the stomach, small & large intestines, and spleen during the submaximal exercise regimen for the O rats when compared to their Y counterparts (Figure 3B).
Discussion

The present investigation is the first to demonstrate that aging causes a profound redistribution of skeletal muscle blood flow within and between muscles comprised of different fiber types during submaximal exercise. Specifically, despite a similar total hindlimb muscle blood flow response, examination of 28 individual muscles or muscle parts revealed a significant reduction in blood flow to six highly oxidative muscles (FOG, SO fiber types; CS activities ranging from 21.3-42.3 µmol \cdot min^{-1} \cdot g^{-1}, ref. 12). In contrast, blood flow was significantly elevated in eight low oxidative muscles (FG fiber types; CS activities ranging from 8.1-20.6 µmol \cdot min^{-1} \cdot g^{-1}). The altered profile of muscle blood flow in the aged rats suggests that there may be a decrement in blood flow and therefore O2 delivery to the oxidative muscle fibers and a greater recruitment of highly glycolytic, low oxidative fibers during submaximal exercise. It is likely that these age-related changes in skeletal muscle blood flow are mechanistically linked to the early onset of fatigue that characterizes the aged population.

In designing an investigation where the experimental conditions affect the exercise capacity of the subjects, it is always debatable whether to examine them at the same absolute or relative work rate. In the present investigation, we chose to exercise both the Y and O rats at the same absolute submaximal workload based on the fact that both Y and O individuals normally perform daily work tasks that are equivalent to one another in absolute terms (i.e., climbing a flight of stairs, riding a bicycle, or walking through the grocery store). Therefore, the present study was designed to answer important questions based upon their practical application pertinent to the daily life style of the elderly (e.g., the elderly do not usually sustain very high workloads for any significant amount of time during their daily lives). It is important to note, that comparison of Y and O rats exercised at the same relative workload (i.e., same percentage of VO2max) raises difficult questions regarding interpretation of blood flow differences between experimental groups. This crucial consideration needs to be kept in mind when interpreting the results of the present investigation.

As demonstrated in our laboratory and the laboratories of others (7,9,35,43,52), rats exercising at 20 m/min up a 5% grade on a motor-driven treadmill elicit a VO2 in the range of 47-
55 ml/min/kg of body weight. If we assume that Fischer 344/Brown Norway rats experience a 
$VO_{2\text{max}}$ reduction similar to that found in the Fischer 344 rat ($VO_{2\text{max}}$: Y = ~75 ml/min/kg of body 
weight vs. O = ~66 ml/min/kg of body weight; 11,38,46), then the O rats in the present investigation 
were exercising at ~71-83% of their $VO_{2\text{max}}$ compared with ~63-73% for the Y rats. Whether this 
~10-20% difference in relative workloads is sufficient to produce significantly disparate regional 
blood flow responses remains unclear. However, as demonstrated previously in the dog (but not 
the rat, 34), a ~10% increase in relative workload (i.e., within the range imposed herein), can 
produce modest, though significant increases in blood flow to some, but not all exercising 
muscles (44). This occurred in the absence of alterations in the exercise-induced reduction in 
blood flow to the kidneys or splanchnic organs (44).

In the present investigation, blood flow per 100g of total hindlimb musculature was not 
different between Y and O rats during exercise. These results are consistent with those reported 
previously for exercising rats (32) and humans performing leg exercise (47). Moreover, these 
results cohere with those found in isolated contracting muscles of Y and O female rats (26), but 
they conflict with those for their male counterparts (25). It should be noted that several human 
studies have shown that the skeletal muscle blood flow response to a given level of exercise is 
reduced in O compared to Y individuals (27,37,48,62). Therefore, it appears that the effects of 
aging on the skeletal muscle blood flow response to exercise may to a certain extent be species 
and/or paradigm specific.

Although our results are aligned with those studies supporting the notion that blood flow 
to the exercising musculature in toto is maintained during the aging process, they are also 
consistent with our original hypothesis that aging produces a redistribution of blood flow within 
and between muscles and muscle fiber types. Accordingly, we found that aging produced a 
redistribution of blood flow from highly oxidative to low oxidative muscles and muscle fibers 
during a given level of submaximal exercise. The factors responsible for this unique response 
remain unclear at this time. However, the recent studies by Muller-Delp and colleagues (41,42) 
suggest that aging may be associated with a fiber type-specific alteration of exercise-induced 
vascular control that may help to explain the present findings. Specifically, these investigators
found that flow- and also acetylcholine(ACh)-mediated vasodilation was attenuated in the isolated soleus arterioles of O compared to Y rats (41). Although similar age-related decrements in flow-induced vasodilation occurred in the arterioles of the white portion of the gastrocnemius muscle, Ach-induced vasodilation was maintained (41). McAllister (39) recently provided evidence that muscles containing a majority of SO and FOG types of fibers (and muscles having a high oxidative potential) possess a greater potential for endothelium-mediated vasodilation when compared to muscles containing a majority of FG fibers (low oxidative potential). Collectively, these findings are consistent with the present results and the hypothesis that endothelium-dependent vasodilation is impaired in the skeletal muscle with advancing age (1,14,18,53,54) and that this impairment occurs preferentially in muscles that have a high oxidative capacity (i.e., muscles containing a majority of SO and FOG types of fibers). The present results suggest that mechanisms of endothelial-mediated vasodilation (i.e., increased shear stress, NO, prostacyclin, hyperpolarization factor) are particularly susceptible to the aging processes (41,42).

Whereas age-related declines in endothelial vasodilatory function can potentially explain the reduction in blood flow to the highly oxidative muscle in aged animals, the mechanistic basis for the increases in blood flow found in the low oxidative highly glycolytic muscle is not obvious. Two potential mechanisms may contribute to this response: 1) Muller-Delp and colleagues have shown that the myogenic component of vasoregulation is attenuated in both the soleus and white portion of the gastrocnemius muscle of O when compared to Y rats, even though the vasoconstrictor responses remain intact (42). 2) Arteriolar rarefaction occurs in the gastrocnemius muscle of O rats (41) and we recently reported that rarefaction occurred at the microcirculatory (i.e., capillary) level within the low-oxidative spinotrapezius muscle (51). Muller-Delp and colleagues suggest that this vascular rarefaction could increase blood flow and shear stress in the individual blood vessels (i.e., the white portion of the gastrocnemius) of O rats thereby producing increases in vessel maximal diameter and potentiating the endothelial-mediated vasodilator response (41). Thus, the increases in blood flow found in the low oxidative, highly glycolytic muscles in the present investigation could be the result of an enhanced endothelial-
mediated vasodilation in conjunction with a diminished myogenic vasoconstrictor response during exercise.

In addition to the proposed mechanistic hypotheses presented above, the possibility remains that the age-related differences in body weight and skeletal muscle mass may have contributed to the differential muscle blood flow responses found in the present investigation through alterations in the recruitment pattern of the locomotory muscles during exercise (4,19). However, results found in the literature along with our own findings suggest that differences in relative work rate along with differences in body size and muscle mass cannot explain the redistribution of blood flow from the highly oxidative to highly glycolytic fibers found in this study.

First, although an age-related muscle atrophy eventually occurs in rats (23), muscle atrophy was not present in the O rats in the present investigation as all except 3 hindlimb muscles of the O rats were significantly heavier than those of their younger counterparts. Therefore, reductions in muscle weight was not a confounding issue in the present investigation. In addition, because of the differences in body weight found between Y and O rats, all blood flows were normalized per 100 g of wet tissue weight. Thus, the assessment of alterations in muscle (organ) blood flows between Y and O rats is not simply a function of altered size.

Second, as the larger O rats would have been running at a greater relative exercise intensity could this have decreased blood flow to the highly oxidative muscles whilst increasing flow to their glycolytic counterparts? Laughlin and Armstrong (34) have demonstrated that rat hindlimb locomotor muscle blood flows are unchanged between running speeds of 15 and 45 m/min. As this range encompasses both the absolute and relative exercise intensities of the Y and O groups examined herein, it is doubtful that different relative work loads would have produced differences in muscle blood flows. Moreover, the O rats examined in the present investigation would have been working at a higher relative intensity than the Y rats. As the O animals actually experienced a decreased blood flow in their oxidative muscles, the directional change is counter to that expected on the basis of relative work intensity. With respect to the increased blood flow found in the highly glycolytic muscles of the O rats, this directional change is consonant with an increased relative work rate. However, Laughlin and Armstrong (34) further
showed that blood flow in these glycolytic muscles does not increase appreciably until the rat is running at speeds that are supramaximal with respect to their aerobic capacity. The running speed of 20 m/min was selected for the present investigation, in part, because it represents a work rate that is clearly submaximal in both Y and O rats.

In conclusion, by reference to the landmark paper of Laughlin and Armstrong (34), a higher (though submaximal) relative work rate and associated muscle fiber recruitment pattern in the O rats cannot explain the divergent blood flow responses measured in the highly oxidative versus highly glycolytic muscles.

The likelihood that age-related changes in the sympathetic control of blood flow underlie the blood flow redistribution found in senescent animals herein cannot be ignored. Specifically, Procter and colleagues (30) demonstrated enhanced sympathetic vasoconstriction in the exercising leg muscles of aged humans. Moreover, functional sympatholysis which is dependent upon nitric oxide production (57) may become impaired with advancing age (63). The primary site of sympathetic vasoconstriction (and therefore sympatholysis) resides at the level of the feed arteries and 1A arterioles (61), at least within hamster muscle, and therefore it is possible that enhanced vasoconstriction of these vessels accounted for the lowered muscle blood flow found in aged rats in the present investigation. However, any such conclusions must be tempered in light of the following: 1. Functional sympatholysis does not exist in the soleus muscle (56) and yet this muscle was one of the oxidative muscles that demonstrated a substantial decrement in flow in aged rats in the present investigation. 2. The presence of functional sympatholysis in different muscles is associated with a high glycolytic capacity and is independent of oxidative capacity (56). Accordingly, if alterations in functional sympatholysis alone accounted for age-related decrements in blood flow we would have expected a similar reduction in blood flow to the plantaris (~94% glycolytic fibers) and tibialis posterior (~98% glycolytic fibers). However, blood flow to the plantaris was reduced whereas that to the tibialis posterior was increased. Thus, whereas the possibility that the blood flow redistribution demonstrated in aged rats herein may be mediated sympathetically cannot be dismissed, elegant prospective studies are required to address this issue mechanistically.
Although the primary focus of the present study was to examine the effects of aging on the skeletal muscle blood flow response to exercise, the present investigation produced several interesting and/or unique observations regarding the renal and splanchnic blood flow response to exercise in Y and O rats that include the following:

First, renal blood flow at rest was reduced in O compared with Y rats and also fell during exercise in the O but not the Y rats (Figure 3). Whereas the response at rest agrees with that reported for humans (29), other studies on rats (13,59) and dogs (21) show no effect of age. It is pertinent that resting renal sympathetic tone (i.e., resting plasma norepinephrine concentrations) does not differ between either Y and O rats (32) or humans (29). With respect to the exercise response, certain studies in rats (32,34) and humans (58) but not dogs (21,44) or humans performing very mild exercise (35% VO$_{2\text{max}}$, ref. 29) demonstrate that renal blood flow decreases during exercise in an intensity-dependent fashion. Moreover, exercise-induced renal blood flow reductions are augmented in aged rats (32) and dogs (21) concomitant with a greater sympathetic response to exercise (31,32) which is possibly related to the greater relative work load imposed by a given exercise condition (60,55,58). Together, the present investigation and the established literature support the notion that aging causes a greater exercise-induced reduction in renal blood flow that is associated with an enhanced sympathetic response to exercise. However, the present investigation cannot discriminate whether the reduced renal blood flow in O animals may have resulted, in part, from the greater relative exercise intensity.

Second, at rest splanchnic organ blood flow was not different between Y and O rats with the exception of stomach and splenic blood flows which were reduced in the O rats. Neither dogs (21) nor humans (29) evidence an effect of age on splanchnic organ blood flows at rest. However, other investigations have noted a reduced splenic but not stomach blood flow in the aged rat (13,59). With respect to the exercise response, the O rats evidenced a more pronounced reduction in splanchnic organ (stomach, intestines, spleen) blood flow than their Y counterparts. This response is consistent with other studies in rats (32) and dogs (21) but not humans (22,29). The mechanistic bases for the differential effect of age on renal and splanchnic blood flows between humans and animals during exercise remains to be resolved.
In conclusion, the present investigation has demonstrated that, despite no differences in overall hind limb blood flow, aging causes a redistribution of blood flow among muscles of different fiber type and/or oxidative capacity. Specifically, in O rats performing moderate-to-heavy intensity exercise, blood flow was reduced to muscles comprised of highly oxidative SO and FOG fibers and increased to select low oxidative FG muscles. This redistribution: 1) cannot be explained on the basis of differences in the relative exercise intensity, but 2) is likely to be of crucial importance in explaining the reduced exercise capacity that characterizes the aged individual.
Acknowledgements

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References


Figure Legends

**Figure 1.** – Blood flow to the total hindlimb musculature measured at rest (solid bars) and during moderate intensity (20 m·min⁻¹, 5% grade) exercise (hatched bars) for young and old rats. No differences were found between young and old rats. Values are mean±SE.

**Figure 2.** – Individual muscles and muscle parts that evidenced significantly different blood flows during moderate intensity exercise (20 m·min⁻¹, 5% grade) in young (solid bars) vs. old (hatched bars) rats. Blood flow was reduced in 6 muscles (Panel A), but increased in 8 muscles (Panel B) of the hindlimb musculature when old rats were compared to young. S, soleus; P, plantaris; GR, red portion of the gastrocnemius; TAR, red portion of the tibialis anterior; VI, vastus intermedius; VLr, red portion of the vastus lateralis; GW, white portion of the gastrocnemius; TP, tibialis posterior; V LW, white portion of the vastus lateralis; BF A, anterior portion of the biceps femoris; AMB; adductor magnus & brevis; GR, gracilis; SM W, white portion of the semimembranosus; SMr, red portion of the semimembranosus. Values are mean±SE. *P<0.05 vs. young rats

**Figure 3.** - Blood flow to the kidneys and organs of the splanchnic region measured at rest (Panel A) and during moderate intensity (20 m·min⁻¹, 5% grade) exercise (Panel B) for young (solid bars) and old (hatched bars) rats. Small Int, small intestines; Large Int, large intestines. Values are mean±SE. *P<0.05 vs. young rats; † P<0.05 vs. resting value
Table 1. Heart rate and mean arterial blood pressure measured at rest and during exercise of old and young rats.

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<th>HR, bpm</th>
<th>MAP, mmHg</th>
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<td><strong>Young</strong></td>
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<tr>
<td>Rest</td>
<td>393±12</td>
<td>123±4</td>
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<tr>
<td>Exercise</td>
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<td>136±3†</td>
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<tr>
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<tr>
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<tr>
<td>Exercise</td>
<td>457±6*†</td>
<td>134±2</td>
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Values are means ± SE, *P<0.05 vs. Young; † P<0.05 vs. Rest
Table 2: Blood flow (ml · min⁻¹ · 100 g⁻¹) measured at rest in selected hindlimb muscles of old and young rats.

<table>
<thead>
<tr>
<th>Muscles</th>
<th>Young</th>
<th>Old</th>
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<td><strong>Ankle extensors</strong></td>
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<tr>
<td>Soleus</td>
<td>112±22</td>
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<tr>
<td>Plantaris</td>
<td>8±2</td>
<td>16±3*</td>
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<td>Gastrocnemius</td>
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<td>Red</td>
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<td>Flexor digitorum longus</td>
<td>8±2</td>
<td>22±7</td>
</tr>
<tr>
<td>Flexor hallucis longus</td>
<td>8±3</td>
<td>20±5</td>
</tr>
<tr>
<td><strong>Ankle flexors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tibialis anterior</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Red</td>
<td>28±11</td>
<td>24±5</td>
</tr>
<tr>
<td>White</td>
<td>13±3</td>
<td>13±2</td>
</tr>
<tr>
<td>Extensor digitorum longus</td>
<td>10±5</td>
<td>15±3</td>
</tr>
<tr>
<td>Peroneals</td>
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<td>22±7</td>
</tr>
<tr>
<td><strong>Knee extensors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vastus intermedius</td>
<td>96±14</td>
<td>81±29</td>
</tr>
<tr>
<td>Vastus medialis</td>
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<td>16±3</td>
</tr>
<tr>
<td>Vastus laterails</td>
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</tr>
<tr>
<td>Red</td>
<td>69±13</td>
<td>52±11</td>
</tr>
<tr>
<td>White</td>
<td>12±7</td>
<td>9±1</td>
</tr>
<tr>
<td>Middle</td>
<td>23±6</td>
<td>21±6</td>
</tr>
<tr>
<td>Rectus femoris</td>
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<td></td>
</tr>
<tr>
<td>Red</td>
<td>25±8</td>
<td>14±2</td>
</tr>
<tr>
<td>White</td>
<td>16±6</td>
<td>10±1</td>
</tr>
<tr>
<td><strong>Knee flexors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biceps femoris</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>7±2</td>
<td>11±1</td>
</tr>
<tr>
<td>Posterior</td>
<td>7±1</td>
<td>11±2</td>
</tr>
<tr>
<td>Semitendinosus</td>
<td>9±2</td>
<td>14±3</td>
</tr>
<tr>
<td>Semimembranosus</td>
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<td></td>
</tr>
<tr>
<td>Red</td>
<td>15±5</td>
<td>24±7</td>
</tr>
<tr>
<td>White</td>
<td>8±2</td>
<td>12±2</td>
</tr>
<tr>
<td><strong>Thigh adductors</strong></td>
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<td></td>
</tr>
<tr>
<td>Adductor longus</td>
<td>158±21</td>
<td>123±24</td>
</tr>
<tr>
<td>Adductor magnus &amp; brevis</td>
<td>18±3</td>
<td>21±6</td>
</tr>
<tr>
<td>Gracilis</td>
<td>10±2</td>
<td>25±6</td>
</tr>
<tr>
<td>Pectineus</td>
<td>26±5</td>
<td>20±9</td>
</tr>
</tbody>
</table>

Values are means ± SE. *P<0.05 vs. young
Table 3: Blood flow (ml min⁻¹ 100 g⁻¹) measured during exercise in selected hindlimb muscles of old and young rats for which there was no effect of age (P>0.05).

<table>
<thead>
<tr>
<th>Muscle Type</th>
<th>Young</th>
<th>Old</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ankle extensors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrocnemius</td>
<td>195±13</td>
<td>216±27</td>
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<tr>
<td>Middle</td>
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<td></td>
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<tr>
<td>Flexor digitorum longus</td>
<td>63±9</td>
<td>139±51</td>
</tr>
<tr>
<td>Flexor hallucis longus</td>
<td>113±11</td>
<td>128±10</td>
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<tr>
<td><strong>Ankle flexors</strong></td>
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<td></td>
</tr>
<tr>
<td>Tibialis anterior</td>
<td>107±8</td>
<td>85±10</td>
</tr>
<tr>
<td>White</td>
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<td></td>
</tr>
<tr>
<td>Extensor digitorum longus</td>
<td>80±6</td>
<td>68±10</td>
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<tr>
<td>Peroneals</td>
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<td>69±7</td>
</tr>
<tr>
<td><strong>Knee extensors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vastus medialis</td>
<td>178±13</td>
<td>234±30</td>
</tr>
<tr>
<td>Vastus lateralis</td>
<td>214±11</td>
<td>232±23</td>
</tr>
<tr>
<td>Middle</td>
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<td></td>
</tr>
<tr>
<td>Rectus femoris</td>
<td>278±24</td>
<td>214±30</td>
</tr>
<tr>
<td>Red</td>
<td>114±7</td>
<td>123±12</td>
</tr>
<tr>
<td>White</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Knee flexors</strong></td>
<td></td>
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</tr>
<tr>
<td>Biceps femoris</td>
<td>84±19</td>
<td>60±5</td>
</tr>
<tr>
<td>Posterior</td>
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</tr>
<tr>
<td>Semitendinosus</td>
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<td>49±11</td>
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<tr>
<td><strong>Thigh adductors</strong></td>
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</tr>
<tr>
<td>Adductor longus</td>
<td>248±19</td>
<td>252±33</td>
</tr>
<tr>
<td>Pectineus</td>
<td>20±2</td>
<td>24±6</td>
</tr>
</tbody>
</table>

Values are means ± SE.
Figure 1.
Figure 2.
Figure 3.

A

Rest

- **Young**
- **Old**
- * P<0.05 vs Young

Blood Flow (ml/min/100g)

- Kidney
- Stomach
- Small Int
- Large Int
- Pancreas
- Spleen

B

Exercise

- **Young**
- **Old**
- * P<0.05 vs Young
- † P<0.05 vs Rest

Blood Flow (ml/min/100g)

- Kidney
- Stomach
- Small Int
- Large Int
- Pancreas
- Spleen

Figure 3.