Blood flow in non-muscle tissues and organs during exercise: Nature of splanchnic and ocular circulation

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Abstract  In response to increased vascular conductance associated with vasodilation in exercising muscles, many non-exercising organs suppress their blood flow by vasoconstriction, thus helping to maintain blood pressure. This vasoconstriction in non-exercising organs contributes to ensuring a favorable distribution of the blood flow. However, a consequent excessive decrease of blood flow in non-exercising organs should be avoided so that they can maintain appropriate functioning during and/or after exercise. There is now evidence of a decrease in splanchnic blood flow with vasoconstriction during dynamic exercise, which indirectly contributes to an increase in flow in exercising muscles. Hypoperfusion in the splanchnic area, induced by such vasoconstriction, may result in gastrointestinal symptoms. On the other hand, such vasoconstriction is suppressed when exercise is performed after food intake, which may be associated with the maintenance of digestive and absorptive functions in the gastrointestinal tract. In contrast to organs that decrease their blood flow, the choroidal flow, which forms part of the ocular blood flow, increases with exercise intensity, but without vasodilation. The relevance of this phenomenon to visual function and the nature of ocular circulation remain unclear. Competition in blood flow between exercising muscles and non-exercising organs should be examined from the viewpoint of the functions of non-exercising organs and exercising condition, such as the postprandial condition.

Keywords: gastrointestinal tract, portal vein, blood flow, ocular flow

Introduction

The aerobic capacity of exercising muscles could be improved if exercising muscles were able to capture all of the increased cardiac output that occurs during dynamic exercise. Shutting down the blood flow to non-exercising organs is impossible, in part, as a result of myogenic autoregulation. The blood flow in non-exercising organs decreases to maintain the blood pressure against the increased vascular conductance that results from vasodilation in vast vessels in exercising muscles. Renal flow decreases proportionally with increasing exercise intensity via vasoconstriction1-3, while cardiac output increases up to fivefold of the resting value in exercising humans3. Even light-intensity exercise decreased renal flow by 20% within 30 s of exercise onset4. In addition, during exercise the blood flow increases in organs other than exercising muscles. The most well known, but still generally unexplained, example is cerebral blood flow, which was originally believed to be stable during exercise, but recent studies have revealed actually increases5.

It is important to be able to increase the blood flow into exercising muscles to enable them to adequately perform a given physical activity. Conversely, it is also important to prevent an excessive reduction in blood flow into non-exercising organs to allow them to maintain their functions both during and after exercise. The question arises, then, as to which of the non-exercising organs allow an exercise-induced reduction in blood flow, which would consequently suppress their function. Evidence is accumulating regarding the actions of the splanchnic and ocular circulations during exercise. The nature of the blood flow of these two circulatory systems is herein discussed, and focus is particularly given to the relationship between the nature and function of each system in the gastrointestinal tract and eyes in humans.

Splanchnic blood-flow response to exercise

The alimentary tract governs digestion and absorption
from the mouth to the anus. Blood flow within the organs from the stomach to the large intestine—including the liver, pancreas, and spleen—is considered a part of the splanchnic circulatory system in the present review. The splanchnic circulatory system accounts for about 25% of cardiac output at rest\(^3\), and is supplied from three major arteries that branch off from the abdominal aorta: the celiac artery (CA), superior mesenteric artery (SMA), and inferior mesenteric artery (IMA). The CA supplies blood to the stomach, liver, and spleen, and its flow at rest is reported to be 460–1080 ml/min\(^6,7\); the SMA supplies the duodenum, jejunum, ileum, ascending colon, transverse colon, and pancreas, and its flow at rest is 220–540 ml/min\(^7,8\); while the IMA supplies the descending colon, sigmoid colon, and upper rectum, and its flow at rest is 80–130 ml/min\(^9,10\). Blood in these three arteries flows through the liver via the portal vein.

Splanchnic blood flow decreases during long-duration exercise. Pulsed-Doppler ultrasonography has revealed the nature of this change in human subjects. Cycling at 40–75% of maximum oxygen consumption (\(\mathrm{VO}_{2\max}\)) for 15 and 120 min was found to decrease the blood flow in the CA and SMA by roughly 30% and 50%, respectively\(^11-13\). However, lower-intensity exercise at 40 watts for 4 min did not affect the blood flow in the SMA as shown in Fig. 1\(^4\).

The portal vein receives blood from the gastrointestinal tract, and its flow at rest is 500–800 ml/min\(^14-16\). This vein is formed by the confluence of the superior mesenteric and splenic veins, and it also receives blood from the inferior mesenteric, gastric, and cystic veins. Thus it is natural that blood flow in the portal vein would decrease during exercise, reflecting a reduced blood flow to the major intestinal organs.

Blood flow in the portal vein was reported to decrease by 35% during 25 min of arm cranking at an exercise intensity of 50% of \(\mathrm{VO}_{2\max}\)\(^8\), and by 26% and 50% during 20 and 60 min of cycling at 70% of \(\mathrm{VO}_{2\max}\), respectively\(^15,17\). Furthermore, after 10 min of treadmill walking at 14 metabolic equivalents (METs), portal vein blood flow was 32% lower than the resting value\(^18\). The duration of exercise therefore appears to affect blood-flow response in the portal vein. Portal-vein flow was observed to decrease, during 60 min of exercise at 70% \(\mathrm{VO}_{2\max}\), relative to the elapsed time\(^19\).

Blood flow response in the proper hepatic artery to dynamic exercise has yet to be reported, probably due to the technical difficulty of measuring the flow therein. Blood is supplied to the liver by the proper hepatic artery and the portal vein. Blood flow in the proper hepatic artery is reported to be about 250 ml/min at rest (as assessed using a noninvasive technique)\(^18,19\). This corresponds to 20% of the total hepatic blood flow. Up to 70% of the blood flow to the liver is thus supplied by the portal vein\(^9\).

The role of sympathetic activation, in vasoconstriction in non-exercising organs, has been demonstrated by comparing blood flow response in the portal vein and femoral artery during arm cranking between normal subjects and subjects with a spinal cord lesion (SCL)\(^20\). The portal-vein flow decreased in normal and low-level SCL patients, but not in high-level SCL patients. Similarly, SMA blood flow and resistance changed in response to isometric exercise, cold pressor testing, and tilting, but not in response to pure autonomic failure or in subjects with multiple system atrophy\(^20\).

The splanchnic blood-flow response to dynamic exercise may be non-uniform among splanchnic regions, although very few studies have examined this. One study found that the blood flow decreased by 30% in the SMA, whereas it decreased by 50% in the CA during dynamic exercise at 75% \(\mathrm{VO}_{2\max}\)\(^17\). In another study, the blood flow decreased by 30% in the spleen, but not in the SMA, during light-intensity exercise\(^6\).

It appears reasonable to assume that non-uniform responses in the splanchnic blood flow are controlled multifactorially by the autonomic, humoral, and local organ-specific regulatory systems. The human splanchnic artery and vein are innervated by the sympathetic nervous system, and sympathetic vasoconstriction occurs during exercise. There is a well-documented close relationship between splanchnic blood flow and serum norepinephrine concentration at different work rates\(^21\).

Some authors consider that the renin-angiotensin system—and in particular angiotensin II (not vasopressin)—plays a role in the vasoconstriction that occurs in the visceral regions during exercise, similar to the systemic effect of the other vessels\(^22\), while others take the
opposite view\textsuperscript{19}. The mechanism underlying the regional differences in blood flow among the splanchnic vessels remains to be established. While there is no clear evidence that the sympathetic nerves, supplying the different vascular beds in the splanchnic organs, are not equally activated during exercise, the differential responses of the sympathetic nerves, and/or their sensitivities, appear to result in a non-uniform redistribution of blood flows to the splanchnic organs.

The decrement in total splanchnic blood flow appears to be mainly due to a decreased inflow to the liver and spleen, rather than to the intestinal tract; although evidence is still accumulating with regard to the local distribution of the blood flow of the supplying vessels among the different splanchnic organs in response to dynamic exercise. Details of the regional differences in the splanchnic circulation during and after exercise need to be resolved.

Effect of food ingestion on the gastrointestinal tract at rest and during exercise

Several researchers have investigated another aspect of human blood distribution during exercise: the prioritization of blood flow to exercising muscles over the gastrointestinal organs in the postprandial condition. This is important from the viewpoint of human behavior, since exercise was originally related to eating behaviors such as hunting and gathering. It is also particularly important for long-duration exercise such as marathon running and cycle road racing, since appropriate supplementation of foods and water is essential during these races. In addition to the provision of appropriate or optimum food intake during exercise, it is clinically important to protect the gastrointestinal organs from unnecessary stress induced by hypoperfusion; although the gastrointestinal organs are less vulnerable to hypoperfusion than other regions—only long-lasting hypoperfusion increases its permeability\textsuperscript{23}.

Exercise exerts both positive and negative effects on the splanchnic organs. It has been well established from large-population studies and meta-analyses that there is an inverse relationship between physical activity and the incidences of colorectal carcinoma, cancer, and diverticulitis\textsuperscript{24-25}. Conversely, gastrointestinal symptoms are a well-known downside of exercise. A mailed questionnaire survey found that 40–70\% of endurance athletes experienced gastrointestinal symptoms during acute exercise, and 11\% of runners suffered from serious gastrointestinal complaints when running\textsuperscript{26-28}. Exercise-induced splanchnic hypoperfusion is assumed to result in gut dysfunction\textsuperscript{27-29}, with the symptoms found to be related to food intake\textsuperscript{30}.

It can be readily assumed that food intake induces an unusual competition for blood flow between the alimentary tract and exercising muscles. Food intake increases splanchnic blood flow, contrary to the effect of exercise; food intake instantly increases the flow in the CA and SMA. According to research, the flow in the CA rapidly peaked at a 38–60\% increase from resting levels\textsuperscript{30}, while that in the SMA increased 1.5- to 3.5-fold at 5–60 min after food ingestion\textsuperscript{31-34}. The effect was greatly affected by the content of the ingested food, such that a richer energy content produced a greater peak\textsuperscript{35}, and either protein or fat intake delayed the peak but increased its value\textsuperscript{32,33}. No increase was observed in the IMA after food intake\textsuperscript{35}.

These increases in blood flow in the splanchnic circulation are affected by the nervous and humoral systems. Cholinergic nerves play a role in postprandial hyperemia\textsuperscript{36}, and beta adrenoreceptors form part of a humoral mechanism\textsuperscript{37}. The effects of these nervous activities on vasodilation in the gastrointestinal tract are relatively small. Several of the gastrointestinal hormones—such as cholecystokinin, secretin, gastrin 17, and glucagon—are candidate mechanisms, although their involvement in postprandial splanchnic hyperemia is not clear\textsuperscript{38}. This is partly because these hormones also activate the nervous system\textsuperscript{39}. Moreover, metabolic products also regulate the splanchnic circulation\textsuperscript{40}.

Food intake could modify blood flow distribution during exercise. Blood flow in the gastrointestinal tract is suppressed during postprandial exercise. Treadmill running for 15 min was reported to reduce the SMA flow by 43\%, whereas food intake increased it by 60\%. Combining exercise and food increased the flow by 40\%, demonstrating the counterbalancing effects of vasodilation by food intake and vasoconstriction by exercise\textsuperscript{41}. Similarly, food ingestion modulates blood-flow response in the portal vein to exercise. Carbohydrate ingestion affected portal vein blood flow during exercise, as well as resulted in a carbohydrate-induced increase at rest. Portal vein flow also decreased after 60 min of cycling at 70\% VO\textsubscript{2max}, whereas the decrease tended to be smaller when carbohydrates were consumed before and during the exercise\textsuperscript{42}.

A positive correlation has also been observed between gluconic level and blood flow. This suggests that eating before and during exercise modulates blood flow in the gastrointestinal tract. On the other hand, no difference in blood flow and conductance was observed in exercising limbs and the splanchnic circulation between the normal and postprandial conditions\textsuperscript{41}. Exercise in the postprandial condition was shown to increase cardiac output, superimposing its increase on the blood flow into the SMA\textsuperscript{42}. The question regarding competition in the blood flow between the splanchnic circulation and exercising muscle remains to be resolved.

Ocular flow during exercise

A continuous supply of blood to the retina is essential for eye function, since it has a high oxygen demand and oxygen is not stored in the retina or surrounding tissues\textsuperscript{43}. Furthermore, it is also necessary to keep the flow stable
so as to maintain visual function.

The ocular circulation comprises the retinal and choroidal circulations. The retinal circulation exists in the inner part of the retina and is characterized by a low blood supply, whereas the choroidal circulation exists on the outside of the retina, and has a very high blood supply - 85% of total ocular flow. The anatomical characteristics of the eye mean that increases in retinal circulation may interfere with light reaching the retina.

It has been shown that submaximal dynamic exercise resulting in a heart rate of 100–140 bpm increases the choroidal flow by up to 30% of the resting baseline, depending upon the intensity, but does not alter retinal flow as shown in Fig. 2. However, the increase in choroidal flow is not associated with an increase in the conductance index, indicating an association with the pressor response to exercise. At dynamic-exercise-induced exhaustion with hypocapnia, findings showed the choroidal flow did not change from the resting baseline value, and the retinal flow decreased by 13%. The conductance index in both the choroidal and retinal flows decreased from the resting baseline, suggesting that ocular blood flow is suppressed by the hypocapnia associated with exhaustion.

Animal studies have led to a general acceptance that autoregulation exists in the retina, but not (or, if so, at a very weak level) in the choroidal circulation. However, whether autoregulation exists in the human retina has yet to be established. One study found no change in the retinal circulation during either the cold pressor test or handgrip exercise, indirectly suggesting the existence of autoregulation. Consistent with the presence of autoregulation, choroidal flow did not change during submaximal dynamic exercise even where there was a pressor response. The choroidal flow increased in these studies, and hence autoregulation seems to be present in the retinal circulation, but not in the choroidal circulation. Nevertheless, autoregulation against short-term fluctuations in arterial pressure has not been observed. Measurements of blood flow in the ophthalmic artery by Doppler ultrasound during an acute fall in systemic pressure induced by thigh cuff deflation did not reveal evidence of autoregulation. The autoregulatory effect on blood flow might have been weakened by choroidal flow, since the ophthalmic artery is upstream of both the choroidal and retinal flows. This matter is difficult to clarify since continuous observation of the ocular flow is impossible simply because subjects can not keep their eyes open for long periods.

Ocular flow and visual function

While the relationships between the ocular circulation and visual function are readily apparent, changes in ocular flow and the effects on visual function have not been elucidated (with the exception of pathological conditions). The chronic loss of ocular blood flow associated with pathological conditions such as diabetes and glaucoma is associated with impaired visual function. In Japan, the prevalence of primary open-angle glaucoma is estimated to be 2% in patients aged in their 40s, and 10% of those older than 70 years. Thus, the correct functioning of the ocular circulation is important, and the administration of certain drugs that alter ocular flow can improve visual function in these patients. However, the effect of regular exercise on ocular circulation remains unclear.

Some researchers have observed acute changes in visual function induced by ocular blood flow in healthy humans. Increases in ocular blood flow induced by either inhalation of high concentrations of CO2 or administration of sildenafil was shown to improve static visual acuity and contrast sensitivity. In addition, an increase in the retrobulbar circulation - which supplies blood to the ocular circulation - by CO2 inhalation, was associated with improved contrast sensitivity. Nevertheless, the effects of acute changes in ocular blood flow on visual function have yet to be established, in part because these changes in ocular flow are also associated with changes in cerebral blood flow, which is strongly related to brain function, including visual information processing.

Changes in visual function during exercise have been reported. An important aim of visual information processing is to judge the speed and distance of objects, which makes it important to be able to maintain visual function during exercise. Visual field and contrast sensitivities were reported to increase after jogging in many subjects, but to decrease after exercise in others. Unclear changes in visual function may be due to the complicated mechanisms underlying the maintenance of eye function, not just in the eyes themselves, where there are several such mechanisms (including pupil diameter regulation), but also in the brain, where major processing of the information from the eyes occurs. Thus, eye functionality is too complex for it to be studied during exercise, although
some researchers have attempted to characterize neurovascular coupling during dynamic exercise. Research into eye function during exercise has really only just begun from the viewpoint of circulatory changes.

Summary and perspective

Blood flow in the splanchnic circulation is reduced during exercise, as in other organs such as the kidney. This decrease is suppressed by food intake, possibly due to efforts by the body to maintain digestive and absorptive functions in the gastrointestinal tract. Conversely, choroidal blood flow increases during submaximal exercise. The relevance of this is unclear. However, retinal blood flow remains unchanged during exercise, presumably so that it does not interfere with light reaching the retina.

Competition in the blood flow between exercising muscles and non-exercising organs should be examined from the viewpoint of the functions of the non-exercising organs and the particular exercising condition (e.g., postprandial). Before recommending regular exercise training to patients or the elderly, it is necessary to determine blood-flow responses to exercise and the significance of such responses regarding the functions of various organs.

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References


