COUNTERPOINT: ACTIVE VENOCONSTRICTION IS NOT IMPORTANT IN MAINTAINING OR RAISING END-DIASTOLIC VOLUME AND STROKE VOLUME DURING EXERCISE AND ORTHOSTASIS

Veins were considered merely as passive conduits of blood until Mellander (13) reported that stimulation of sympathetic nerves supplying the cat’s hindquarters resulted in a decrease in regional blood volume. This and other work led Folkow and Mellander (4) to assert that veins were “at least as active and important a part of the regulatory mechanisms as arteries.” Since then it has been assumed that the control of veins provides a major role in cardiovascular regulation. The gastrointestinal tract made only a very small contribution to the active response, although the volume change in response to sympathetic nerve activity would reduce venous volume and enhance cardiac filling. However, veins are highly distensible (30 times more so than arteries) and so their volume can also be changed by changes in transmural distending pressure. In humans, a 5 mmHg change in venous pressure would be associated with a change in venous volume of ~1 liter (9).

Changes in venous volume may be regarded as active (capacitance change) when they result directly from contraction of venous smooth muscle or passive when changes result from changes in transmural distending pressure (9). These two mechanisms are interlinked. An increase in sympathetic activity not only constricts veins but also constricts arterioles. This reduces flow of blood into veins, resulting in less venous distension and consequently a passive decrease in venous volume. These “active” and “passive” effects are difficult to separate, but it seems reasonable to assume that if blood flow to a region is forced to remain constant despite resistance vessel constriction, by isolation of the region and constant flow perfusion, any change in volume would be mainly active. We (10) compared the volume changes in the dog’s hindlimb to direct and reflex sympathetic stimulation, during constant flow and constant pressure perfusion, and found that changes occurred only during constant pressure. The conclusion, therefore, is that the circulation in the limb does not make any significant contribution to the control of vascular capacitance and that changes reported by others (1, 3) were just secondary passive effects from changes in flow.

Capacitance in the abdominal circulation. The absence of appreciable venoconstriction in musculocutaneous circulations may actually be of physiological benefit because when flow is high, as during exercise, venoconstriction would impede rather than enhance venous return. The situation in the abdominal circulation, however, is quite different. Even during exercise, increases in sympathetic activity would reduce blood flow, so both active and passive effects would reduce regional blood volume. We (11, 12) reported that changes in volume of 7.5 and 5 ml/kg were expelled from the abdominal circulation of the dog in response to direct and reflex stimulation, respectively. These occurred during constant flow perfusion and assumed to be active.

Despite the existence of active capacitance responses in the abdominal circulation, passive effects may be greater. Just decreasing blood flow to the splanchic region resulted in a decrease in volume only a little less than that during sympathetic stimulation (14). In dogs with intact spleens, we showed that at low frequencies of stimulation the decrease in abdominal blood volume was mainly active, but at high frequencies, active and passive responses were similar. After splenectomy, the active response was greatly reduced but the passive change was unaffected (14). The estimated active capacitance responses at stimulus frequencies of 1 and 8 Hz were only 1.4 and 2.7 ml/kg. The significance of results is that humans, unlike dogs, do not possess a large contractile spleen, so to extrapolate dog results to humans we should exclude the splenic contribution.

In an attempt to determine the regions responsible for the capacitance responses, Noble et al. (15, 16) separated the circulations to the liver, gastrointestinal tract, and remainder of the abdominal circulation (excluding spleen) and found that most of the active response (average 88%) arose from the liver. The gastrointestinal tract made only a very small contribution to the active response, although the volume changed considerably with changes in flow (Fig. 2). Thus it is mainly the liver that is responsible for the active response and the intestine for the passive response.

![Figure 2](http://jap.physiology.org/)

**Fig. 2.** Summary diagram showing responses calculated from splanchnic circulation to changes in carotid pressure and to changes in blood flow. Values are means ± SE from 6 splenectomized dogs. This shows that, of the total volume change in the region, the active component (during constant flow) made only a small contribution. The difference in the responses at constant flow and constant pressure was not significantly different from the change in volume occurring when flow was changed by a similar amount by altering the pump speed (reproduced with permission from Ref. 15).
Physiological importance of active vasoconstriction. To ascertain the importance of active venoconstriction in relation to end-diastolic volume and stroke volume, we need to consider the following: 1) the magnitude of the volume of blood returned, 2) the effects of this on end-diastolic and stroke volumes, 3) the circumstances under which this would occur. Unfortunately, as it is not possible to obtain accurate quantitative data from humans, we have to rely on results extrapolated from animal studies, mainly dogs and cats. As discussed above, in the splenectomized dog, the maximum capacitance response amounts to only ~3 ml/kg, mostly from the liver. If we assume that humans behave similarly to this (admittedly an unvalidated assumption!), a 70-kg man could have a response of 200 ml. The effect of this can be estimated by calculating its effect on mean circulatory filling pressure (MCFP, the pressure in the circulation seen after equilibration at zero flow). Assuming mean circulatory compliance to be 2.5 ml·kg$^{-1}$·mmHg$^{-1}$, a change in effective circulatory volume of 3 ml/kg would change MCFP by 1.2 mmHg. From Guyton’s curves (7) this would increase cardiac output by ~20%.

Next, is a change in cardiac output of 20% important in cardiovascular control during exercise and orthostatic stress? Note that active venoconstriction occurs at low levels of sympathetic activity; about one-half the maximum response occurs at 1 Hz and 75% at 2 Hz (14). The implication for exercise is that if, before exercise, the bursts of sympathetic activity equate to, say 1 Hz, there is very little reserve, possibly only 100 ml, and this would be unlikely to have much effect at all in such a dynamic state.

This leaves the question of the possible role of venous constriction in orthostasis. Supine humans have irregular bursts of sympathetic activity averaging ~1 Hz (5). On standing, this may increase to 2 Hz and this would reduce capacitance by ~100 ml. This could make a small contribution to maintaining cardiac output. However, during active standing, rather than passive tilting, venous compression due to leg movement is likely to be much more important (see recent debate, Ref. 17). Indeed, we recently showed that asymptomatic subjects who have a poor tolerance to artificial orthostatic stress (head-up tilting and lower body suction) compensate by having greater leg movements during normal standing than subjects with good tolerance to the abnormal stress (3).

In conclusion, on the basis of the evidence presented above we would suggest that active venous constriction only has the potential for a small enhancement of venous return and that this occurs at low levels of sympathetic inactivity. Therefore, under most circumstances there would be little reserve. It is hard to see how this small change could have any noticeable effect during exercise when other far greater changes occur. During orthostasis, venous constriction may make a small contribution. However, even then it is likely that external influences on veins, caused by external compression by muscles or reductions in arterial inflow due to resistance vessel constriction, would be of much greater importance.

REFERENCES


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REBUTTAL FROM DR. ROTHEN

Hainsworth and Drinkhill (2) concluded that active venoconstriction is not important in raising end-diastolic volume (EDV) or stroke volume during exercise and orthostasis. They do admit that active venoconstriction exists, but in their last paragraph, they conclude that it only provides a small venous return enhancement. I fully agree with the following. 1) The skeletal muscle pump during exercise can provide the major part of the maintenance or increase in EDV (7). 2) Active venoconstriction occurs primarily in the abdominal splanchnic bed. 3) Skin and skeletal muscle venous responses are minimal. 4) The spleens of dogs are much larger than that of humans. 4) In response to changes in flow and venous distending pressure, passive changes in venous volume are indeed important.

However, Hainsworth and Drinkhill did not support the assumption that constant pressure perfusion eliminates concurrent active venoconstriction in assessing the magnitude of the passive venous responses. Changing the carotid sinus pressure between 60 and 195 mmHg, Hainsworth and Drinkhill (2)