

Changes in Superior Mesenteric Blood Flow Produced by Splanchnic Nerve and Hypovolemic Stimulation in Rats

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Summary. Changes in superior mesenteric venous blood flow (SMVF) were examined in rats following splanchnic nerve and hypovolemic stimulation. The splanchnic nerve branch to the liver was sectioned in all rats tested. SMVF was decreased after electrical stimulation of the left splanchnic nerve, and SMVF was reduced in parallel with the volume of blood withdrawn (1.0, 2.0 and 2.5 ml per body). The SMVF response after nerve stimulation was decreased according to the volume of blood withdrawn. Noradrenaline injected into the superior mesenteric vein reduced SMVF in a dose-dependent fashion. Splanchnic nerve stimulation decreased superior mesenteric arterial blood flow (SMAF), but the reduction in SMAF was similar for all three degrees of hypovolemia.

These results suggest that the sympathetic nerve directly moderates blood flow in the superior mesenteric vein through adrenergic fibers. With blood loss, sympathetic mesenteric control of the venous but not the arterial circulation is moderated.

Key words—splanchnic circulation, bleeding, sympathetic nerve.

INTRODUCTION

Intraabdominal organs including the liver, spleen and intestine have been shown to act as a blood reservoir. The sympathetic nerve plays an important role in mobilizing blood in the abdominal cavity.¹⁻³ Recently, it has been demonstrated in cats, rabbits and dogs that the splanchnic nerve directly regulates portal blood flow through constriction of the portal vascular

walls.⁴⁻⁷ Moreover, it has been reported that blood flow in the portal vein in a rat model is regulated by changes in portal venous pressure, and that this is reflected in the pressure in the superior mesenteric vein.^{8,9} It has been shown, in histochemical experiments in rats and guinea pigs, that there is sympathetic innervation to the superior mesenteric vasculature.¹⁰⁻¹² However, there are no reports concerning sympathetic contribution to superior mesenteric venous circulation. On the other hand, hypovolemia caused by bleeding stimulates the sympathetic nerve.^{13,14} The intense vasoconstriction caused by nerve stimulation in the splanchnic area shifts blood from the visceral reservoir into the systemic circulation.

The present study was designed to investigate how the stimulated splanchnic nerve influences blood flow in the superior mesenteric vessels in consideration of hypovolemia.

MATERIALS AND METHODS

Animals

Twenty male Wistar rats weighing between 350 and 400 g were housed individually (12 h light-12 h dark cycle) in a room at temperatures ranging from 22.0 to 24.0°C. They were fed *ad lib* on a standard diet with free access to tap water prior to the experiments. The experiments were carried out in the afternoon (between 1:00 and 6:00 p.m.) to eliminate diurnal changes in sympathetic nerve activity.¹⁵

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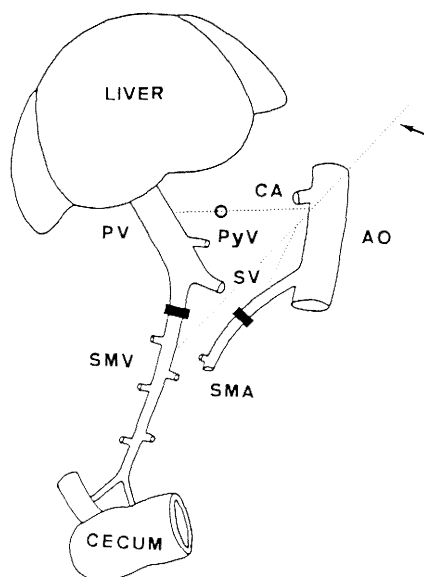


Fig. 1. Schematic diagram of splanchnic nerve pathways. Dotted lines show the neural pathway. Arrow indicates electrical stimulation site. The hepatic branch has been sectioned at the open circle. The probes of the flowmeter have been placed at the filled rectangles. AO; aorta, CA; celiac axis, PV; portal vein, PyV; pyloric vein, SMA; superior mesenteric artery, SMV; superior mesenteric vein, SV; splenic vein.

Anesthesia and general monitoring

The rats were anesthetized initially with pentobarbital sodium (45 mg/kg, i.p.). Further doses of this agent (10 mg/kg) were injected intramuscularly every 30 min to maintain the strength of anesthesia.⁹⁾ The trachea was intubated to allow adequate ventilation. The anal temperature was maintained at $37.5 \pm 0.5^\circ\text{C}$ with a heating lamp throughout the experiments.

Estimation of blood flow and pressure

A portion of the superior mesenteric vein and artery were cleaned of surrounding connective and fatty tissues, keeping the nerves intact. Probes for blood flow estimation were placed around the superior mesenteric vein and the superior mesenteric artery (Fig. 1). Superior mesenteric venous blood flow (SMVF) and superior mesenteric arterial blood flow (SMAF) were measured with an ultrasonic blood-flow meter (Transonic T201, Advance, NY, USA).^{16,17)} The systemic arterial pressure (SAP) was recorded from the left femoral artery. The data were recorded

continuously using a pen recorder (SR6221, Graphtec, Tokyo).

Sympathetic activation with electrical stimulation

The left side of the splanchnic nerve was exposed and sectioned, with a stimulation electrode¹⁸⁾ then placed around the distal cut end of the nerve (Fig. 1). Based on the results of a previous experiment,⁸⁾ electrical stimulation which produced saturated blood flow response (frequency; 10 Hz, width; 1 ms, strength; 15 V) was applied for 20 s. Because electrical stimulation of the hepatic branch of the splanchnic nerve has been shown to alter portal venous blood flow,⁸⁾ the branch to the liver was cut in all animals tested.

Blood withdrawal and infusion

A catheter was inserted into the right jugular vein. The tip of the catheter was located in the right atrium of the heart. Blood withdrawal and infusion were performed with the same catheter. When blood was withdrawn, the same volume of blood was infused after testing. These procedures were performed in about 30 s, for a total test time of 15 min.

Adrenalectomy

The adrenal glands were resected bilaterally using previously described methods.¹⁹⁾ The experiments started 20 min after adrenalectomy.

Noradrenaline injection

Noradrenaline (Wako, Osaka, Japan) was dissolved in physiological saline (5.9 mM) and injected into the superior mesenteric vein or the portal vein. Injection was performed over a period of 20 s using an infusion pump.⁸⁾ Physiological saline was used as the control.

Data analysis

The data were ANOVA analyzed, and specific values were evaluated by Duncan's multiple range test: a $p < 0.05$ was regarded as significant.

RESULTS

Control values of SMVF, SMAF and SAP are shown in Table 1.

The SMVF decreased after electrical stimulation of the splanchnic nerve (Fig. 2A), reaching a nadir at approximately 15 s. The SMVF returned to the

Table 1. SMVF, SMAF and SAP 2 min after the withdrawal of 0 ml (I), 1.0 ml (II), 2.0 ml (III) and 2.5 ml (IV) of blood

	I	II	III	IV
SMVF (ml/min)	11.6±1.2	8.6±1.6	5.2±0.6 ^a	4.4±0.6 ^b
SMAF (ml/min)	6.6±0.5	4.0±0.7 ^c	3.8±0.3	2.9±0.4
SAP (mmHg)	108±3	7±4 ^d	57±3	55±4

Values are the mean ± SEM (n=6). ^ap<0.05 vs I and II. ^bp<0.01 vs I and II. ^cp<0.01 vs I and IV. ^dp<0.01 vs I and III.

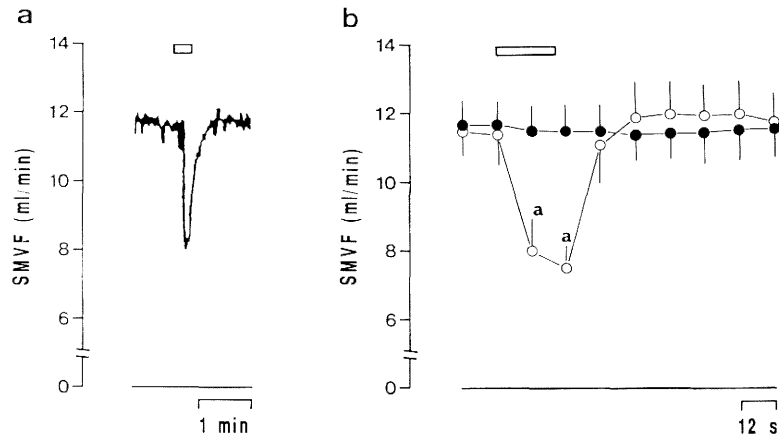


Fig. 2. Changes in SMVF caused by electrical stimulation of the left splanchnic nerve. **a.** A representative SMVF response following electrical stimulation of the nerve. The bar indicates the time of stimulation. **b.** Mean SMVF after electrical stimulation of the nerve (○). Control had no stimulation (●). The bar indicates the time of stimulation. Values are the mean ± SEM (n=6). ^ap<0.01 vs ●.

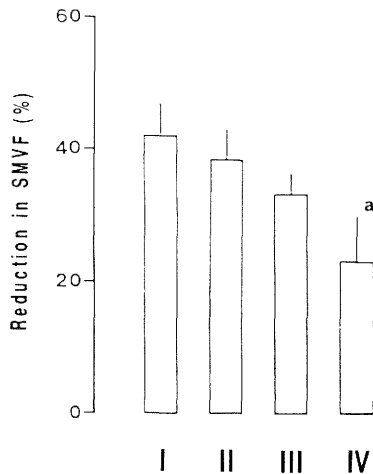


Fig. 3. Changes in SMVF after splanchnic nerve stimulation after the withdrawal of 0 ml (I), 1.0 ml (II), 2.0 ml (III) and 2.5 ml (IV) of blood. Values are the mean ± SEM (n=6). ^ap<0.01 vs I and II.

control value within another 60 s (Fig. 2B). Based on this information, the SMVF at 20 s after stimulation was used for comparative evaluation.

The SMVF was decreased when the volume of blood drawn was increased (Table 1). The SMVF after splanchnic nerve stimulation was compared for the three different volumes of blood withdrawn (1.0, 2.0 and 2.5 ml). The reduction in SMVF did not significantly differ between the control and after 1.0 ml of blood was withdrawn. The SMVF response was significantly attenuated after 2.5 ml of blood was withdrawn (Fig. 3). The SMVF response with nerve stimulation was reduced according to the volume of blood withdrawn.

Bilateral adrenalectomy did not affect the decreases in SMVF produced by splanchnic nerve stimulation (Table 2).

Injection of noradrenaline into the superior mesenteric vein resulted in a reduction in SMVF. The response was dose-dependent (Fig. 4).

Table 2. Maximal percentages of reduction in SMVF and SMAF caused by splanchnic nerve stimulation immediately before (I) and 30 min after (II) adrenalectomy

	I	II
SMVF	41.5±4.8	41.3±4.9
SMAF	38.0±4.6	41.0±3.7

Values are the mean ± SEM (n=6).

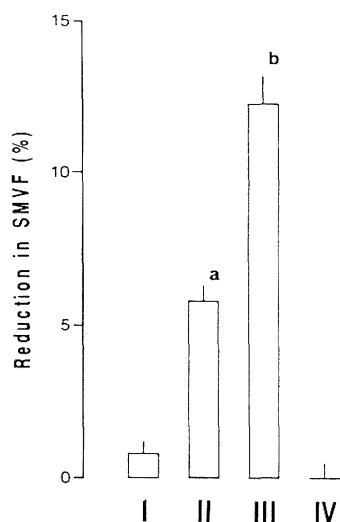


Fig. 4. Responses in SMVF caused by noradrenaline (5.9 mM). (I) Control: NaCl (154 mM) injection. (II) Noradrenaline (250 nl) injected into the superior mesenteric vein. (III) Noradrenaline (500 nl) injected into the superior mesenteric vein. (IV) Noradrenaline (250 nl) injected into the portal vein. Values are the mean ± SEM (n=6). ^ap<0.01 vs I and IV. ^bp<0.01 vs II.

Splanchnic nerve stimulation reduced SMAF. The reduction in SMAF with nerve stimulation was similar after 1.0, 2.0 and 2.5 ml of blood were withdrawn (Fig. 5).

DISCUSSION

We found that the sympathetic nerve directly modulates blood flow in the superior mesenteric vein; electrical stimulation applied to the nerve effectively reduced SMVF under conditions in which the hepatic splanchnic branch was interrupted (Fig. 2). Histochemical studies have identified adrenergic fibers in the superior mesenteric vein.¹⁰⁻¹² Nerve stimulation causes vasoconstriction resulting in the inhibition of blood flow.

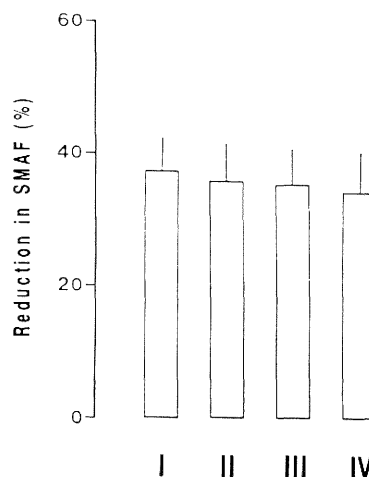


Fig. 5. Responses in SMAF caused by splanchnic nerve stimulation in animals after the withdrawal of 0 ml (I), 1.0 ml (II), 2.0 ml (III) and 2.5 ml (IV) of blood. Values are the mean ± SEM (n=6).

The systemic circulating volume of blood in the rat is estimated to be 21 to 24 ml.²⁰ Up to 10 to 12 percent of the blood volume was withdrawn in this study.

A decrease in SMVF was observed with splanchnic nerve stimulation when the volume of blood withdrawn was increased to 10 to 12 percent (Fig. 3). Why the effect of nerve stimulation on blood flow was reduced is not clear. Mechanical changes in the vasculature may have affected the response. It has been demonstrated that blood flow in the portal vein is regulated by changes in portal venous pressure, and that the pressure in the superior mesenteric vein is tonically reflected in the portal venous pressure.^{8,9}

Adrenaline causes vasoconstriction. It has been shown that adrenaline is released from the adrenal glands after splanchnic nerve stimulation.²¹ However, there was no difference in the magnitude of the SMVF response caused by nerve stimulation with or without adrenalectomy (Table 2). Thus, the effect of adrenaline released as a result of nerve stimulation is negligible.

Noradrenaline injection into the superior mesenteric vein caused a dose-dependent inhibitory response in SMVF (Fig. 4). Histochemically, fibers sensitive to noradrenaline have been identified in the superior mesenteric vein.¹⁰ It appears that noradrenergic fibers in the vessels are involved in the observed flow response.

The reduction in SMAF in response to splanchnic nerve stimulation is similar regardless of the volume of blood withdrawn (Fig. 5). This could be interpreted as evidence that the splanchnic nerves are more

effective than the circulating blood volume in the control of SMAF.

As mentioned above, responses in SMVF caused by nerve stimulation varied according to volume status (Figs. 3 and 5) although both splanchnic nerve and blood withdrawn stimulation cause activation of the nerves innervating the mesenteric vein and artery.³⁾ One interpretation of this difference is that the density of innervation of the artery is much higher than that of the vein.¹⁰⁾

The fact that splanchnic nerve and blood withdrawn stimulation evoked a constant SMAF response, but a decreased SMVF response, does not justify conclusions about the pathophysiological significance of these effects. However, it is reasonable to note that the SMAF response primarily contributes to maintaining the systemic arterial pressure, and that the SMVF response maintains the splanchnic blood volume.¹⁴⁾

Clinically, blood withdrawal simulates acute hypovolemia from bleeding. The data obtained in this study provide valuable knowledge which may be used in the care of patients suffering bleeding.

The sympathetic nerve directly regulates blood flow in the superior mesenteric vein through adrenergic fibers. When the circulating blood loss is not more than 10 to 12 percent, the regulation is active in the arterial vessels, but is attenuated in the venous vessels.

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