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Traumatic Brain Injury Creates Biphasic Systemic Hemodynamic and Organ Blood Flow Responses in Rats

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ABSTRACT

Traumatic brain injury affects systemic circulation as well as directly damages the brain. The present study examined the effects of fluid percussion brain injury on systemic hemodynamics and organ arterial blood flow in rats. Rats were prepared for fluid percussion injury under anesthesia. Twenty-four hours later, rats were anesthetized (1.0% halothane in N₂O:O₂) and prepared for radioactive microsphere measurement of cardiac output and organ blood flow. After baseline blood flow and physiological measurements were established, the rats were injured (2.47 ± 0.02 atm, $n = 17$) or not injured ($n = 20$). Additional blood flow determinations were made at two of the following four time (T) points: 5, 15, 30, and 60 min after the injury or sham injury. Fluid percussion brain injury produced an immediate systemic hypertension followed by a hypotension and low cardiac output. Organ blood flows remained constant or increased for 30 min and then declined. Decreased blood flow was most pronounced in the kidneys and the spleen and was less severe in the liver. The reduced cardiac output was redistributed to favor blood flow through the heart and pancreas. These data suggest that traumatic brain injury creates a hyperdynamic period followed by a hypodynamic state with a heterogeneous hypoperfusion among organs.

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INTRODUCTION

TRAUMATIC BRAIN INJURY (TBI) OFTEN RESULTS in multiple organ system damage in addition to brain injury (Matjasko, 1986; Deutschman, 1987). Management of most head injuries is nonsurgical, and functional survival may depend on attention to these multisystem derangements (Matjasko, 1986; Deutschman, 1987; Weinand, 1988). A number of investigators have reported the systemic physiological responses to severe closed head injury (Clifton et al., 1983; Fell et al., 1984; Miller, 1984; Robertson et al., 1984; Waters et al., 1984). A hyperdynamic cardiovascular state characterized by increased cardiac output, hypertension, decreased or normal systemic vascular resistance, and increased oxygen consumption has been noted in patients with isolated TBI (Clifton et al., 1983; Robertson et al., 1984; Deutschman et al., 1986; Deutschman, 1987). The cardiovascular response to closed head injury is similar to that noted in multisystem trauma without brain injury (Robertson et al., 1984; Deutschman, 1987).

Despite this frequent clinical observation, recent experimental evidence indicates that a hypodynamic state could occur following TBI (Dixon et al., 1987; McIntosh et al., 1987). Furthermore, no experimental data are available currently to describe the changes of individual organ blood flow immediately after TBI. Since severe disturbance of vital organ blood flow would contribute to posttraumatic multiple organ failure and eventually affect outcome, it is very important for clinicians to have some knowledge about the pattern of organ blood flow changes after TBI. The present study was designed to examine the sequential effects of TBI on systemic hemodynamics and organ arterial blood flows in the rodent fluid percussion TBI model.

MATERIALS AND METHODS

Animal Preparation

Thirty-seven male Sprague-Dawley rats (371–523 g) were used in the study. The guidelines of the Animal Welfare Act (P.L. 89–544) and the Institute of Laboratory Animal Resources (National Research Council) were observed, and the research protocol was approved by the Animal Care and Use Committee of Bowman Gray School of Medicine of Wake Forest University. Rats were randomly assigned to control ($n = 20$) or trauma groups ($n = 17$).

Rats in the trauma group were anesthetized with ketamine (50 mg/kg i.m.) and xylazine (10 mg/kg, i.m.), and a 5 mm craniotomy was trephined over the superior sagittal sinus. Two stainless steel screws (length 4 mm, tip OD 1 mm) were placed in the left parietal bone 4 mm lateral to bregma and in the occipital bone 2 mm caudal to lambda, respectively. A modified Luer-Lok syringe hub, 5 mm OD, was placed over the exposed dura and was secured to the bone and the screws with dental acrylic. The rats were returned to their cages and allowed to recover for 24 h. The following day, anesthesia was induced (ketamine and xylazine i.m.), and the rats were intubated and ventilated with a mixture of 1% halothane in 70% nitrous oxide and 30% oxygen using a volume mechanical ventilator (EDCO Scientific, Inc.). Rectal temperature was monitored continuously and maintained at 36.5–37.5°C using a heating pad. The right femoral artery was cannulated for blood pressure monitoring using a quartz transducer (Hewlett Packard) and an eight-channel polygraph (Hewlett Packard 8890A). Arterial blood gases were analyzed using a 1306 pH/Blood Gas Analyzer and a IL282 Co-Oximeter (Allied Instrumentation Laboratory). By adjusting ventilatory rate and tidal volume, and by administering sodium bicarbonate, P_{aO_2} , P_{aCO_2} , and pH were maintained within the normal range during the entire experiment. A second cannula was inserted into the left femoral artery to withdraw the reference sample during microsphere injection. A left atrial cannulation was performed through a left thoracotomy. The catheter consisted of a Silastic tubing (0.02 inch ID $\times$ 0.037 inch OD, Dow Corning) with a 2-mm silicon sleeve 0.5 cm from the tip. The cannula was inserted through a hole punctured in the wall of the left atrium with a 23-gauge needle and sutured in the left

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atrium with a 7-0 silk suture previously sewn through the silicon sleeve of the cannula. The sham-injury rats were prepared identically, but without the craniotomy.

Following surgery, the concentration of halothane was reduced to 0.5%, and the rats were paralyzed with pancuronium bromide (0.1 mg/kg, i.a., q 15 min). Thirty minutes later, baseline hemodynamic values were recorded, and the baseline radiolabeled microspheres were injected. Fifteen minutes later, the rats were subjected to fluid percussion injury (2.47 ± 0.02 atm) or no injury. Each rat was randomly assigned to receive additional injections of microspheres at two of the following four time (T) points: 5, 15, 30, and 60 min after injury or no injury. All animals were killed after T60 by injection of a lethal dose of potassium chloride into the left atrial catheter. The organs were removed, dissected, weighed, and counted in a gamma counter.

Fluid Percussion Brain Injury

The fluid percussion injury device consisted of a Plexiglas cylinder (60 cm long and 4.5 cm in diameter) with a cork-covered piston mounted on O-rings at one end. The other end of the cylinder was fitted with a 2-cm long metal housing on which a transducer was mounted. The transducer housing was connected to a right angle tube that ended with a male Luer-Lok fitting, which was connected to a female Luer-Lok syringe hub implanted over the craniotomy. The system was then filled with isotonic saline, and the injury was produced by dropping a weighted metal pendulum from a preset height. The magnitude of the injury was regulated by varying the height of the pendulum. At the time of injury, pressure pulse was measured extracranially by the transducer and recorded on a storage oscilloscope. The fluid percussion injury device transiently injected a constant (depending on level of injury) volume of saline into the closed cranial cavity, thereby producing brief displacement and deformation of the brain. The fluid percussion injury device has been described in detail elsewhere (Sullivan et al., 1976; Dixon et al., 1987; Dewitt et al., 1988).

Radioactive Microsphere Technique

Blood flows in the kidneys, spleen, liver, pancreas, heart, and lungs were measured with microsphere (15 μ m, Dupont New England Nuclear Products) labeled with ^{113}Sn , ^{85}Sr , or ^{46}Sc , which were injected in a rotated sequence. Microspheres suspended in saline with 0.01% Tween 80 were shaken vigorously for 3 min, and an aliquot (0.12–0.22 ml) was withdrawn into a length of PE tubing, which was sealed and counted. Before injection, the tubing was sonicated for 20 min to maintain even suspension. The tubing was opened. One end was attached to the left atrial catheter, and the other end was attached to a 1-ml flush syringe. Approximately 230,000–299,000 spheres were injected into the left atrium over a 15-sec period, followed by a 35-sec flush with 1 ml of saline. Beginning 10 sec before the microsphere injection and continuing for 30 sec after the flush, a reference arterial blood sample was withdrawn from the left femoral artery at a rate of 0.68 ml/min using a syringe pump (EDCO Scientific, Inc). Following the injection, the microspheres in the PE tubing were counted and subtracted from the preinjection count to determine the number of microspheres injected.

At the end of the experiment, the rats were killed. The organs were removed, placed in preweighed counting vials, weighed, and counted in an Auto-Gamma 5000 gamma counter (Packard Instruments). Corrections for isotope overlap were performed automatically by a microcomputer connected to the gamma counter. Organ blood flow or cardiac index was calculated using the following equation (Malik et al., 1976; Rothwell and Stock, 1984; Proctor and Busija, 1985; Lee et al., 1986).

$$\text{Organ blood flow or cardiac index (ml/min/100 g)} = \frac{C_o \times \text{RBF} \times 100}{C_r \times W_o}$$

C_o = counts in the organ or total counts injected

C_r = counts in reference sample

RBF = reference blood withdrawal rate

W_o = weight (g) of organ or whole body

Statistical Analysis

Individual organ blood flow and other physiological variables from the two groups were compared at baseline using an unpaired *t*-test. A one-way analysis of variance for each group was performed on individual organ blood flow and other physiological variables to assess the overall time effect over five preset time points. When significant time effects were present, the means between the baseline and any of the four time points (T5, T15, T30, and T60) were compared further within the group using Dunnett's test. To assess intergroup comparison, a two-way analysis of variance was performed using absolute values at five preset time points for the hemodynamic variables, and percentage of baseline values at four postinjury or sham injury time points for the individual organ blood flows. In the event of a significant intergroup difference or time-group interaction, a Newman-Keuls test was performed to locate the difference between the groups at each time point. An unpaired Student's *t*-test with pooled estimate of variance was used to compare the peak mean arterial pressure and its corresponding heart rate during the posttraumatic hypertensive response with their respective baseline values and counterparts in the control groups. Since the hypertensive responses were usually maximal at 30 sec after injury, the mean arterial pressure and heart rate at 30 sec after sham injury in the control group were used as counterparts. A *p* value less than 0.05 was regarded as significant.

To correct for intergroup variability among rats, values of organ blood flow in both groups were expressed as percentage of baseline and presented as mean $\pm$ SEM percentage in the graphs.

RESULTS

There were no significant differences between the two groups in body weight, blood gases, body temperature, or hemoglobin concentration at any time during the experiment (Table 1). The only significant change over time in these parameters was reduced hemoglobin concentration in the trauma group at T60.

Hemodynamic changes

Mean arterial blood pressure (MAP) did not change significantly over time in the control group (Fig. 1). Fluid percussion brain injury produced a transient, significant increase in MAP from 80 ± 4 to 131 ± 7 mm Hg ($p < 0.001$ for the intragroup and intergroup comparison). MAP peaked in 30 ± 11.5 sec, returned to baseline level within 367 ± 128 sec after injury, and then continued to decline for the rest of the experiments.

Heart rate increased from 287 ± 6 to 334 ± 18 beats/min ($p < 0.01$) during the postinjury hypertensive period in the trauma group as opposed to no significant change in the control group.

Cardiac index in the trauma group rose initially and then decreased over time to 78% of baseline at T60. In contrast, cardiac index in the control group was reduced to 89% of the baseline at T60.

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TABLE 1. PHYSIOLOGICAL STATUS OF RATS DURING EXPERIMENT

Variable	Group	Baseline	Posttrauma (min)			
			5	15	30	60
Body temperature (°C)	C ^a	37.0 ± 0.1 ^b	37.0 ± 0.1	37.4 ± 0.2	37.2 ± 0.1	37.0 ± 0.3
	T	37.0 ± 0.1	37.1 ± 0.1	37.2 ± 0.1	37.2 ± 0.1	37.2 ± 0.1
pH	C	7.38 ± 0.01	7.38 ± 0.01	7.36 ± 0.01	7.35 ± 0.01	7.35 ± 0.01
	T	7.37 ± 0.01	7.36 ± 0.01	7.39 ± 0.01	7.36 ± 0.01	7.36 ± 0.01
PCO ₂ (mm Hg)	C	39.4 ± 0.7	38.3 ± 0.9	40.2 ± 1.1	39.9 ± 1.0	37.7 ± 0.8
	T	40.2 ± 0.7	39.8 ± 1.0	40.3 ± 1.0	39.2 ± 1.3	39.4 ± 0.9
PO ₂ (mm Hg)	C	94 ± 5	89 ± 6	84 ± 4	89 ± 9	98 ± 13
	T	99 ± 4	98 ± 7	87 ± 6	109 ± 5	104 ± 13
Hb (g/dl)	C	11.2 ± 0.4	11.0 ± 0	10.4 ± 0.3	10.7 ± 0.4	10.5 ± 0.5
	T	11.7 ± 0.4	—	10.2 ± 0.3	9.4 ± 1.8	9.8 ± 0.7
Body weight	C	440 ± 06				
	T	456 ± 12				

^apH, arterial blood acidity; PCO₂, arterial carbon dioxide partial pressure; PO₂, arterial oxygen partial pressure; Hb, hemoglobin concentration in arterial blood; C, control group; T, trauma group.

^bData are presented as mean ± SEM.

There were no significant differences between the two groups in any of these parameters. Changes over time in each group were only statistically significant for the reduced Hb in trauma group at T60 ($p=0.04$ vs baseline).

Organ Blood Flow Changes

There were no significant differences between the control and the injury groups in baseline organ blood flows except splenic blood flow (Table 2). Organ blood flow responses to TBI are shown in Figure 2 and Table 3. Organ blood flows remained constant over time in the control group.

In the trauma group, blood flows remained constant or increased for the first 30 min in most organs and then decreased progressively over time. There was a heterogeneity in blood flow responses to brain injury among different organs and even different parts of the same organ. Total renal blood flow was significantly reduced (intragroup and intergroup $p<0.025$). This decrease was asymmetrical. At T60, left renal blood flow decreased ($p<0.025$) more than right renal blood flow ($p>0.05$). Hepatic arterial blood flow increased 50% at T5 (intergroup $p=0.05$) and 40% at T15, with the most pronounced rise in the right hepatic arterial blood flow. As shown in Table 3, the right hepatic arterial blood flow increased almost 70% at T5 (intergroup $p<0.025$). Hepatic arterial blood flow declined in the last 30 min after injury to about 70% of baseline at T60. A similar biphasic pattern was seen with splenic blood flow changes (Fig. 2), showing a 50% decrease at T60 ($p<0.05$). Pancreatic and total coronary blood flow did not change over time. Pulmonary (bronchial arterial) blood flow showed a 30% increase at T5 and then decreased progressively to 40% of preinjury values at T60 (intragroup and intergroup $p<0.025$).

DISCUSSION

Microsphere Technique

The microsphere technique has been validated for simultaneous measurements of cardiac output and organ blood flows in rats (Sasaki and Wagner, 1971; Rakusan and Blahitka, 1974; Tsuchiya et al., 1978; Malik et al., 1976; Flaim and Minter, 1980; Stanek et al., 1983; Rothwell and Stock, 1984; Proctor and Busija, 1985; Lee et al., 1986). The four major concerns over the

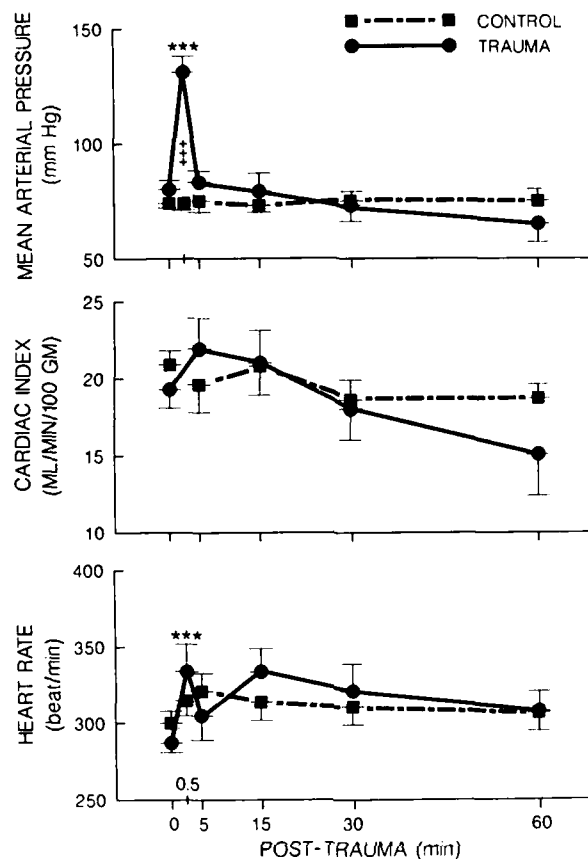


FIG. 1. The hemodynamic responses to fluid percussion brain injury over 1 h. There were significant but transient increases in mean arterial blood pressure and heart rate immediately after the percussion. Cardiac output was slightly elevated or maintained for the first half hour. A hypotensive trend with a declining cardiac output followed. Bars indicate standard error of the mean. Intragroup comparison (vs baseline): *** $p < 0.01$; intergroup comparison: +++, $p < 0.01$.

use of the microsphere method include (1) uniform mixing of microspheres with blood, (2) complete extraction of microspheres from the blood by the tissues, (3) lodging of sufficient particles in the organs of interest to provide accurate measurement, and (4) absence of a significant effect of injected microspheres on systemic or local hemodynamics.

Left atrial injection of spheres achieves better mixing than ventricular or aortic injection (Kajhara et al., 1968; Stanek et al., 1983). Both absolute values and percent changes in our study indicated that mixing was adequate, since there were no appreciable differences between the left and right renal blood flows in the control group throughout the entire time course nor in the trauma group at the baseline.

The size of microspheres used in other studies to measure organ blood flow varies from 15 to 50 μm . Using larger microspheres has the advantage of minimizing the possibility of shunting and recirculation. Experiments using a sphere population with a wide range of diameters from 5 to 50 μm showed that spheres greater than 15- μm diameter did not appear in the venous blood, whereas smaller spheres recirculate (Maxwell et al., 1985). According to Rothwell and Stock (1984), less than 5% of the total number of 15- μm microspheres are shunted to the lungs. Our values (6.3% for the control group and 6.5% for the trauma group) were slightly higher (Buckberg et al., 1971). Buckberg et al. advocate the use of 15- μm microspheres because they

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TABLE 2. BASELINE ORGAN BLOOD FLOW (ML/MIN/100 G, MEAN $\pm$ SEM)

Organ	Group ^a	
	Control (n=20)	Trauma (n=17)
Kidney		
Left	421.1 $\pm$ 16.0	458.2 $\pm$ 30.3
Right	434.6 $\pm$ 25.3	487.4 $\pm$ 36.1
Total	428.0 $\pm$ 19.7	472.2 $\pm$ 31.8
Liver		
Middle lobe	30.0 $\pm$ 3.2	34.3 $\pm$ 3.2
Left lobe	30.0 $\pm$ 3.1	34.0 $\pm$ 3.3
Right lobe	41.2 $\pm$ 3.6	48.2 $\pm$ 6.5
Total	32.7 $\pm$ 3.1	37.2 $\pm$ 3.7
Spleen	341.0 $\pm$ 38.4*	597.8 $\pm$ 53.3
Pancreas	41.4 $\pm$ 2.7	33.6 $\pm$ 3.5
Heart		
Left	310.5 $\pm$ 23.7	320.6 $\pm$ 31.7
Right	229.3 $\pm$ 19.0	263.9 $\pm$ 27.9
Total	285.1 $\pm$ 21.4	304.4 $\pm$ 29.3
Lung		
Left	240.5 $\pm$ 23.0	239.7 $\pm$ 38.1
Right	278.1 $\pm$ 34.2	277.6 $\pm$ 48.1
Total	261.1 $\pm$ 28.5	261.8 $\pm$ 43.2

^aIntergroup comparison: * $p < 0.01$.

have rheological properties similar to erythrocytes, they occlude less of the vascular bed, and they are less likely to affect local hemodynamics.

The precision of the microsphere method depends on the number of microspheres in the reference and tissue samples (Buckberg et al., 1971; Dole et al., 1982). It has been calculated theoretically and confirmed experimentally that errors due to nonrandom distribution are minimized if at least 400 spheres are present in each tissue and reference sample (Buckberg et al., 1971). We injected approximately 250,000 microspheres for each determination. This number yielded approximately 2000 beads in each reference sample and more than 400 microspheres in each organ studied.

Stanek et al. (1983) demonstrated that up to 360,000 microspheres per injection and up to 1,440,000 microspheres per rat can be injected without significant hemodynamic consequences. We injected considerably fewer beads, and we observed no appreciable changes in monitored hemodynamic parameters.

The baseline cardiac index in the present study was 20.9 ± 0.9 ml/min/100 g for the control group and 19.3 ± 1.2 ml/min/100 g for the trauma group. These values are within the reported ranges of 20.4 to 32 ml/min/100 g using the Fick method and indicator-dilution techniques (Popovic and Kent, 1964; Dawson et al., 1968). Our control blood flow values for the kidney, liver, pancreas, and lungs agree with reported data under similar conditions (Tsuchiya et al., 1978; Flaim and Minter, 1980; Stanek et al., 1983; Rothwell and Stock, 1984; Proctor and Busija, 1985).

Head Trauma

Secondary injury following head trauma includes all events other than the actual mechanical injury sustained at impact. This secondary injury may be divided into systemic and intracranial insults (Miller and Becker, 1982). Systemic insults include hypoxemia, anemia, hypertension,

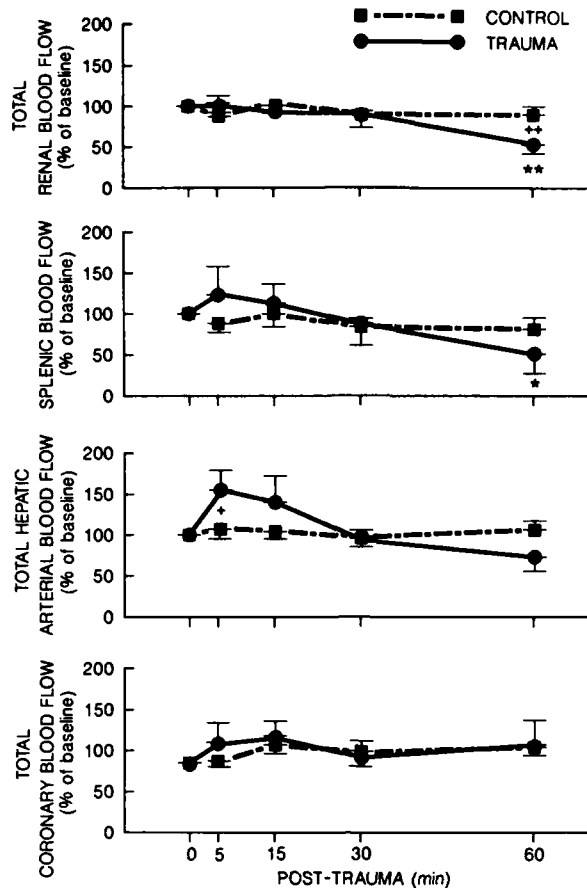


FIG. 2. Organ blood flow responses to fluid percussion brain injury over 1 h. Total renal blood flow exhibited progressive decrease over time, with a 50% drop at T60. Splenic blood flow was maintained in the initial epoch and declined in the later phase, with a 50% decrease by the end of the experiment. There were 50% and 40% increases in total hepatic arterial blood flow at T5 and T15, respectively. Substantial decreases were observed during the rest of the observation period. Total coronary arterial blood flow was well maintained for the entire observation period. Intragroup comparison (vs baseline): * $p < 0.05$, ** $p < 0.025$; intergroup comparison: + $p < 0.025$.

hypotension, hypercarbia, hyperthermia, and electrolyte imbalance (Miller and Becker, 1982; Matjasko, 1986). The most significant advance in managing severe head trauma in the last quarter-century has been the recognition of the importance of secondary insults to patient outcome.

The physiological response to traumatic brain injury involves immediate and major hemodynamic changes. Immediate systemic hypertension always occurs with concussion (Rosner et al., 1984). In the present study, moderate fluid percussion brain injury produced transient but significant hypertension, followed by a progressive hypotension. The transient hypertensive response immediately following TBI in our study was similar to other reports of experimental head injury (Dixon et al., 1987; Shapira et al., 1988; Sullivan et al., 1976).

The coexistence of a brain injury and systemic derangement is a potentially lethal combination. MAP declined steadily after the initial hypertensive response in our trauma group. Although there was no significant difference in MAP between baseline and T60, the steady decrease suggests that MAP would have fallen significantly had we continued the studies for longer periods. Posttraumatic hypotension has been observed in a number of experimental models of TBI, including compression (Meyer et al., 1970), missile injuries (Crockard et al.,

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TABLE 3. ORGAN BLOOD FLOW RESPONSES TO TRAUMATIC BRAIN INJURY (% OF BASELINE)

Organ	Group	Postinjury (min)			
		5	15	30	60
Kidney					
Left	C ^a	94.1 ± 4.6	97.9 ± 06.4	117.6 ± 30.2	88.3 ± 11.3
	T	102.1 ± 8.5	90.7 ± 10.5	86.8 ± 15.3	48.3 ± 07.3**
Right	C	92.2 ± 7.5	105.8 ± 15.1	108.0 ± 19.0	91.8 ± 08.7
	T	105.3 ± 9.0	93.6 ± 07.3	91.5 ± 17.8	56.6 ± 13.9
Liver					
Middle	C	108.1 ± 13.4	103.8 ± 10.1	89.2 ± 09.0	108.5 ± 11.1
	T	149.9 ± 28.6	137.6 ± 36.5	95.3 ± 14.3	79.3 ± 22.3
Left	C	109.8 ± 11.9	106.4 ± 09.1	99.8 ± 10.6	105.5 ± 11.1
	T	156.4 ± 23.0	144.3 ± 33.3	96.0 ± 13.7	62.4 ± 11.9
Right	C	101.9 ± 10.4	100.6 ± 09.0	98.1 ± 09.2	105.1 ± 09.5
	T	167.7 ± 25.5 ⁺⁺	138.1 ± 31.5	103.0 ± 14.5	78.4 ± 18.7
Pancreas	C	106.6 ± 7.6	103.4 ± 08.9	100.9 ± 8.0	95.3 ± 08.1
	T	108.8 ± 9.6	95.9 ± 10.8	88.9 ± 6.2	99.3 ± 17.1
Heart					
Left	C	102.2 ± 07.6	125.3 ± 13.2	115.9 ± 15.2	113.5 ± 10.8
	T	126.4 ± 25.4	131.2 ± 19.1	107.6 ± 10.9	116.9 ± 28.7
Right	C	102.4 ± 06.6	107.9 ± 07.7	109.9 ± 07.8	130.8 ± 10.6
	T	133.9 ± 19.9	140.1 ± 13.0	112.3 ± 16.2	140.8 ± 35.3

^aC, control group, T, trauma group.

⁺⁺. $p < 0.025$ (intergroup comparison).

^{**} $p < 0.025$ (vs baseline).

1977), and fluid percussion injury (McIntosh et al., 1987; Dixon et al., 1987). Hypotension following TBI has been recognized as a major secondary complication following severe clinical closed head injury (Eisenberg et al., 1983). Overall, 13–15% of head-injured patients experience shock in varying degrees of severity (Miller and Becker, 1982). These patients are doubly at risk, since systemic hypotension and elevated ICP lower cerebral perfusion pressure, and the traumatized brain does not autoregulate well (Lewelt et al., 1980). Experimental studies indicate that cerebral oxygen delivery is compromised seriously if TBI is followed by even moderate hemorrhagic hypotension (Dewitt et al., 1989a,b). Furthermore, TBI itself will produce a progressive decline of cerebral blood flow immediately after the injury in rats (Yuan et al., 1988; Yamakami and McIntosh, 1989). Hypotension in association with severe head injury will result in a significant increase in mortality to 83%, as opposed to 45% when head injury is unassociated with shock (Newfield et al., 1980).

Head injury may impair cardiac function in humans. Experimental TBI produced a steady decline in cardiac index after a slight rise immediately following TBI (Fig. 1). Of 30 patients with severe head injury, 28 demonstrated an elevation in the myocardial isoenzyme CK-MB (Hackenberry et al., 1982), suggesting ongoing myocardial cell injury possibly resulting from sustained sympathetic hyperactivity (Hackenberry et al., 1982; Cruickshank et al., 1988). Clifton et al. (1981) noted the presence of subendocardial hemorrhages in 50% of autopsies performed on patients who died of severe head injury. These findings are similar to the pathological findings in animals infused with high levels of catecholamines (Reichenbach and Benditt, 1970). Consistent with these findings is the evidence that epinephrine and norepinephrine are significantly elevated after fluid percussion TBI (Rosner et al., 1984).

The present study demonstrated that fluid percussion brain injury produced blood flow decreases in most organs, especially in the kidneys and the spleen. However, during the initial period (up to 30 min), blood flow in most organs appeared to be normal or increased. This is

quite different from the pattern of cerebral blood flow that showed progressive decline following fluid percussion brain injury (Yuan et al., 1988; Yamakami and McIntosh, 1989). The pattern of the organ blood flow changes was somewhat consistent with the pattern of changes in systemic blood pressure and cardiac output. Therefore, it appears that the preservation of normal organ blood flow in the very early posttraumatic period is the consequence of systemic hemodynamic compensation, and the later decreases in organ blood flow could be, in part, attributable to reduced cardiac output and mean arterial blood pressure. Changes in organ blood flows were neither uniform nor proportional to the decreases in blood pressure and the cardiac output. Thus, blood flow redistribution may have occurred in the posttraumatic period, with the greatest vasoconstriction in the kidneys and the spleen, less in the liver, and no substantial changes in the heart and the pancreas. These changes coincide with the redistribution of cardiac output observed in experimental hemorrhagic shock (Newfield et al., 1980).

Although we did not monitor sympathetic efferent nerve discharge nor plasma catecholamine levels, the hypertensive response that we observed and catecholamine release reported by other investigators (Clifton et al., 1983; Robertson et al., 1984; Rosner et al., 1984; Hamill et al., 1987; Woolf et al., 1987; Cruickshank et al., 1988) indicate a massive sympathetic response to TBI. Thus, elevated catecholamine levels were likely present throughout the observation period in our study. Since sympathetic vasoconstrictor fibers are distributed unevenly to all segments of the circulation (Guyton, 1986), the net effects of sympathoadrenal hyperactivity on different effector organs may be determined by the distribution density and type of sympathetic nerve endings, the ratio of epinephrine and norepinephrine in the circulation, and the dominant type of receptors in a particular organ. There are more sympathetic vasoconstrictor fibers in the kidneys, spleen, and digestive system than in the heart and the brain (Guyton, 1986). Furthermore, renal arterial smooth muscles possess both α - and β -adrenergic receptors with α -type predominating (Yao et al., 1987). In the intact cardiac circulation, sympathetic activation dilates coronary arteries because myocardial metabolism increases secondary to the increase in heart rate and contraction (Guyton, 1986), and β_2 -receptor dominates in the resistance vessels of the coronary circulation (Bevan et al., 1980). Thus, the net result of sympathoadrenal hyperactivity is a widespread but selective vasoconstriction, whereby flow is decreased through certain regions of the circulation, especially in kidneys and splanchnic organs but not to the heart (Kaihara et al., 1969). Therefore, as indicated in the present study, the organ blood flow response to traumatic brain injury is heterogeneous. The perfusion to the heart and pancreas is preserved when blood flow to other vital organs is reduced substantially.

These findings have physiological and clinical implications. Our study suggests that coronary perfusion inadequacy is not an obligatory etiological factor in head trauma-induced cardiac dysfunction. The diminution in cardiac pump function is not simply a consequence of global myocardial hypoperfusion. In fact, a recent study demonstrated that sympathetic nervous system overreaction decreases myocardial contractility by catecholamine-derived oxidant injury, causing an excitation-contraction coupling derangement (Chen and Downing, 1990). Therefore, restoration of the optimal myocardial cellular or subcellular environment should be given a higher priority than just maintenance of coronary blood flow, which has been shown in our study unlikely to be reduced in response to TBI. It is apparent that improvement of organ blood flow following TBI should be emphasized on renal and hepatic systems. As indicated in our study, these two vital organs sustain a reduction in blood flow after TBI. With decreased blood perfusion, dysfunction of kidneys and other affected organs eventually may occur (Klin et al., 1983; Bourguignat et al., 1983; Yao et al., 1987). In order to treat systemic effects of head injury and improve the outcome, maintaining a sufficient organ blood flow to avoid secondary organ failure is vitally important. Our data about peripheral circulation following TBI can be a basis for considering an appropriate strategy in managing this situation.

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CONCLUSIONS

The most consistent systemic response to fluid percussion TBI in rats is an immediate and transient arterial hypertension followed by a hypotension. Blood flow to most organs is maintained or increased for approximately 30 min and then is gradually decreased. The responses of organ blood flows to TBI are heterogeneous. Reduced organ blood flows are most marked in kidneys and spleen and less severe in liver. The reduced cardiac output is redistributed to favor blood flows through the heart and pancreas.

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