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Cardiac output and muscle blood flow during rest-associated apneas of elephant seals

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Abstract

In order to evaluate hemodynamics and blood flow during rest-associated apnea in young elephant seals (*Mirounga angustirostris*), cardiac outputs (CO, thermodilution), heart rates (HR), and muscle blood flow (MBF, laser Doppler flowmetry) were measured. Mean apneic COs and HRs of three seals were 46% and 39% less than eupneic values, respectively (2.1±0.3 vs. 4.0±0.1 mL kg^{-1} s^{-1}, and 54±6 vs. 89±14 beats min^{-1}). The mean apneic stroke volume (SV) was not significantly different from the eupneic value (2.3±0.2 vs. 2.7±0.5 mL kg^{-1}). Mean apneic MBF of three seals was 51% of the eupneic value. The decline in MBF during apnea was gradual, and variable in both rate and magnitude. In contrast to values previously documented in seals during forced submersions (FS), CO and SV during rest-associated apneas were maintained at levels characteristic of previously published values in similarly-sized terrestrial mammals at rest. Apneic COs of such magnitude and incomplete muscle ischemia during the apnea suggest that (1) most organs are not ischemic during rest-associated apneas, (2) the blood O_2 depletion rate is greater during rest-associated apneas than during FS, and (3) the blood O_2 store is not completely isolated from muscle during rest-associated apneas.

Keywords: Apnea; Cardiac output; Heart rate; Laser Doppler flow; Muscle; Seal; Stroke volume; Temperature

1. Introduction

Cardiac output (CO), stroke volume (SV), and muscle blood flow (MBF) of seals are important parameters in the modeling of O_2 store depletion during dives (Scholander, 1940; Davis and Kanatous, 1999). However, there have been few investigations of these parameters because of the difficulty of obtaining such measurements in these animals. Most data have been obtained during forced submersions (FS), in which, COs and SVs have varied between 0.2 and 0.8 mL $kg^{-1}s^{-1}$, and 0.8–1 mL kg^{-1}, respectively (Murdaugh et al., 1966; Sinnett et al., 1978; Zapol et al., 1979; Blix et al., 1983; Thornton et al., 2005). As might be expected due to the extreme bradycardia during FS, such values are less than typical values (CO: 1.5–2 mL kg^{-1} s^{-1}, SV: 1.5–2 mL kg^{-1}) of terrestrial mammals at rest (Taylor et al., 1987). In addition, the severe peripheral vasoconstriction which accompanies the bradycardia during FS abolishes MBF (Zapol et al., 1979; Blix et al., 1983). However, in harbor seals at rest (*Phoca vitulina*), apneic CO and SV are near typical mammalian values; during eupnea, CO is elevated (Ponganis et al., 1990). Similarly, during submergence of flume-swimming harbor seals, CO and SV are near values of other mammals at rest, and, during eupnea, they are increased, on average, three-fold, and two-fold, respectively, above values during submersion (Ponganis et al., 1990). In addition, MBF is greater during submersions after seals undergo a submersion training protocol than during naïve FS (Jobsis et al., 2001).

These findings indicate that it is essential to determine hemodynamics and MBF if we are to model O_2 transport and depletion during spontaneous apneas of seals (Ponganis et al., 2002). In addition to apnea during diving, spontaneous, rest-associated apneas are common during the terrestrial, on-shore time of seals (Bartholomew, 1954; Blackwell and LeBoeuf, 1993; Castellini et al., 1994b). Indeed, during sleep in the

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northern elephant seal (*Mirounga angustirostris*), apnea can comprise up to 60% of time (Blackwell and LeBoeuf, 1993). Because of the frequency of these apneas, the associated changes in HR (Castellini et al., 1994a,b; Andrews et al., 1997), and the coupling of HR with organ perfusion and oxygen consumption, it is important to know the magnitude of hemodynamic alterations between apnea and eupnea in order to (1) fully understand the on-shore physiology of the seal, (2) assess the management and depletion of O_2 stores during such breath holds, and (3) perhaps better interpret the results of many on-shore physiological/metabolic studies (Castellini et al., 1987, 1994a; Houser and Costa, 2001a; Houser et al., 2001b; Noren, 2002; Ortiz et al., 2002, 2003; Ponganis et al., 2002). The latter is important because kinetic modeling is influenced by the vascular distribution of tracers used in many of these studies. Therefore, we investigated CO, SV, and MBF during rest-associated apneas of young elephant seals (*Mirounga angustirostris*).

2. Materials and methods

Juvenile elephant seals (*Mirounga angustirostris* Gill, 4–6 mo old), obtained from Sea World's Rehabilitation Program, were maintained at the ring tank facility at Scripps Institution of Oceanography during one- to two-month periods and then released at sea. They were maintained on a daily diet of smelt (5–10% of body mass) and vitamin supplements. These seals had previously beached themselves during their first trip to sea, and had been successfully rehabilitated at the Sea World program. All studies and procedures were approved in a UCSD Animal Subjects Committee protocol, and a federal marine mammal permit (#732-1487).

Cardiac output studies were conducted in three seals of 66–69 kg body mass. Catheterizations were conducted under general anesthesia maintained with isoflurane (1–2%)–oxygen anesthesia after mask induction and intubation. Pulmonary artery (PA) catheterization was performed percutaneously with a 7.5-Fr. Swan Ganz VIP catheter (Baxter, Edwards Life Sciences, Irvine, CA, USA), and introducer (9 Fr., 13 cm; Cook, Bloomington, IN, USA) with fluoroscopic guidance via an upper lumbar, paravertebral approach (Elsner et al., 1971). Catheter port positions were confirmed by characteristic pressure traces in the heart, and PA. Intravascular pressures were transduced with a Hewlett-Packard blood pressure transducer system (H-P 78304A/78205D), calibrated daily by manometer with transducers at the level of the seal's heart. The extradural vein (EDV) was also catheterized percutaneously with 14-g, 13-cm Angiocath catheter (Becton Dickinson, Sandy, UT, USA). Catheters were affixed to the fur with neoprene patches and Loctite glue.

For MBF studies, three other seals (70–90 kg) were sedated with 1 mg kg^{-1} intramuscular ketamine. A Transonic (Ithaca, NY, USA) laser Doppler flow (LDF) probe (Type N), connected to a Transonic ALF 21 Flowmeter, was then inserted percutaneously with local skin anesthesia (1% xylocaine) into the longissimus dorsi–iliocostalis muscle complex above the iliac crest, and affixed to the fur with neoprene and Loctite. An EDV catheter was also inserted under local anesthesia. The LDF probe response was also evaluated at no flow by insertion into muscle of a seal carcass available through the Sea World Rehabilitation Program.

For all studies, seals were equipped with transthoracic skin electrocardiogram (ECG) electrodes (attached with Loctite glue) connected to an ECG/impedance monitor (RespI/ECG, UFI, Morro Bay, CA, USA).

Prophylactic cephalexin was administered intravenously (1 g every 6 h) while the seals were instrumented, and then orally (250 mg four times day^{-1}) for two days afterward. Catheters, probes, and ECG electrodes were removed after 0.5 mg kg^{-1} ketamine intravenous sedation.

After extubation, seals were placed unrestrained but restricted by a plastic pipe cage. The animals were left undisturbed, usually with hose water running over the bottom of the cage. A blind along one side of the cage allowed access to catheters. After four to six hours of recovery after anesthesia, hemodynamic and MBF data were collected when spontaneous, long apneas occurred in the seals.

Electrocardiogram and impedance outputs were recorded on a Dell Dimension 8100 personal computer with AcqKnowledge software and a Biopac MP100 System interface (Santa Barbara, CA, USA). The LDF output was recorded with an Axon Instruments A-D interface (TL-2) and Axotape software (Axon Instruments, Union City, CA, USA). Thermodilution COs were determined as previously described (Ponganis et al., 1990) with the use of a COM2 cardiac output computer (Baxter, Edwards Life Sciences, Irvine, CA, USA) and 10 mL ice cold saline injections into the right atrial port of the Swan–Ganz catheter.

Data were processed, graphed, and statistically analyzed with Excel, Origin, and SPSS software. The grand means of individual variables in all seals were analyzed for apneic versus eupneic differences with two sample *t*-tests, unless otherwise noted.

Table 1
Heart rate, cardiac output, stroke volume and pulmonary artery temperature during eupnea and apnea

Seal	BM (kg)	Heart rate (beats min^{-1})		Cardiac output (mL kg^{-1} s^{-1})		Stroke volume (mL kg^{-1})		PA temperature (°C)		*N*		DUR (min)
		E	A	E	A	E	A	E	A	E	A	
Z	69	105 (6)	59 (5)	4.1 (1.4)	2.4 (0.6)	2.2 (0.9)	2.5 (0.6)	36.7 (0.4)	36.6 (0.4)	7	6	7.8 (1.3)
K	66	84 (12)	57 (7)	3.9 (0.9)	2.0 (0.4)	2.8 (0.5)	2.1 (0.3)	36.4 (0.1)	36.4 (0.2)	16	21	4.8 (1.1)
W_7	66	78 (9)	47 (4)	4.0 (0.6)	1.9 (0.6)	3.1 (0.7)	2.3 (0.6)	36.5 (0.2)	36.5 (0.2)	9	7	6.3 (2.0)
Grand Mean		89 (14)	54*(6)	4.0 (0.1)	2.1* (0.3)	2.7 (0.5)	2.3 (0.2)	36.5 (0.2)	36.5 (0.1)			

Values are means and (S.D.).
Abbreviations: BM body mass, PA pulmonary artery, DUR duration of apnea, E eupnea, A apnea, *significant difference ($P<0.05$) between eupnea and apnea.