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Left-ventricular performance in man during breath-holding and simulated diving

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Gross, P. M., R. L. Terjung, and T. G. Lohman. 1976. Left-ventricular performance in man during breath-holding and simulated diving. Undersea Biomed. Res. 3(4):351–360.—We measured left-ventricular (LV) systolic time intervals (STI) to determine whether breath-holding and simulated diving evoke a depression of LV performance in man similar to that previously demonstrated in natural divers. Records of STI were obtained by a noninvasive procedure in 15 adult males who had breath-holding diving experience during supine rest, at 30 and 60 s of simple breath-holding (BH) and at 30 and 60 s of BH combined with cold, wet facial stimulation (FS). Changes in both BP and HR during FS reflected cardiovascular behavior typical of simulated diving. The isovolumic contraction period increased 13% and 31% after 60 s of BH and FS, respectively. LV ejection time shortened by 30 ms during BH and by 37 ms during FS. These measurements of STI represent the first description of cardiac cycle components during the human diving response. The alterations in STI suggest that a reduction in LV performance, as seen by a decreased rate of preejection pressure development and a diminished stroke volume, had occurred during the apneic maneuvers. In addition, there was a trend in these measures indicating that FS potentiated the response over that which occurred during BH. Thus, it appears that man exhibits a depression of LV performance during simulated diving similar to that found in natural divers.

apnea
diving response
systolic time intervals

Profound changes in cardiovascular function enable diving species to endure extended periods of apnea during submersion (Andersen 1966; Strauss 1970). Distinct features of this circulatory adjustment to breath-hold diving are extensive constriction of peripheral resistance vessels and pronounced bradycardia with a corresponding decrease in cardiac output. In addition to the bradycardia, there is evidence for a negative inotropic effect on ventricular performance during diving (Folkow and Yonce 1967; Ferrante and Opdyke 1969; Folkow, Lisander, and Oberg 1971). These adjustments during a dive restrain blood flow to the periphery while maintaining perfusion of the heart and brain.

Although the diving response is less well-developed in man, bradycardia and peripheral vasoconstriction have been observed during breath-holding and simulated diving (Elsner and Scholander 1965; Heistad, Abboud, and Eckstein 1968; Folinsbee 1974). Evidence for changes

in cardiac output and ventricular performance in apneic man, however, remains equivocal. Hong, Lin, Lally, Yim, Kominami, Hong, and Moore (1971) and Paulev and Wetterqvist (1968) found no significant changes, whereas Skillman, Olson, Lyons, and Moore (1967) and Kawakami, Natelson, and DuBois (1967) found large decreases in cardiac output and stroke volume during apnea and simulated diving. Clear interpretation of these conflicting reports of cardiac function during apnea may be confounded by the use of invasive techniques that can elevate sympathetic activity; thus, atraumatic measurements may better reflect subtle changes in ventricular performance during breath-holding.

Externally recorded systolic time intervals (STI) have been recently validated as sensitive and reliable indices of left-ventricular function in animals and man (Weissler, Harris, and Schoenfeld 1969; Metzger, Chough, Kroetz, and Leonard 1970; Martin, Shaver, Thompson, Reddy, and Leonard 1971; Van der Werf, Piessens, Kesteloot, and DeGeest 1975). These simultaneous measurements of the electrocardiogram (ECG), heart sounds, and central arterial pressure waves permit assessment of cardiac-cycle intervals that demonstrate significant predictive relationships with various indices of cardiac pump function, e.g., the rate of rise of isovolumic left-ventricular pressure (dP/d*t*) (Martin et al. 1971; Ahmed, Levinson, Schwartz, and Ettinger 1972), left-ventricular ejection fraction (Garrard, Weissler, and Dodge 1970; Ahmed et al. 1972), stroke volume (Weissler, Peeler, and Roehll 1961; McConahay, Martin, and Cheitlin 1972) and cardiac output (Weissler, Harris, and White 1963).

In measuring STI, we were able to document previously unreported changes in cardiac-cycle components of man during breath-holding. Additionally, we designed the present study to evaluate alterations in STI during breath-holding and simulated diving to determine if the characteristic depression of left-ventricular function in diving animals is engendered in man.

METHODS

Recordings of noninvasive STI were made from supine, fasting subjects under each of five conditions during an experiment: rest, 30 s of continuous simple breath-holding (BH), 60 s of continuous BH, 30 s of continuous BH with facial stimulation (FS), and 60 s of continuous FS. The BH and FS treatments were separated by an interval of approximately 15 min. During this time we monitored the subject's HR periodically to assure resumption of resting rate before beginning FS. Our procedure for FS was a modification of a technique reported by Whayne and Killip (1967) and consisted of placing a wet, ice-packed towel (towel–face interface temperatures = 4–9°C) over the subject's face during a breath-hold at approximately 80% of inspiratory capacity. Subjects were encouraged to relax against the closed glottis to avoid a Valsalva maneuver. The above experiment was repeated for each individual at least 24 hours later at the same time of day.

Fifteen males (mean age $\pm$SE = 22.7 $\pm$ 1.0 yr), who were experienced breath-holders (skin and scuba divers), served as subjects for this study. They were in good health and had no known history of cardiac disease.

The durations of the phases of the cardiac cycle were measured from simultaneous recordings of the ECG, phonocardiogram (PCG), and carotid arterial-pulse tracing by the method of Weissler, Harris, and Schoenfeld (1968) as described by Tavel (1972). The records were obtained at a paper speed of 100 mm/s on a multichannel direct-writing recording system (Hewlett—Packard Thermal-tip, Model 7754A).

The ECG signal was received from standard bipolar limb leads (usually lead II) or from the augmented unipolar limb lead, aVF. Heart sounds were recorded from a piezoelectric microphone (E & M Instruments), strapped firmly over the upper precordium to the left of the

sternum. The exact position of the microphone was critical for each individual and was determined by its ability to clearly detect the initial high-frequency vibrations of the first and second heart sounds. Effective lower cutoffs on the filtration range for the PCG were between 15 and 150 Hz, while the high pass was usually set at 300 Hz. The signal of the carotid arterial pulsation was recorded from a Beckman crystal transducer through a filtration range of 0.5 to 300 Hz. The transducer was manually held in place over the left carotid artery by an investigator.

The following phases of the cardiac cycle were determined according to definitions by Weissler et al. (1968): (*1*) total electromechanical systole (QS_2) was measured from the onset of the QRS complex of the ECG to the aortic-valve component of the second heart sound; (*2*) left ventricular ejection time (LVET) was measured from the beginning of the upstroke to the trough of the dicrotic notch on the carotid arterial-pulse tracing; (*3*) from the foregoing components, the preejection period (PEP) was derived by subtracting LVET from QS_2; (*4*) mechanical systole (S_1S_2) was determined as the interval between the mitral-valve component of the first heart sound and the aortic-valve component of the second heart sound; (*5*) electromechanical lag (QS_1) was determined as the difference between QS_2 and S_1S_2; (*6*) isovolumic contraction period (IVCP) was derived by subtracting LVET from S_1S_2.

Individual STI were corrected for HR using the regression equations of Weissler et al. (1968). The duration of IVCP was left uncorrected inasmuch as it demonstrates no significant regression with respect to HR (Weissler et al. 1968). The ratio of PEP to LVET (PEP:LVET) was calculated directly from the uncorrected means for these two intervals. HR was determined from the R–R intervals of the ECG.

We measured blood pressure (BP) externally from the brachial artery either automatically (Electrosphygmograph, E & M Instruments) or manually at rest and during the last few seconds of each apneic maneuver. BP measurements were made simultaneously with recordings of STI.

The data were analyzed using a single-factor analysis of variance in a repeated-measures design. Upon finding a significant treatment effect, we used Tukey's multiple comparison test to determine statistical significance ($P < .05$) between any two treatment groups (Steel and Torrie 1960).

RESULTS

Reproducibility of measurements

Comparisons of results obtained from duplicated experiments conducted on different days demonstrate the reproducibility of our measurements (Table 1). To test for day-to-day differences, we made paired comparisons (Student's t test) and found no day effect in any measurement ($P > .05$). Therefore, the analyses of BH and FS responses were performed on averaged data collected from both days.

Additionally, the STI obtained in our subjects at rest (Table 2) are similar to those reported from other laboratories for normal man (Weissler et al. 1968; Stafford, Harris, and Weissler 1970; McConahay et al. 1972).

Circulatory responses

In our studies, we were able to demonstrate (Fig. 1) the typical human circulatory response to simulated diving (Kawakami et al. 1967; Heistad et al. 1968; Folinsbee 1974). A marked

TABLE 1
Reproducibility of day-to-day measurements

		HR (beats/min)	QS_2 (ms)	LVET (ms)	S_1S_2 (ms)	BP_s (mm Hg)	BP_d (mm Hg)
Rest	*Day 1*	64±2	529± 5	400± 4	471± 5	117±3	72±2
	Day 2	65±2	532±7	402± 6	467± 5	116±2	72±1
BH_{60}	*Day 1*	62±3	512±11	369±11	447±12	131±4	89±3
	Day 2	62±3	516± 9	372±10	448±12	126±2	85±2
FS_{60}	*Day 1*	55±2	508±12	360±11	448±12	136±3	92±2
	Day 2	57±3	514±12	366±11	451±13	128±2	92±2

Mean values ± SE for 15 subjects. Systolic time intervals were corrected for HR according to Weissler et al. (1968). BH_{60} = 60-s breath-hold; FS_{60} = 60-s breath-hold with cold, wet facial stimulation; BP_s = systolic blood pressure; BP_d = diastolic blood pressure. See text for other abbreviations.

TABLE 2
Effects of breath-holding with and without cold, wet facial stimulation on systolic time intervals, heart rate, and blood pressure

Conditions	HR (beats/min)	BP_s (mm Hg)	BP_d (mm Hg)	QS_2 (ms)	QS_1 (ms)	S_1S_2 (ms)	LVET (ms)	IVCP (ms)	PEP (ms)	PEP:LVET
Rest	64±2	117±2	72±2	530±2	67±2	469±3	401±3	62±2	129±1	0.355±0.006
BH_{30}	64±3	--	--	506±5	71±2	442±5	371±6	65±3	136±2	0.426±0.015
BH_{60}	62±3	129±3	87±2	514±5	73±4	447±6	371±5	70±3	144±2	0.452±0.014
FS_{30}	64±3	--	--	510±7	70±3	446±6	366±6	74±3	144±2	0.465±0.014
FS_{60}	56±2	132±2	92±2	512±6	67±2	450±6	364±5	81±3	148±2	0.471±0.011
$\bar{x}_d$*	5	4	3	12	6	13	11	7	6	0.032

Mean values ± SE for 15 subjects. Systolic time intervals (excluding IVCP and PEP:LVET) were corrected for HR using the regression equations of Weissler *et al.* (1968). BH_{30} and BH_{60} = 30- and 60-s breath-holds. FS_{30} and FS_{60} = 30- and 60-s breath-holds with cold, wet facial stimulation; BP_s = systolic blood pressure; BP_d = diastolic blood pressure. See text for other abbreviations.

*Mean difference needed between any two treatment means to be significantly different ($P < .05$). Calculated by the Tukey method for multiple comparisons (Steel and Torrie 1960).

arterial hypertension was evident after 60 s of both BH and FS. Systolic pressure increased 10% and 13%, whereas diastolic pressure increased 21% and 28% during BH and FS, respectively. Bradycardia was found after 60 s of apnea accompanied by FS.

In contrast to the cardiac and vascular effects of airway straining (Valsalva) (Gorlin, Knowles, and Storey 1957; Skillman et al. 1967; Paulev and Wetterqvist 1968; Flessas, Kumar, and Spodick 1970; Spodick, Meyer, and Quarry-Pigott 1974), our observed circulatory events during apnea—unaltered or decreased heart rate, elevated systolic blood pressure, insignificant changes in pulse pressure, and lengthened PEP— indicated that our subjects executed these prolonged bouts of apnea without influencing their central hemodynamic status by Valsalva maneuvers.

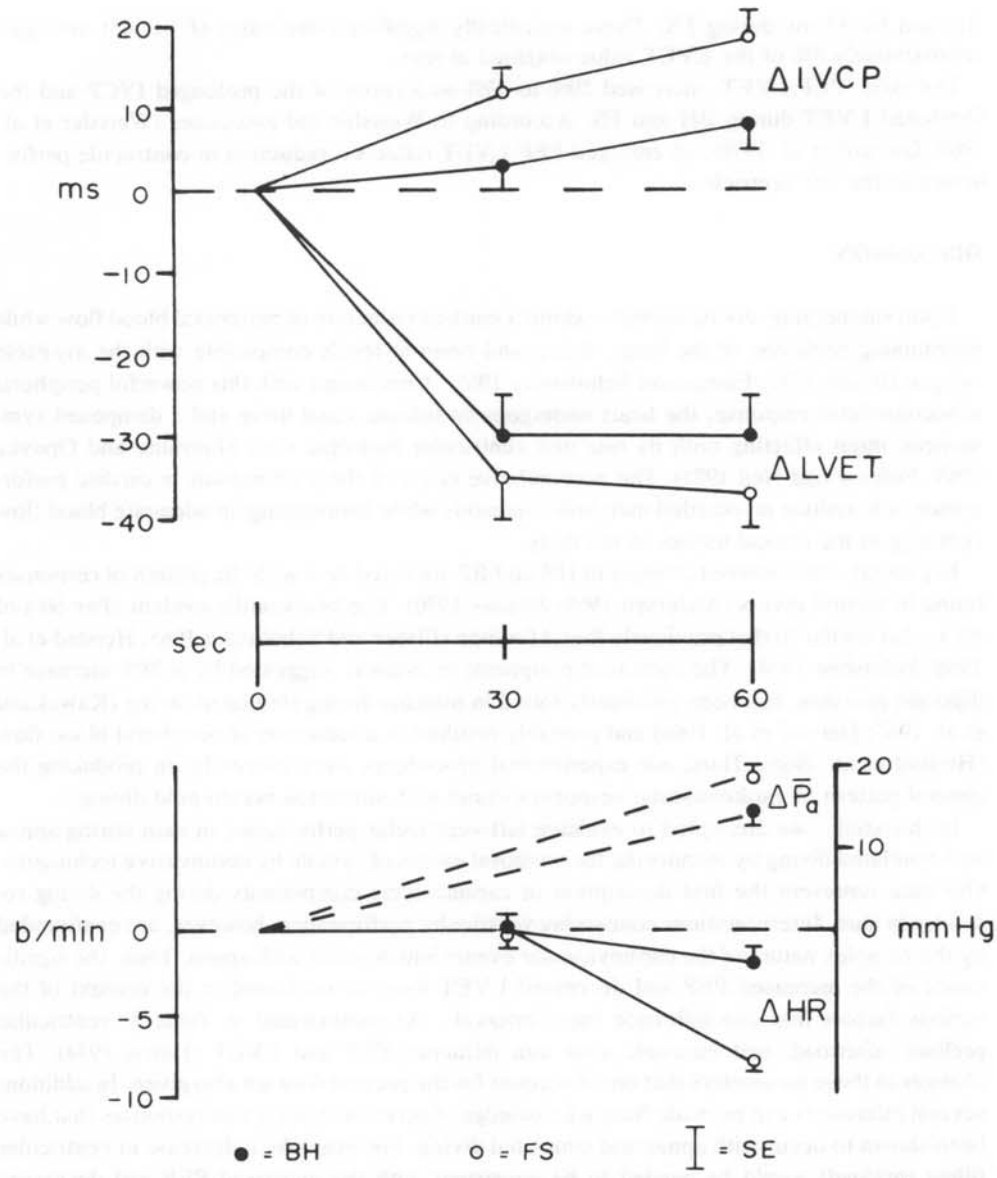

Fig. 1 Mean changes from rest in IVCP, LVET, HR, and mean arterial blood pressure ($\bar{P}_a$) during breath-holding (BH) with and without cold, wet facial stimulation (FS) in 15 subjects.

Alterations in STI

Notable changes in the STI during BH and FS appear to center around the times for left-ventricular isovolumic contraction and ejection (Table 2). Significant prolongations of IVCP by approximately 13% and 31% occurred after 60 s of BH and FS, respectively. FS, after both 30 s and 60 s produced a significant increase in IVCP over the BH response (Fig. 1). Thus, it appears that the added stimulus of a cold, wet application to the face further provoked an increase in IVCP over that found during simple BH. The LVET shortened by 30 ms during

BH and by 37 ms during FS. These statistically significant decreases ($P < .05$) averaged approximately 8% of the LVET value obtained at rest.

The ratio, PEP:LVET, increased 20% to 33% as a result of the prolonged IVCP and the shortened LVET during BH and FS. According to Weissler and associates (Weissler et al. 1969; Garrard et al. 1970), an enlarged PEP:LVET reflects a reduction in contractile performance of the left ventricle.

DISCUSSION

Upon submerging, diving animals exhibit a marked reduction of peripheral blood flow while maintaining perfusion of the lungs, heart, and brain at levels compatible with the available oxygen (Irving 1939; Elsner and Scholander 1965). Concurrent with this powerful peripheral vasoconstrictor response, the heart undergoes an intense vagal drive and a dampened sympathetic input affecting both its rate and ventricular inotropic state (Ferrante and Opdyke 1969; Folkow and Neil 1971). The accumulative effect of these alterations in cardiac performance is to reduce myocardial metabolic demands while maintaining an adequate blood flow centrally to the critical tissues of the body.

In general, our observed changes in HR and BP are consistent with the pattern of responses found in natural divers (Andersen 1966; Strauss 1970). The bradycardia evident after 60 s of FS is also similar to that previously found for man (Elsner and Scholander 1965; Heistad et al. 1968; Folinsbee 1974). The increased peripheral resistance, suggested by a 28% increase in diastolic pressure, has been previously found in humans during simulated diving (Kawakami et al. 1967; Heistad et al. 1968) and probably resulted in a reduction of peripheral blood flow (Heistad et al. 1968). Thus, our experimental procedures were successful in producing the general pattern of cardiovascular responses found with simulated breath-hold diving.

In this study, we attempted to evaluate left-ventricular performance in man during apnea and simulated diving by monitoring the temporal events of systole by noninvasive techniques. Our data represent the first description of cardiac-cycle components during the diving response in man. Interpretations concerning ventricular performance, however, are confounded by the complex nature of the cardiovascular events which occur with apnea. Thus, the significance of the increased PEP and decreased LVET must be evaluated in the context of the various factors that can influence these intervals. As summarized in Table 3, ventricular preload, afterload, and inotropic state can influence PEP and LVET (Harris 1974). The changes in these parameters that could account for the present data are also given. In addition, several inferences can be made from a knowledge of other cardiovascular responses that have been shown to occur with apnea and simulated diving. For example, a decrease in ventricular filling (preload) would be needed to be consistent with the increased PEP and decreased LVET found in our study (Harris 1974). However, this is opposite to the effect generally considered part of the overall diving response. Folkow, Nilsson, and Yonce (1967) found a greatly elevated central venous pressure in a natural diver during submersion. While subsequently evaluating parasympathetic involvement in the diving response, Folkow and Yonce (1967) observed a similar elevation in left ventricular end-diastolic pressure when the diving response was simulated by vagal nerve stimulation. Thus, in all likelihood, the elevated central venous pressure during diving establishes an elevated left-ventricular filling pressure. Other studies have shown that central venous pressure is increased in man during breath-holding and simulated diving (Skillman et al. 1967; Paulev and Wetterqvist 1968; Hong et al. 1971). Thus, we would expect that the ventricular preload would have been enhanced in our subjects. In addition, any increased time for ventricular filling, as would occur with bradycar-

TABLE 3
Factors that influence systolic time intervals

Hemodynamic factor	Relationship with:		Response needed to:		Response during breath-holding
	PEP*	LVET*	↑PEP	↓LVET	
Preload (*ventricular filling*)	Varies indirectly	Varies directly	Decrease	Decrease	Probably increases†
Afterload (*aortic diastolic pressure*)	Varies directly	Varies directly	Increase	Decrease	Increases‡
Inotropic state	Varies indirectly	Varies indirectly	Decrease	Increase	Probably decreases§

PEP = preejection period
LVET = left-ventricular ejection time
*Harris 1974
†As inferred from increased central-venous and right-atrial pressures: Folkow et al. 1967; Skillman et al. 1967; Cohn et al. 1968; Paulev and Wetterqvist 1968; Hong et al. 1971
‡Kawakami et al. 1967; Heistad et al. 1968
§As inferred from increased vagal drive (Folkow and Neil, 1971) and decreased sympathetic input to the heart: Lin, 1974

dia, would further promote an increased ventricular end-diastolic volume. It is reasonable, therefore, to turn our attention to other more plausible factors that could account for the changed STI.

It is well-known that an increased aortic diastolic pressure would, by itself, lead to a prolongation in both PEP and LVET (Shaver, Kroetz, Leonard, and Paley 1968). Thus, the 21% and 28% increases in diastolic blood pressure during BH and FS, respectively, could account for the prolonged PEP; the abbreviated LVET found in our studies, however, is opposite to the response elicited by an elevated ventricular afterload. The increased diastolic pressure, therefore, cannot by itself adequately explain our data. We are left with a third factor that may influence STI, namely, the inotropic state of the heart (Table 3). A reduction in inotropism could prolong PEP, but LVET would be lengthened if stroke volume was maintained. That is, a decreased inotropic state would again account for only half of our results. However, a combination of an elevated afterload and a depressed contactile state lead to a shortened LVET and a prolonged PEP. Harris, Schoenfeld, and Weissler (1967) found a substantial increase in PEP during bradycardia evoked by propranolol while peripheral resistance was increased by norepinephrine. Similarly, Matsuura and Goodyer (1973) reported an 18% increase in the duration of preejection contraction and an 8% decrease in LVET after aortic constriction in atrial-paced dogs given propranolol in doses sufficient to depress left-ventricular dP/dt. These conditions of a reduced ventricular function in the face of elevated arterial pressure seem consistent with the results of the present work. As a consequence of the combined effects, stroke volume is diminished (Matsuura and Goodyer 1973). Therefore, we suggest that the cardiovascular effects of apnea and simulated diving include a reduced left-ventricular function that may manifest itself as a smaller stroke volume. This reduction in left ventricular performance may originate from afferents arriving from proprioceptive sites in the lungs and thoracic wall (Cohn, Krog, and Shannon 1968; Song, Lee, Chung, and Hong 1969),

from thermal and tactile receptors in the face (Song et al. 1969), and from carotid chemoreceptors (Daly and Angell James 1975). These afferent inputs could activate a train of vagal discharge to the heart, consequently affecting rate (Song et al. 1969; Daly and Angell James 1975) and, to a minor extent, myocardial inotropic function (Higgins, Vatner, and Braunwald 1973).

The primary negative influence on contractile performance during diving could be due to reflex withdrawal of sympathetic input to the heart, a response which has been shown to be a component of diving bradycardia in the unanesthetized rat (Lin 1974). The afferent site of this mechanism could be the carotid chemoreceptors which, when activated, depress cardiac sympathetic activity (Downing, Remensynder, and Mitchell 1962).

Our suggestion of a reduction in left-ventricular function in apneic man is consistent with previous observations in natural divers (Ferrante and Opdyke 1969; Folkow and Neil 1971) and other terrestrial mammals (Lin and Baker 1975). This interpretation does not agree, however, with the data of Paulev and Wetterqvist (1968) and Hong et al. (1971) who did not find any significant changes in stroke volume or cardiac output during breath-holding in humans. In both cases, however, bradycardia was not established during their breath-hold experiments when cardiac output was measured. In addition, during the experiments of Hong et al. (1971), preapneic HRs were considerably higher than in our study. These observations suggest that sympathetic discharge to the heart may have had a more influential role during their cardiac-output measurements than during our protocol that used noninvasive procedures for evaluating cardiac function.

On the other hand, previous investigations in man lend support to the interpretation of our data. Studies that examined cardiovascular function during breath-holding (Skillman et al. 1967) and apneic face immersion (Kawakami et al. 1967) showed reductions in cardiac output and stroke volume. Thus, with the conclusions of these studies and our data, we suggest that part of the cardiovascular response to prolonged apnea in man is a decreased left-ventricular performance that manifests as a reduced stroke volume.

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Gross, P. M., R. L. Terjung, and T. G. Lohman. 1976. La fonction ventriculaire gauche en apnée et en plongée fictive chez l'homme. Undersea Biomed. Res. 3(4):351–360. Les intervalles systoliques (STI) du ventricule gauche ont été mesurés pour déterminer les effets de l'apnée et de la plongée fictive sur le fonctionnement du ventricule gauche humain. Une dépression de la performance ventriculaire a été démontré au cours de la plongée réelle.) Les STI ont été enrégistrées par un procédé noninvasif chez 15 hommes adultes expérimentés en plongée en apnée, au repos, aprés 30 et 60 secondes en apnée simple ou en apnée accompagné d'une stimulation faciale par un objet froid et mouillé. Les altérations de la pression artérielle et de la fréquence cardiaque au cours de la stimulation ressemblaient à celles rencontrées en plongées fictives. Le temps d'éjection du ventricule gauche a diminué de 30 msec pendant l'apnée et de 37 msec pendant l'apnée avec stimulation. Ces mesures des intervalles systoliques représentent la premiére déscription des composants du cycle caridaque humain au cours de la plongée. Les altérations des STI suggérent que la performance ventriculaire gauche, traduite par la vitesse réduite du développement de la pression pré-éjection, et par le débit cardiaque diminué, avait subi une réduction au cours des exercises en apnée. De plus, la tendance de ces paramètres parait indiquer que la stimulation faciale a potentié la réponse au delà de celle observée pendant l'apnée simple. Il paraît donc qu'il existe chez l'homme

une dépression de la performance ventriculaire gauche en plongée fictive semblable à celle constatée en plongée réelle.

intervalles systoliques
apnée
réponse du plongeur

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