Heart-Rate Complexity is Decreased During Apnea and Respiratory Acidosis

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Objectives

We previously showed that heart-rate complexity (HRC) is decreased following trauma/hemorrhage. Because respiratory arrest frequently coincides with trauma, we sought to investigate the effects of prolonged apnea and respiratory acidosis on different measures of HRC and heart-rate variability.

Materials and Methods

- Swine (n=6, 35.4 +-1.1 kg SEM) were anesthetized (ketamine/propofol), intubated, paralyzed (pancuronium), and mechanically ventilated in volume-control mode at baseline (PRE).
- After baseline, the animals were ventilated by tracheal gas insufflation with intermittent pressure release at 25 cm H_20 twice a minute (apnea phase) for 2 hours or until their pH reached 7.1 and then maintained there for at least 10 minutes. Next, the animals were returned to mechanical ventilation for over 30 minutes to normalize their ventilation.
- Electrocardiogram (ECG) was recorded to a computer at 500 Hz at 4 timepoints: baseline (PRE), after 30 min of apnea (AP1), end of apnea at 120 min or when pH=7.1 (AP2), and recovery (POST).
- Off-line the following HRC methods were applied to ectopy-free sections of the ECG:

1. Approximate entropy (ApEn) and sample entropy (SampEn) which measure the irregularity of the R-to-R interval time series (RRI) of the ECG.
2. Bit-per-word Entropy (BPWEn), which calculates the irregularity of the signal distribution encoded into arbitrary words.
3. Fractal dimension by curve lengths (FDCL) which assesses the fractal-like self-similarity of the signal.
4. Signal stationarity (StatAv), that assesses changes in the mean and standard deviation of the signal over time in each dataset.

- Heart rate variability (HRV) by frequency-domain analysis was also calculated:

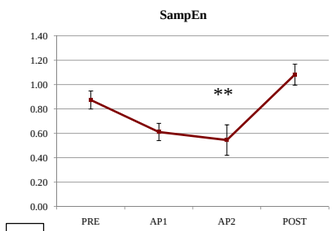
1. RRI spectral power at low-frequency range (LF, 0.05-0.15 Hz ms^2)and high-frequency (HF, 0.15-0.4 Hz ms^2).
2. Complex demodulation, measuring the amplitude of low- (CDM LF), and high-frequency oscillations (CDM HF). The HF and CDM HF variables correlate with vagal cardiac control, whereas the LF and CDM LF variables describe both vagal and sympathetic inputs to the heart.

Materials and Methods cont…

- Heart rate (HR), mean arterial pressure (MAP), cardiac output (CO), partial pressure of oxygen (PO_2) and carbon dioxide (PCO_2), and pH of arterial blood were also recorded at each time point.
- All variables are means ± SEM. Statistics by one way ANOVA with repeated measures and Dunnett adjustment to baseline.

Measures/ Time point	PRE	AP1	AP2	POST
HR, b/p/min	118±5	118±8	140±10*	121±5
MAP, mmHg	89±12	105±6	100±7	102±6
CO, L/min	6.6±0.1	4.9±0.5	6.7±0.3	6.0±0.3
PO_2, mmHg	527± 14	522 ± 9	473±15***	576±14***
PCO_2, mmHg	44±1	66±3.7***	129±4***	44±2
pH	7.49±0.01	7.32±0.02	7.10±0.01***	7.50±0.01

Table 1. Changes in conventional vital signs and blood gas values. Significance levels: *, p<0.05; **, p<0.01; ***, p<0.001.



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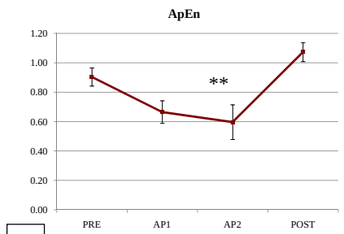

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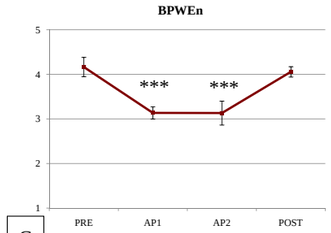

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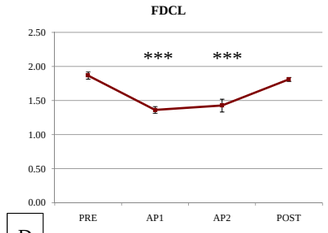

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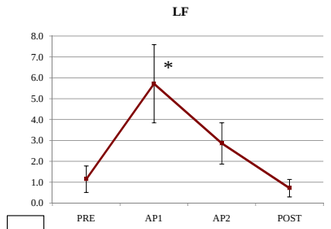

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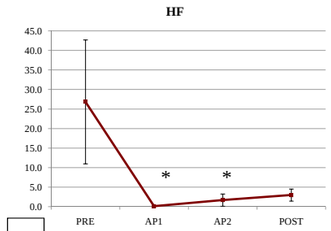

F

Figure. Changes in ECG-derived metrics: **A.** ApEn; **B.** SampEn; **C.** BPWEn; **D.** FDCL, all of the above unitless; **E.** LF, Hz ms^2; **F.** HF, Hz ms^2.

Measures/ Time point	PRE	AP1	AP2	POST
RRI, ms	527±26	505±37	438±31**	489±17
CDM LF	0.71±0.36	2.43±0.53*	2.57±0.65*	0.71±0.29
CDM HF	5.14±2.11	0.57±0.20**	1.29±0.68*	2.00±0.62
StatAv	0.71±0.08	0.94±0.02*	0.93±0.07**	0.85±0.07

Table2. Changes in ECG-derived metrics. CDM LF, CDM HF, StatAv all unitless. Significance levels: *, p<0.05; **, p<0.01; ***, p<0.001.

Observations

- HR increased at AP2. MAP did not change (Table 1).
- PO_2 was well-maintained by O2 insufflations, decreasing only slightly at AP2 (Table 1).
- PCO_2 increased at AP1 and again at AP2 to very high levels (Table 1).
- pH decreased at AP2 to the 7.1 target (Table 1).
- ApEn and SampEn decreased at AP2 then returned to baseline at POST (Figure A and B).
- BPWEn decreased at AP1 and Ap2 and returned to baseline at POST (Figure C).
- FDCL decreased at both AP1 and AP2 then returned to baseline at POST (Figure D).
- LF increased at AP1 then decreased (Figure E).
- HF decreased at AP1, AP2 and POST (Figure F).
- CDM LF increased at both AP1 and AP2 which means that the amplitude of EKG increased with apnea.
- CDM HF decreased at AP1 and AP2 (Table 2).
- StatAv increased at AP1 and AP2 (Table 2).

Conclusions

- Apnea and respiratory acidosis led to reversible decreases in multiple measures of HRC, pointing to simplification of cardiovascular regulatory feedback. It's often assumed that HRC is a function of vagal cardiac control, but comparison of the HRC and HF HRV results does not reveal a direct relationship.
- The power (HF) and amplitude (CDM HF) of vagal input to the heart were decreased, whereas measures reflecting sympathetic input (LF and CDM LF) increased during apnea signifying vagal withdrawal and sympathetic activation.
- The decrease in HF seen during apnea in the present study may be the result of a loss of respiration-induced blood-pressure oscillations.
- Decreased HRC is not specific for trauma/hemorrhage, but may also be useful for monitoring of patients at risk of respiratory arrest.
- These findings complement the ongoing effort in assessment of noninvasive ECG-derived measures of HRC and HRV as new vital signs reflecting physiologic perturbation under a variety of conditions.