Atrioventricular coupling and ventricular interval regularity during atrial fibrillation: A frequency-dependent phenomenon

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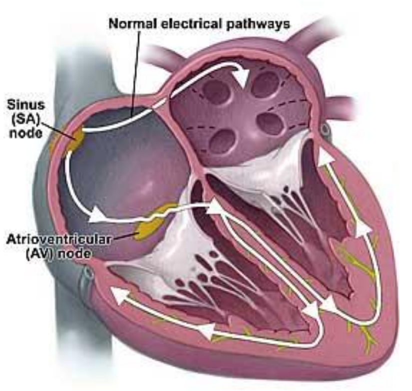
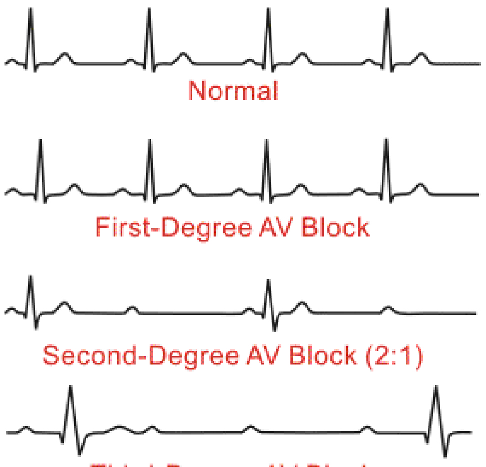
BACKGROUND: AV node - Clinical Perspective



AV node

specialized conduction system of the heart, which connects the atria and ventricles



Functions

-> time delay to optimize the coupling between ventricular filling and contraction

-> filtering of high-rate atrial inputs, safeguard against life-threatening ventricular arrhythmias

BACKGROUND: AV node - Nonlinear Dynamics Perspective

Nonlinear dynamics provide a unified framework to describe block processes in AV conduction

J. Math. Biology (1983) 18: 69–88

Journal of Mathematical Biology

The Heart as a System of Coupled Nonlinear Oscillators

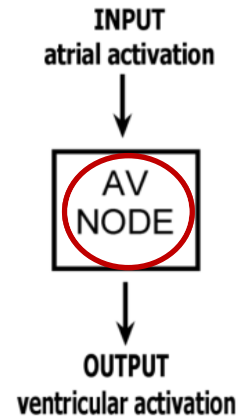
J. Honerkamp

Fakultät für Physik, Universität Freiburg, Hermann-Herder-Str. 3, D-7800 Freiburg i. Brsg., Federal Republic of Germany

Prediction of complex atrioventricular conduction rhythms in humans with use of the atrioventricular nodal recovery curve

Alvin Shrier, Ph.D., Howard Dubarsky, B.Sc., Michael Rosengarten, M.D., Michael R. Guevara, Ph.D., Stanley Nattel, M.D., and Leon Glass, Ph.D.

Circulation 76, No. 6, 1196–1205, 1987.

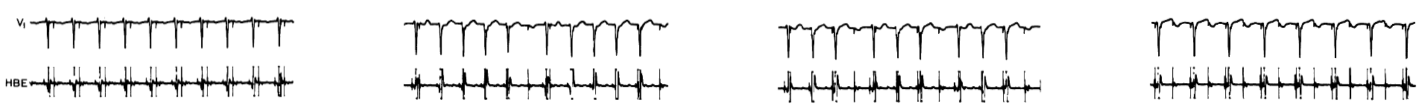


Nonlinear properties

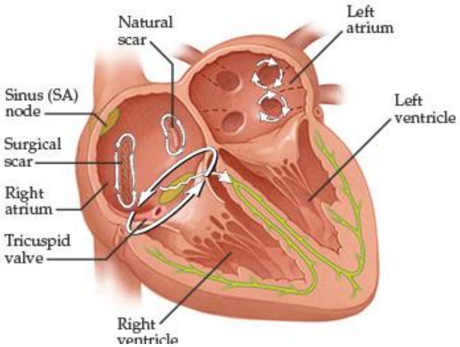
ATRIAL STIMULATION at increasing atrial rate →

AV block processes resembling phase-locking transitions in dynamical systems

1:1 **6:5** **4:3** **2:1**

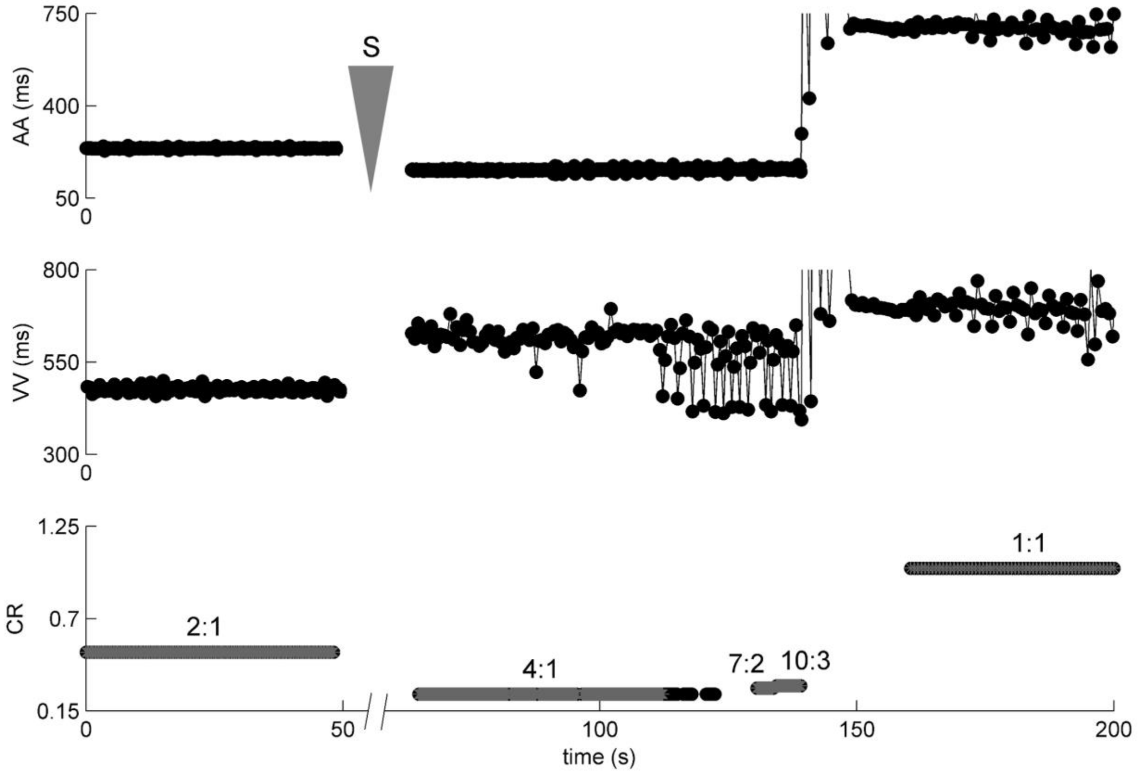


BACKGROUND: AV node in Regular TachyArrhythmias



ATRIAL FLUTTER

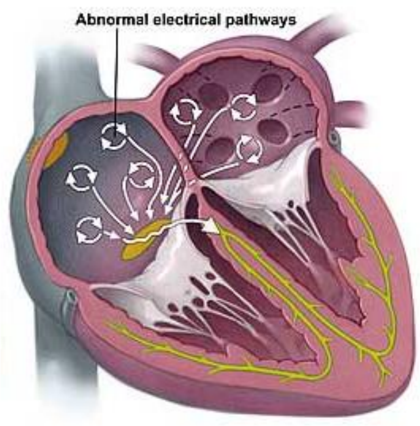
Phase-locking transitions can be observed during regular, high-rate spontaneous arrhythmic condition



Masè M. et al., Am J Physiol Heart Circ Physiol, 303 (10): H1219-H1228, 2012

What happens during AF?

BACKGROUND: AIMS



Atrial Fibrillation

- **Irregular high-rate atrial impulses (400-600 bpm) due to the «chaotic» propagation of multiple wavelets**
- Lost of 1:1 AV conduction
- Irregular ventricular activation, usually with incessant tachycardia

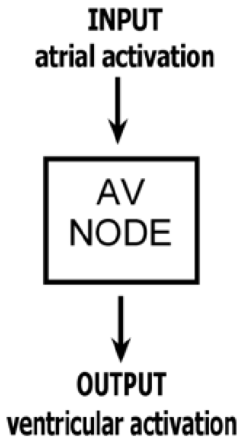
AIMS

1. To investigate the dynamics of AV coupling during AF

2. To assess the influence on the variability and regularity of ventricular interval

METHODS

METHODS: Experimental Setting



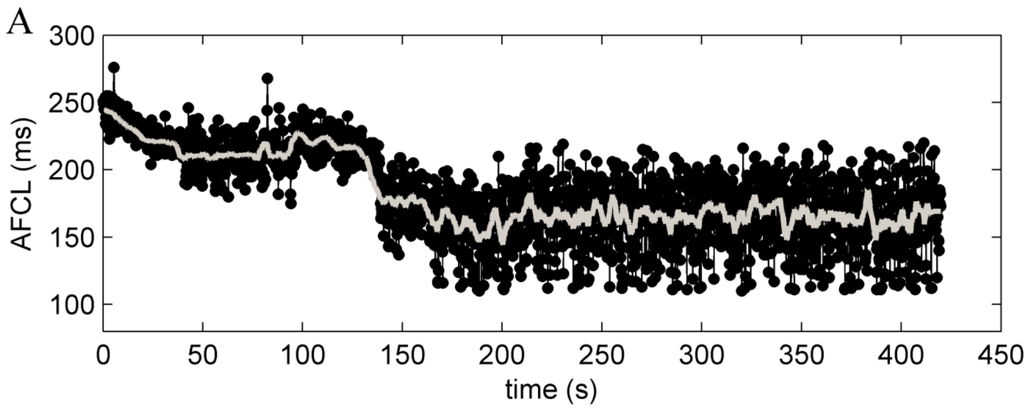
To study the AV node in a dynamical sense

↓

Different atrial input rate should be tested

TO USE

Spontaneous atrial rate changes in the first minutes of an AF episode



Ravelli F et al., JCE, 18, 60-65, 2007

METHODS: Population and EP Study

Patient Population

10 patients with paroxysmal atrial fibrillation (age 54 ± 22 yrs, 1 female)

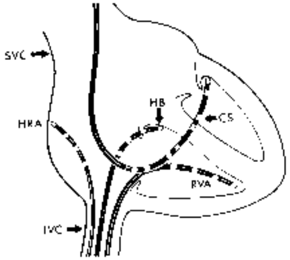
Electrophysiological study

Induction of AF by **burst atrial pacing**

- 5 s bursts, 4mA output, 2 ms pulse width
- from 400 ms cycle length to atrial refractoriness (step 20 ms)

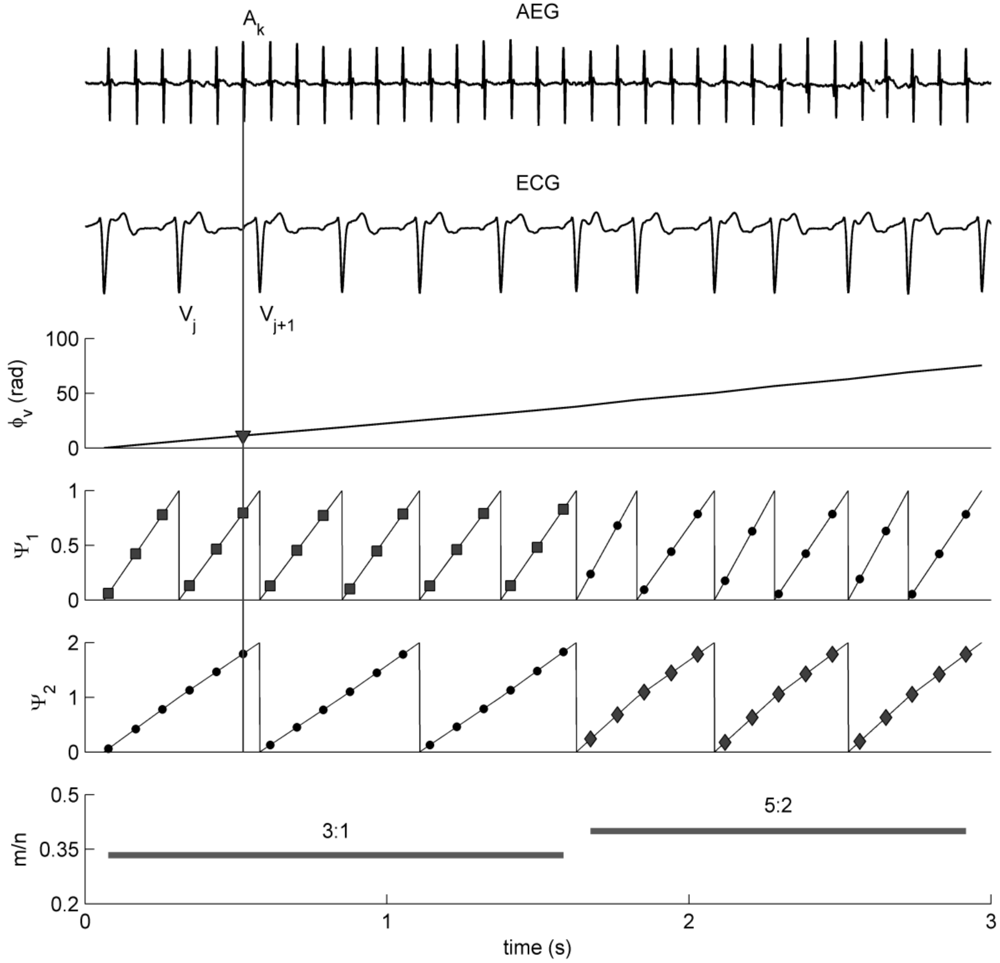
Recordings of few minute length

- Atrial activity by a quadrupolar catheter in the right atrium
- Ventricular activity by surface ECG



METHODS: Construction of the AV synchrogram

AV synchrogram **->** identifies instances of *n:m* atrioventricular coupling by a stroboscopic observation of the ventricular phase at times triggered by atrial activation



Extract A_k atrial and V_j ventricular activation times

$$\phi_v(t) = 2\pi \frac{t - V_j}{V_{j+1} - V_j} + 2\pi j \qquad V_j \le t < V_{j+1}$$

$$\psi_m(A_k) = \frac{1}{2\pi}\left[\phi_v(A_k) \bmod 2\pi m\right]$$

$$\exists k \ge 1 \quad \left|\Psi_m(A_{i+n}) - \Psi_m(A_i)\right| < \varepsilon$$
$$i \in \{l, \ldots, l + kn - 1 \mid 0 < l < N - kn + 1\}$$

Pattern assessment by testing with shuffled surrogate phase series

Masè M. et al., Biomed Sign Proc Control, 8 (6): 1008-1016, 2013
Schafer C et al, Phys Rev E, 60(1): 857–870, 1999; Cysarz D et al, Biomed Eng Online 4, 2004; Lotric MB, Physica A, 283: 451- 461, 2000

METHODS: Characterization of the AV synchrogram

Average parameters

- percentage of coupled beats

$$p_c = \frac{\sum_{j=1}^{M} \left(A_{ej} - A_{1j} \right)}{T} \cdot 100\%$$

- maximal duration of coupled epochs

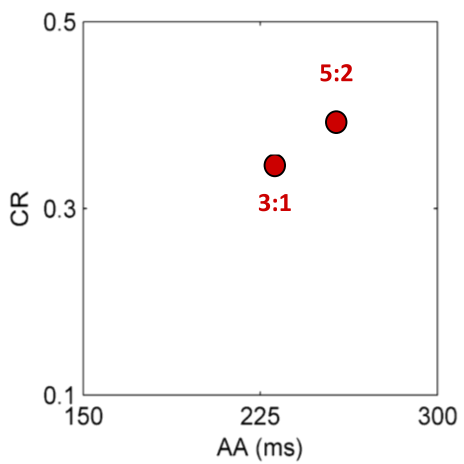
$$l_{\max} = \max_j \left(A_{ej} - A_{1j} \right)$$

- average nodal conduction ratio

$$CR_m = \frac{\sum_{j=1}^{M} \left(m_j / n_j \right) \cdot \left(A_{ej} - A_{1j} \right)}{\sum_{j=1}^{M} \left(A_{ej} - A_{1j} \right)}$$

AV response curve

To outline frequency-dependences, CR displayed as a function of AA



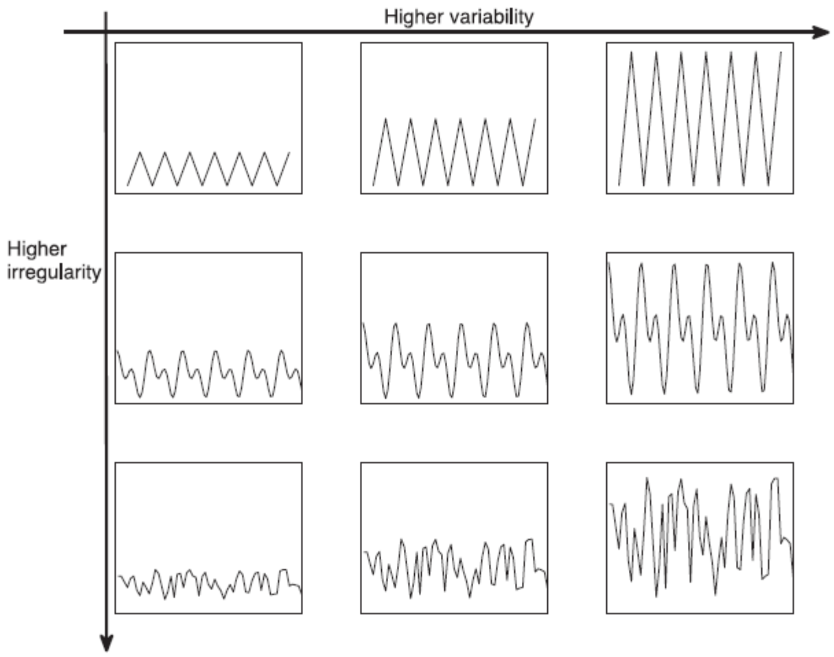
Masè M. et al., Biomed. Sign. Proc. And Control, 8 (6): 1008-1016, 2013

METHODS: Quantification of Ventricular Variability/Regularity

RR series Analysis

VARIABILITY in Time-domain

SD_{RR}
$RMSSD_{RR}$
pRR 10-90



Corino VD et al., JCE, 26(2):137-41, 2015

IRREGULARITY in Entropy-domain

$$SampEn(m, r) = -\log A / B$$

where

A = n. of template vector pairs of length *m+1* having $d[X_{m+1}(i), X_{m+1}(j)] < r$

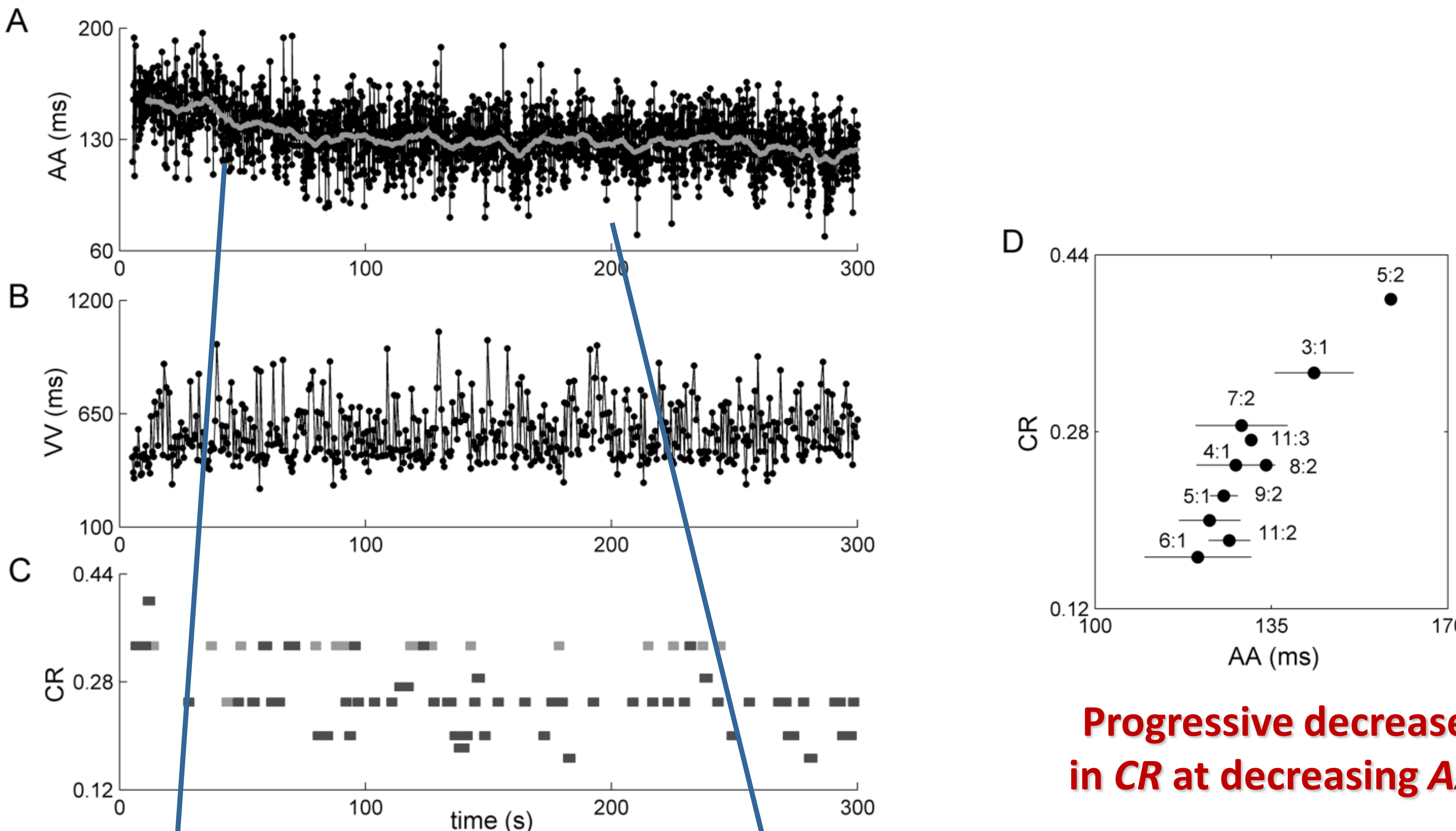
B = n. of template vector pairs of length *m* having $d[X_m(i), X_m(j)] < r$

m = 1, 2; r = 0.15, 0.2, 0.25*SD; *N* = 100 and 150

Richman JS and Moorman JR, Am J Physiol Heart Circ Physiol, 278 (6): H2039–49, 2000

RESULTS

RESULTS: AV coupling 1



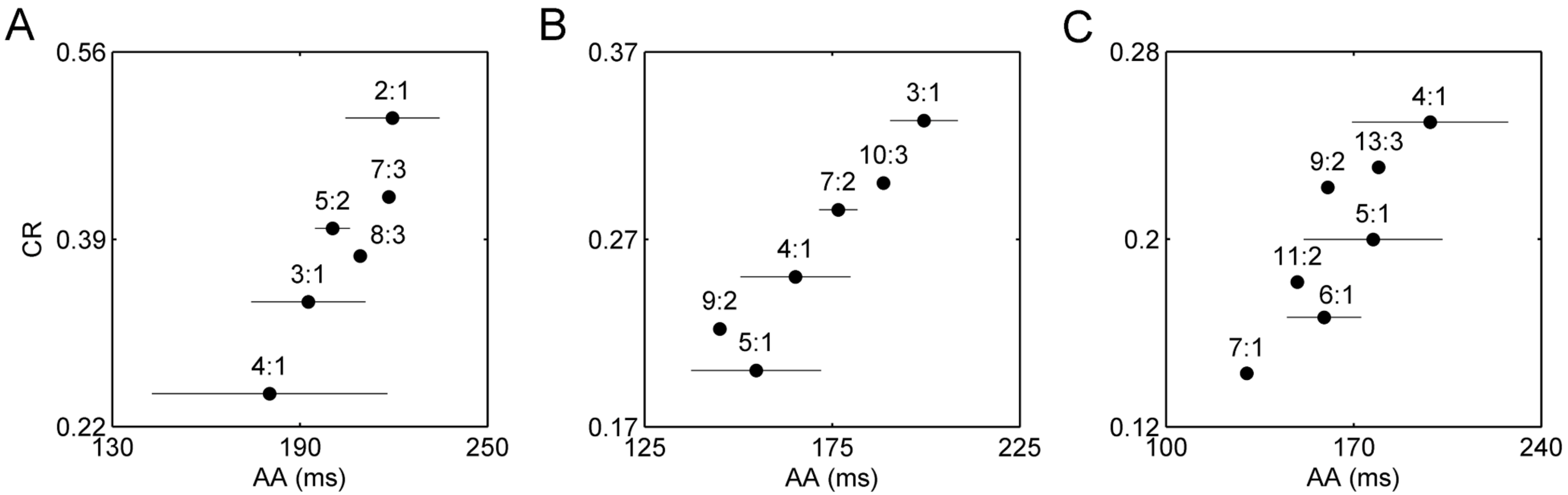
Progressive decrease in *CR* at decreasing *AA*

Existence of significant synchronized epochs (p_c=26.3%, l_{max}=4.2 s)

m_{AA} = 137.0 ± 19 ms
CR_m = 0.27

m_{AA} = 124 ± 16 ms
CR_m = 0.23

RESULTS: AV coupling 2

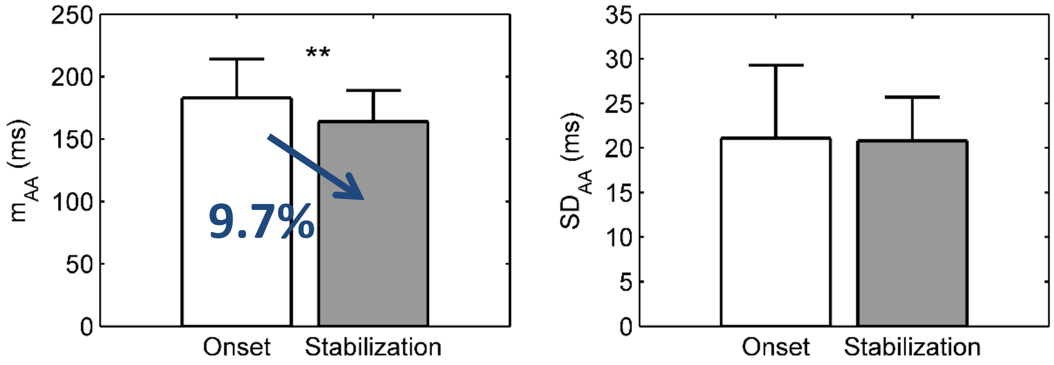


1. **Decrease in CR at the shortening of atrial intervals**
2. **Higher order patterns less common than *n:1* patterns**
3. **Farey sequence ordering of *n:m* patterns as a function of atrial rate (*n+N:m+M* orders between *n:m* and *N:M*)**

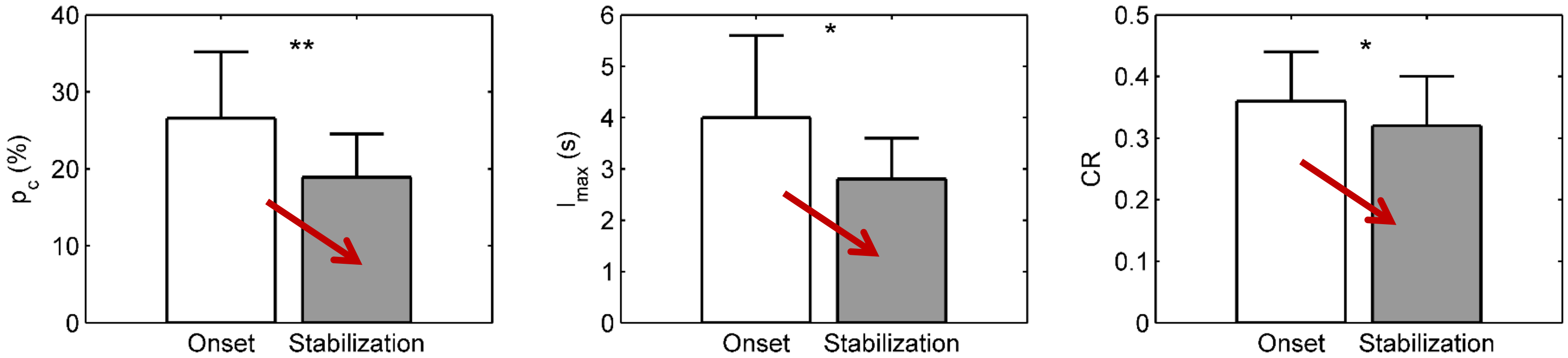
These features are consistent with the nonlinear recovery properties of the AV node

RESULTS: AV coupling 3

ATRIAL RATE PROPERTIES



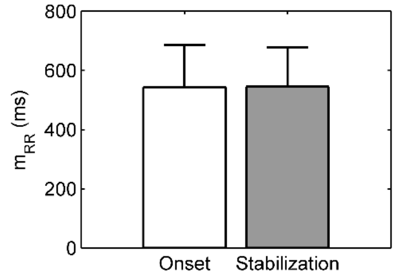
AV SYNCHROGRAM INDICES



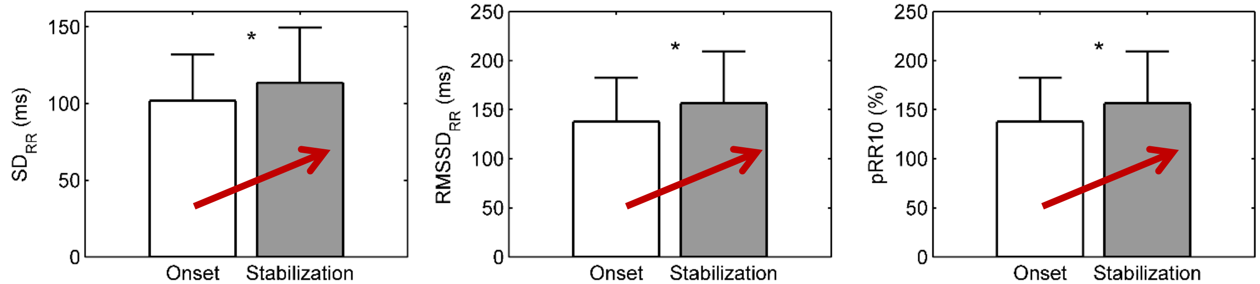
Atrial rate increase determines a decrease in the occurrence, stability and locking ratios of AV coupling patterns

RESULTS: Ventricular Response

VENTRICULAR RATE =

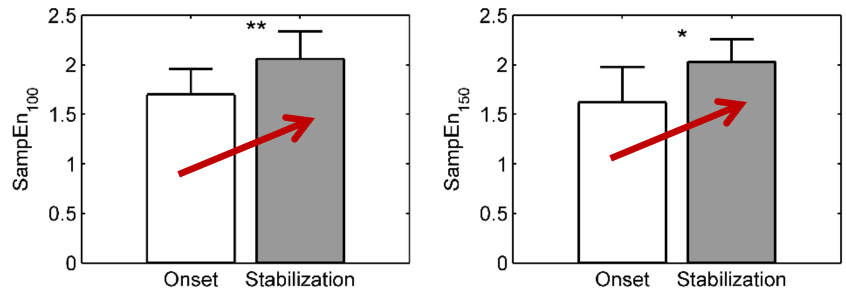


VENTRICULAR VARIABILITY ↑



VENTRICULAR IRREGULARITY ↑

m=2, r=0.2 (significant differences also for 0.15 and 0.25)



Advanced levels of AV block at higher atrial rates determine an increase in the variability and irregularity of ventricular intervals

CONCLUSIONS

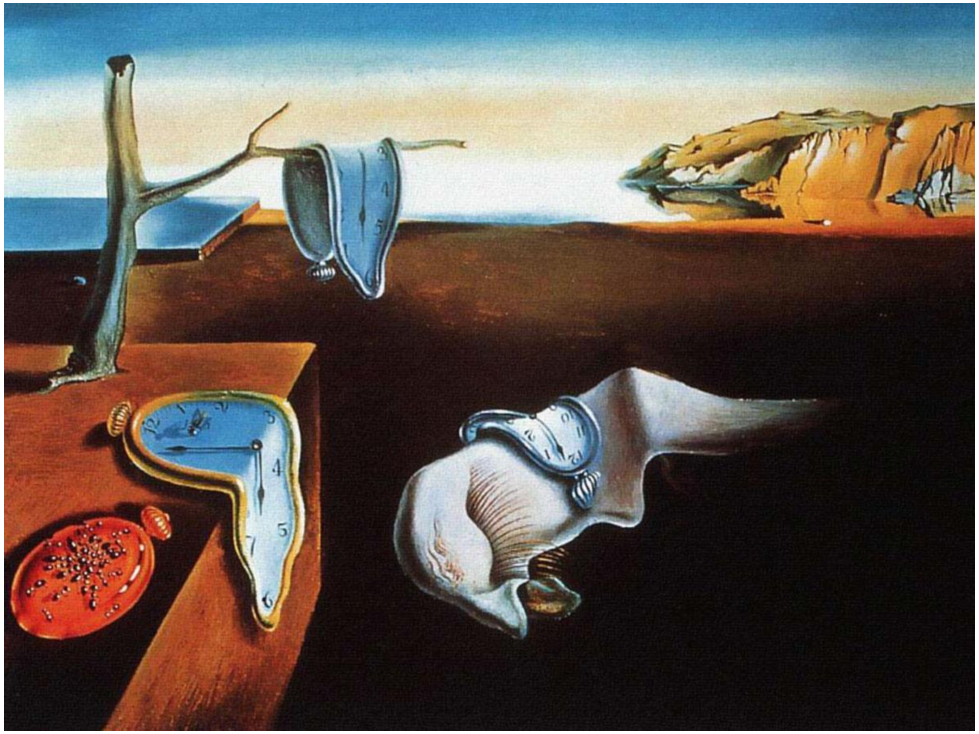
- Instances of AV coupling exist during AF, whose dynamics can be described by AV synchrogram analysis.
- AV coupling during AF is a frequency-dependent phenomenon:
  - AV coupling occurrence and stability decrease at increasing atrial rate
  - AV locking ratios are ordered according to a Farey sequence as a function of atrial rate.

- Instability of AV coupling and advanced levels of blocks at higher atrial rates determine higher variability/irregularity of ventricular intervals.
- Acute changes occurring during AF may determine adverse hemodynamical effects, increasing acute risks in AF patients.
- These factors should be taken into account in the development of rate control strategies for AF.

ACKNOLEDGEMENTS

THANKS
for your attention

QUESTIONS?



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