

Characterising Atrial Arrhythmias in the Hypertensive Heart using High Resolution Optical Mapping

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BACKGROUND

There is a strong association between atrial structural remodelling and risk of atrial fibrillation [1]. However, its role in the initiation and maintenance of atrial rhythm disturbance is not well understood. The spontaneously hypertensive rat (SHR) is a genetic animal model that replicates key features of human hypertensive heart disease (HHD) over a well-established time-course [2]. Progression of HHD in SHR is accompanied by bi-atrial dilation, fibrosis and increased propensity to atrial arrhythmia. Therefore, the SHR provides a potentially powerful model for studying the relationship between structural remodelling and risk of atrial arrhythmia.

AIMS

The goal of this study is to characterise the effects of HHD progression on atrial electrical function and to investigate the relationship between structural remodelling and risk of atrial arrhythmia.

MATERIALS & METHODS

- Age-matched SHRs were studied at 6/7 months, 12/13 months and 18 months.
- Hearts were rapidly excised and mounted on a Langendorff perfusion apparatus. Connective tissue and fat were carefully dissected from the atrial surface.
- The atria were then isolated and immersed in warm (37°C), oxygenated Tyrode's solution in a superfusion chamber.
- After mechanical uncoupling with blebbistatin, the atria were stained with voltage sensitive di-4-ANEPPS for 10 minutes.
- Silver stimulus electrodes were positioned in superior right and left atrial appendages (RAA and LAA, respectively), while atrial electrograms were recorded with Ag/AgCl electrodes at the edge of RAA and LAA.
- Restitution kinetics were characterised using S1-S1 stimulus protocol over a range of intervals.
- Arrhythmia susceptibility was tested using a train of S1 pulses (250 ms intervals) followed by a single S2 pulse until loss of capture or induction of arrhythmia.
- Processing steps involved: binning, spatial Gaussian filtering,

background fluorescence removal, temporal wavelet denoising, and temporal smoothing using Savitsky-Golay filters.

RESULTS AND DISCUSSION

Activation time (AT) maps during SR and stimulation (Fig 1) were consistent with previous studies [3,4], with activation spreading from the sino-atrial node (SAN) and activation of the posterior LA via Bachmann's bundle (BB). In 18-month old animals, however, we consistently observed electrically quiescent patches in the left atrial appendage (LAA) that markedly perturbed activation spread (Fig 2). In 18 month old animals, conduction slowing was markedly greater in the LA (Fig 4 & Fig 4). Atrial hypertrophy (weight of isolated atria/tibial length) occurred with age in SHRs (Fig 5). We also observed an increase in total activation time with age when animals were paced at the same S1-S1 interval (Fig 6).

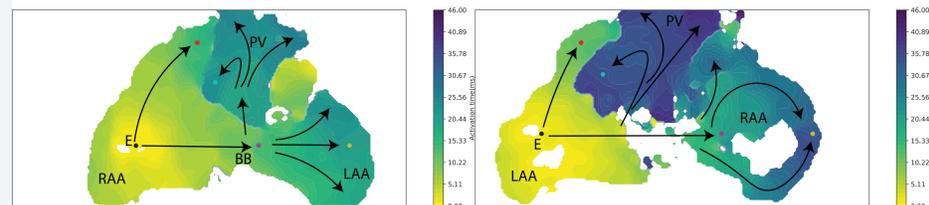


Fig 1: AT map of a 6 month old SHR paced from the RAA (point E) at 100ms S1-S2 interval.

Fig 2: AT map of 18month old SHR paced from the RAA (point E) at 100ms S1-S2 interval. The white blob in the LAA shows inactive regions.

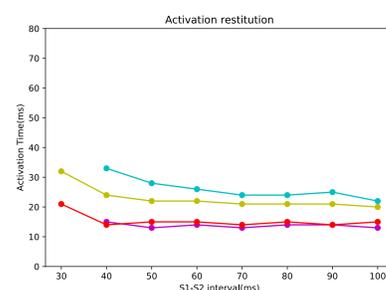


Fig 3: Restitution of AT (corresponding points on Fig 1) with increasing S1-S2 pacing interval

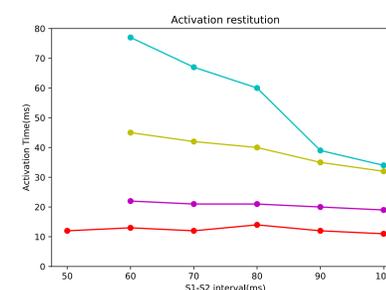


Fig 3: Restitution of AT (corresponding points on Fig 2) with increasing S1-S2 pacing interval. Delays in activation become more prominent in the LA at low S1-S2 intervals.

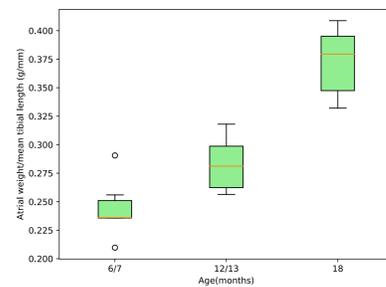


Fig 5: Increase in hypertrophy in the atria with age.

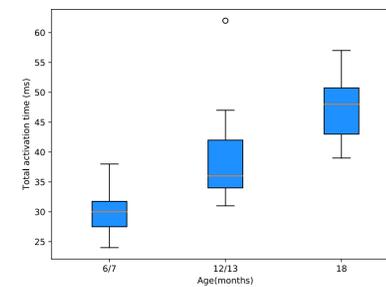


Fig 6: Change in total activation (250ms S1-S1 pacing from the RAA) time with age.

The susceptibility to arrhythmia increased with age, and occurred at lower frequencies in older hearts. For 6 and 12 month olds animals, atrial tachycardia was functional and centred on the stimulus site (Fig 7).

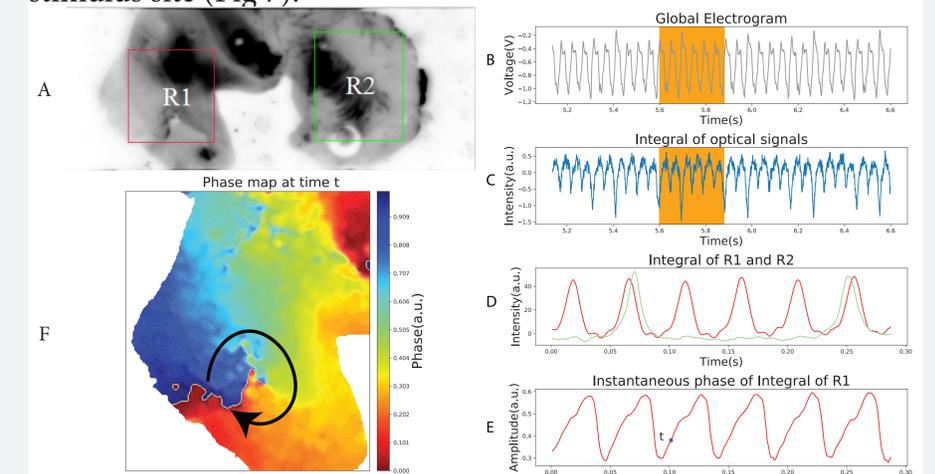


Fig 7: Micro-reentry around electrode site in a 12 month old SHR (QR code a.). Electrical activity is conducted through BB to the LA every 2 or 4 beats (alternating). A, Image defining ROIs in each side of the atrium; B, Global electrogram of the arrhythmia; C: Integral of the optical signals; D, Integral of R1 (red) and R2 (green). E, Instantaneous phase in R1; F: Phase map at time t (see QR code b.)

At 18 months however, rate-dependent macro-reentry was more frequent with heterogeneous and appeared to be driven from the posterior left atrium (Fig 8).

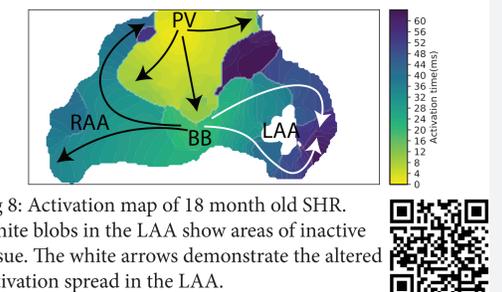


Fig 8: Activation map of 18 month old SHR. White blobs in the LAA show areas of inactive tissue. The white arrows demonstrate the altered activation spread in the LAA.

CONCLUSIONS

This work illustrates the unique capabilities of our high resolution optical mapping set-up for characterising global activation spread in the atria. Our preliminary results indicate progressive electrical dysfunction and increasing risk of atrial arrhythmia with age in SHR.

FUTURE WORK

High resolution imaging to investigate the extent and nature of structural remodelling in SHRs with age.

REFERENCES

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