Effects of Acetylcholine Release and Spatial Distribution on the Frequency of Atrial Reentrant Circuits: a Computational Study.

Chiara Celotto, Carlos Sánchez, José F Rodríguez, Pablo Laguna, Esther Pueyo

University of Zaragoza
Zaragoza, Spain

Electrical activation during atrial tachyarrhythmias is reflected in the electrocardiogram as the fibrillatory waves (f-waves), whose frequency (F_{f}) shows significant variation over time. Cardiorespiratory interactions through the autonomic nervous system have been suggested as a potential cause of this modulation, due to evidences of reduction in F_{f} modulation after full vagal blockade by atropine injection. In this study we tested the hypothesis that the spatial distribution associated with the release of the parasympathetic neurotransmitter acetylcholine (ACh) could affect the frequency of atrial reentrant circuits.

We performed computational simulations in a 3D model of human atria including structural and electrical remodeling. We tested two different patterns of atrial parasympathetic innervation: uniform random spatial distribution in 30% of nodes and ACh release only at the area of the ganglionated plexi (GP) and the nerves departing from it (7% of model nodes), according to the octopus hypothesis. To model respiratory modulation of [ACh], the temporal pattern of ACh release was simulated following a sinusoidal waveform of frequency equal to 0.125 Hz and an amplitude range from 0 to 0.1 μM.

Reentrant circuit frequency was strongly modulated by ACh release when ACh release was uniformly randomly distributed throughout the atria (0.35 Hz peak-to-peak F_{f} variation). In this case rotor frequency variations followed the induced [ACh] modulation pattern, with frequency reductions following [ACh] increases. When ACh release was spatially distributed following the octopus hypothesis, however, the effects of ACh on F_{f} were minor (0.015 Hz peak-to-peak F_{f} variation).

In conclusion, ACh could play a role in F_{f} modulation, but this is strongly dependent on the amount and spatial distribution of released ACh.

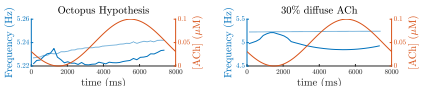

Figure 1. F_{f} (blue) and [ACh] (red). In both panels the dotted line represents F_{f} in the absence of ACh, as reference.