Abstract: 3055

Interactions between metabolism regulator adiponectin and intrinsic cardiac autonomic nervous system: a potential treatment target for atrial fibrillation

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Topic(s):
Atrial Stressors Causing Atrial Fibrillation

Citation:
Background: Previous studies indicated that inhibiting the cardiac autonomic nervous system (CANS) suppressed atrial fibrillation (AF). Clinical research revealed that high levels of serum adiponectin (APN) could exert a beneficial influence on sympathetic and vagal tone in patients with type 2 diabetes. The aim of this study was to elucidate whether APN could regulate CANS and subsequently suppress rapid atrial pacing (RAP)-induced AF.

Methods: Eighteen anesthetized male beagles were randomly divided into three groups: the control group (saline plus sham RAP, N=6), the RAP group (saline plus 3 h RAP, N=6) and the APN + RAP group (APN plus 3 h RAP, N=6). Multielectrode catheters were attached to all atria and pulmonary veins. After bilateral thoracotomy, APN (10 µg, 0.1 µg/µL) or saline was microinjected into 4 fat pads, each containing one of the major atrial ganglionated plexi (GP), prior to RAP. Electrophysiological parameters including atrial effective refractory period (ERP), cumulative window of vulnerability (SWOV), anterior right GP (ARGP) function and neural activity were measured at baseline and 3 h after pacing. The fat pads containing the GP were excised for molecular biological testing and pathological staining at the end of the protocol.

Results: Compared with the control treatment, RAP markedly shortened ERP values at all tested sites and increased SWOV, ARGP function and neural activity, whereas APN injection into the GP reversed these changes. Mechanistically, APN treatment ameliorated the increased inflammatory response induced by RAP. In addition, the APN receptors AdipoR1 and AdipoR2 were detected both in neurons and in non-neuronal cells. Downstream of the AdipoRs, AMPK signaling was significantly activated and NF-κB signaling was significantly inhibited. More importantly, binding between APN and AdipoRs promoted macrophage phenotype switching from proinflammatory to anti-inflammatory.

Conclusion: This study demonstrates that local administration of APN into atrial GP suppress RAP-induced AF by regulating the activity of the CANS. AMPK activation and macrophage phenotype switching may contribute to the attenuation of GP inflammation after APN injection. Therefore, APN signaling may provide a potential therapeutic target to AF.
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