KO hearts develop significantly larger infarctions following lethal ischaemia and reperfusion (25.1±1.97% in PINK1+/+ hearts vs 38.9±3.42% (p<0.01) and 51.5±4.3% (p<0.001) in PINK1+/− and PINK1−/− hearts, respectively). Interestingly, electron microscopic images showed significantly more vacuole-like structures that contained cellular material (indicative of autophagy) in PINK1−/− hearts. We further observed that PINK1−/− hearts had significantly more Beclin1 and total LC3b than hearts from PINK1+/+ littermate controls (Beclin1: 0.674±0.065 in PINK1+/+ vs 0.85±0.019 in PINK1−/− hearts, p<0.05) total LC3b: 0.946±0.139 in PINK1+/+ vs 1.445±0.141 in PINK1−/− hearts, p<0.05; values are in arbitrary units of densitometry). In conclusion, our results suggest that during ischaemic-reperfusion PINK1 acts as an endogenous protective kinase with the regulation of mitophagy being a possible mechanism of its protection.

**Rationale** Oxidative stress has an important role in atrial fibrillation (AF)-induced myocardial remodelling, suggesting that specific oxidases may represent a novel therapeutic target in AF. Here we evaluated how the duration of AF affects the level, sources and localisation of superoxide.

**Results and methods** Our previous work in patients with predominantly paroxysmal AF showed that increased superoxide was produced by NOX2/NADPH oxidase. Here, in patients with permanent AF (n=25) versus matched controls in sinus rhythm (n=25), increased superoxide (assessed by lucigenin-enhanced chemiluminescence and 2-hydroxyethidum detection) was maintained by mitochondrial oxidases and uncoupled nitric oxide synthase (NOS), but not NOX2/NADPH oxidase; although NOX4/NADPH oxidase was upregulated (real-time RT-PCR). Immunoblotting revealed increased protein expression of the mitochondrial complexes I–V and mitochondrial antioxidant peroxiredoxin-3; NOS ‘uncoupling’ was associated with reduced tetrahydrobiopterin by 40% (BH4, HPLC). In the goat, after 14 days of AF, NADPH oxidase activity and protein expression were increased in the left atrium (LA). After 6 months of AF, superoxide release was doubled in both atria and originated from mitochondrial oxidases and ‘uncoupled’ nitric oxide synthase (NOS), which was associated with ipsilaterally reduced BH4 and increased arginase activity.

Manganese superoxide dismutase was reduced by 50% at this stage. **Conclusion** Activation of LA NOX2/NADPH oxidase occurs early in AF and is transient, since mitochondrial oxidases and ‘uncoupled’ NOS account for the increased superoxide production in permanent AF in both models. This suggests that NADPH oxidases may be a valuable target for ‘upstream’ treatment in short-term AF, but not once AF is established.

**Introduction** In health, perivascular adipose tissue (PVAT) has an anticontractile function on adjacent small arteries. We have recently shown that adipocyte hypoxia and inflammation in obesity attenuates PVAT anticontractile function. In animals, PVAT function has only been examined in genetic models of obesity, which are rare in clinical practice.

**Methods** 11 Sprague–Dawley rats were fed a high-fat diet (HF; n=11) over 15–18 weeks. Seven control animals received a normal diet. Weight and blood pressure were monitored. The HF rats were split into two groups: (a) diet-induced obese (DIO; n=6): significantly gained weight after a 10-week period, and diet resistant (DR; n=5): weight comparable to control group. Mesenteric arteries were studied using wire myography with construction of cumulative dose response curves for vessels with intact PVAT and without. Manganese superoxide dismutase was reduced by 50% at this stage. **Conclusion** Activation of LA NOX2/NADPH oxidase occurs early in AF and is transient, since mitochondrial oxidases and ‘uncoupled’ NOS account for the increased superoxide production in permanent AF in both models. This suggests that NADPH oxidases may be a valuable target for ‘upstream’ treatment in short-term AF, but not once AF is established.

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