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Investigating the beneficial effects of voluntary exercise in rats with pulmonary artery hypertension

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Voluntary wheel running can delay the onset of right ventricular failure (RVF) in rats with pulmonary artery hypertension (PAH) induced by monocrotaline (MCT) (Natali *et al*., Am. J. Physiol. 309:H421-4;2015). Although the mechanisms associated with this benefit are unknown, electrical, Ca^{2+}-handling and structural remodelling are associated with cardiac dysfunction in MCT rats.

Male Wistar rats (175-191 g) were injected with 60 mg/kg MCT to induce PAH and RVF, or an equivalent volume of saline as controls (CON). Animals were randomly assigned free access to a running wheel (exercise; ex) or not (sedentary; sed). SedMCT animals were sacrificed upon external signs of heart failure; CON and exMCT animals were sacrificed on matched days to sedMCT animals, unless heart failure signs developed earlier in exMCT animals. Isolated hearts were Langendorff perfused and epicardial membrane potential optically mapped using RH237, and Ca^{2+} transients were simultaneously measured using Rhod-2. Signals were recorded with external pacing at 5 Hz. Following optical mapping, hearts were fixed in 5% paraformaldehyde by immersion and imaged with diffusion tensor MRI using a Bruker 9.4 T system and a diffusion weighted spin-echo protocol to reveal myocardial fibre structure at a resolution of 200 μm isotropic.

Preliminary studies confirm voluntary exercise prolongs survival: no exMCT animals developed heart failure signs on the day of such signs in sedMCT animals (21±0.26 days, n=6). MCT treatment significantly increased RV action potential duration (APD80, MCT 71.6±7.7 ms; CON 42.3±5.4 ms, $p<0.05$ n=10) and fibre disarray (R^2, MCT 0.84±0.04; CON 0.47±0.04, $p<0.001$, n=10). No exMCT values were above the median MCT value, suggesting a trend for attenuation of these effects by exercise.

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