Depolarizing hyperkalemic arrest reduces Mn^{2+}-induced MRI signal enhancement in pig hearts

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Aim: To assess whether sarcolemma depolarization affects MRI contrast enhancement by $MnCl_2$ in pig hearts.

Background: Mn^{2+} is an intracellular type contrast agent, uptake of which is mediated by Ca^{2+} channels [1]. Therefore sarcolemmal depolarization that inactivates Ca^{2+} channels and reduces the driving force for cation influx should affect Mn^{2+} accumulation and contrast development.

Methods: 1. ***Animal model.*** In domestic pigs weighing 25-35 kg (n = 22) 1st and 2nd diagonal branches of the left anterior descending coronary artery (LAD) were acutely or chronically (3, 7 & 14 days) ligated. The hearts were excised and perfused *ex vivo* with 50:50 mixture of blood and Krebs-Henseleit buffer at constant flow. Five hearts were arrested by increasing $[K^+]$ from 4.7 to 16 mM. Cardiac function was recorded via the LV balloon. **2.** ***MRI.*** *Ex vivo* experiments were performed on a 7T magnet, interfaced to a Bruker Biospec console using spin-echo multislice sequence (FOV of 16x16 cm^2, TE = 8 ms, data matrix a 128x128 points). The heart and 2 reference test tubes containing H_2O and H_2O + 10 mM $CuSO_4$ were placed into the perfusion chamber within the birdcage coil. For beating hearts the signal acquisition was gated by the LV dP/dt (TR=800 ms). Six 8-mm thick slices separated by 2 mm were obtained. Following the baseline image, 0.2 mM $MnCl_2$ was added and serial images were taken every 5 min over a 20-min period. Signal intensities in normal areas for each slice were normalized to those of the H_2O reference.

Results: In beating hearts intensities increments (ΔI) in normal areas were greater than those in arrested hearts after 15-20 min Mn^{2+} loading (Figure & Table). Time courses of ΔI were fitted to an exponential function: $\Delta I=\Delta I_{max}[1-\exp(-t/t1)]$. The rates of ΔI rise ($\Delta I_{max}/t1$) and maximal increments (ΔI_{max}) were significantly lower during KCl arrest whereas t1 values did not differ (Table). In ischemic/infarcted areas, intensity increases were much smaller and were not significantly affected by KCl arrest.

Conclusions: Inhibition of Mn^{2+} enhancement development by KCl arrest implies that sarcolemmal depolarization inhibits Mn^{2+} uptake by normal myocytes.

Group (n)	Parameters				
	ΔI(15-20)	ΔI_{max}, %	t1, min	$\Delta I_{max}/t1$, %/min	R^2
Beating (17)	103±26	111±2.2	6.6±0.35	16.8±0.9	0.999
KCl-arrested (5)	67±23	67±6.9	5.2±1.44	12.9±3.57	0.98
p	*0.0003*	*<0.05*		*<0.05*	

Reference: 1. Wendland MF. *NMR Biomed,* **17**:581-594;2004.