RELAXOGRAPHIC ANALYSIS OF THE EFFECTS OF MANGANESE INFUSION AND STRESS IN RAT MYOCARDIUM

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Introduction. Manganese ions (Mn^{2+}) enter cardiomyocytes via calcium (Ca^{2+}) channels in the sarcolemma, and a main fraction is distributed from cytosol to mitochondria via a Ca^{2+} uniport. Both Mn^{2+}-fluxes may be enhanced by inotropic stimuli [1]. The aim of the present study was to examine MR relaxation of myocardium subjected to Mn^{2+}-infusion and a simultaneous or delayed β-adrenergic stress. A working hypothesis is that redistribution of Mn^{2+} from cytosol to mitochondria might enhance relaxation considerably due to binding to mitochondrial macromolecules.

Material and Methods. Wistar ♂ rat hearts were perfused a.m. Langendorff with Krebs buffer containing $MnCl_2$ (25μM) and the stressor isoprenaline (10^{-7} M) at time intervals shown in Figure 1. Ventricular myocardium was excised and relaxation measured by Saturation Recovery (T_1) and Carr-Purcell-Meiboom-Gill (T_2) methods using a Maran Ultra instrument (Resonance Instruments, 23MHz, 37°C). Relaxography was performed within 5 min after excision to avoid major ischemic changes, and data were fitted in a two-component model [2,3] revealing the apparent intracellular (ic) and extracellular (ec) relaxation times.

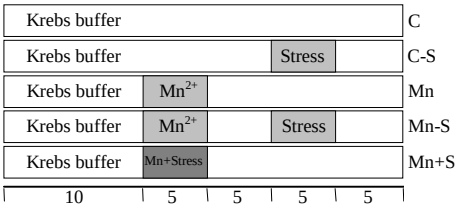

Figure 1: Time course in min.

Results. Mn^{2+}-infusion shortened ic T_1 from 590 ms (C) to 290 ms (Mn) and ec T_1 from 1800ms (C) to 1200 ms (Mn). By a simultaneous stress (Mn-S) T_1 was further shortened to 190 ms (ic) and 1000 ms (ec) while a delayed stress (Mn+S) did not alter T_1-relaxation. The effects on T_2 were minor with ic-T_2 ~70 ms and ec-T_2 ~650 ms for all groups. Population fractions were almost similar in all groups (62 % for ic-p_1 and 72 % for ic-p_2).

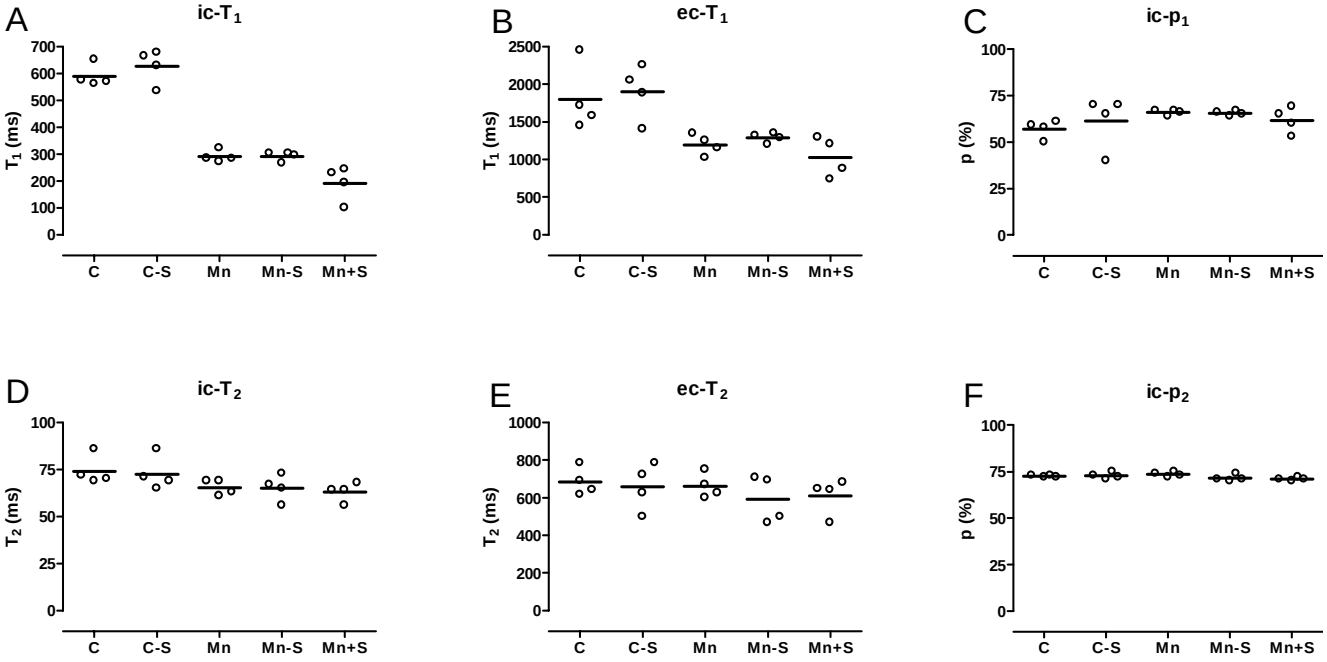

Figure 2: Values for T_1, T_2 and population fractions (p).

Conclusions. We confirmed [4] that simultaneous Mn^{2+}-infusion and β-adrenergic stress lead to a major (68/45 % ic/ec) reduction in myocardial T_1 and showed that a main part of this reduction (51/33 % ic/ec) results from Mn^{2+}-infusion only. Stress did not influence T_1 whether induced alone or delayed after Mn^{2+}-infusion. The absence of further relaxation enhancement in the latter group may indicate that residual cytosolic Mn^{2+}, after cell efflux via the Na^{+}-Ca^{2+} exchanger, was reduced below a critical value necessary for redistribution to mitochondria. Altogether, our results confirm the role of mitochondria as a major sink for Mn^{2+} ions.

References.

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