micro-regional signals (''$Ca^{2+}{}_i$ ripples'') at selected eight time points that were analyzed for dynamic changes in peak $Ca^{2+}{}_i$ amplitudes and frequencies across both STS exposure times and CCh treatment with standard methods consisting of nonlinear curve-fitting and fast Fourier transform, respectively, and with a novel method of recurrence quantification analysis. Their results, although at times mixed or conflicting, showed that there may indeed be alterations in local $Ca^{2+}{}_i$ signaling/dynamic which are biologically valid and sometimes differ from the global $Ca^{2+}{}_i$ signaling/dynamic of whole cytoplasms.
I propose, then, that, at least for intrinsic apoptosis, an early activation of caspases leads to cleavages of increasingly more IP3 receptors and sarco-/endoplasmic reticulum Ca^{2+} ATPase of ER which may enhance $Ca^{2+}{}_i$ release by the former and inhibit uptake by the latter. Ultimately, this results in the accumulation of the ion that starts locally and heterogeneously until spreading by waves and becoming more apparent at the whole cytoplasmic scale.

2784-Pos Board B754

External Sodium Affects SOCE Activation In Mouse FDB Muscle Fibers

Pura Bolaños, Alis Guillen, Reinaldo DiPolo, Carlo Caputo.
Instituto Venezolano de Investigaciones Cientificas, IVIC, Caracas, Venezuela.

We report experiments carried out to study the possible contribution of the Na^+/Ca^{2+} exchanger activity to $[Ca^{2+}]_{myo}$ levels during SOCE activation in mouse muscle fibers. Enzymatically dissociated FDB fibers, loaded with FURA-2 AM, and treated with 5 μM CPA, were submitted to a SR Ca^{2+} store depletion procedure, in the absence of external Ca^{2+}. Exposure to external Ca^{2+} (2mM) activated SOCE under two different modalities. In 9 fibers, $[Ca^{2+}]_{myo}$ increased at a rate of 0.9 ± 0.1 nM/s showing saturation. In 7 other fibers the rate of $[Ca^{2+}]_{myo}$ increase was 1.5 ± 0.3 ($p<0.05$), with no sign of saturation at 115 ± 11 s after SOCE activation. Exposure to a $0Na^+$ solution caused a fast, partial reversal of the SOCE dependent $[Ca^{2+}]_{myo}$ increase. Activation of SOCE was much depressed in the absence of external Na^+; subsequent re-exposure to Na^+ greatly increased $[Ca^{2+}]_{myo}$ and its rate of rise. TRIS was about twice more effective than Li^+ as Na^+ substitute. Thus, $[Ca^{2+}]_{myo}$ decreased by 76.6 ± 6.4 or 33.8 ± 21.4 nM, ($p<0.05$) in the presence of TRIS or Li^+ respectively. In both cases however, the effect occurred with similar time constants: 32.3 ± 2.2 *vs* 29.9 ± 3.6 s^{-1}. When TRIS was used, Na^+ dependent SOCE activation showed a Kd of about 25 mM. Preliminary experiments with the Na^+ sensitive compound benzofuran isophtalate (SBFI) indicate that simultaneously with SOCE activation there is an increase in the myoplasmic Na^+ concentration. If so, the possibility arise that high myoplasmic Na^+ could activate the sarcolemmal Na^+/Ca^{2+} exchanger in its reverse mode, or even the mitochondrial Na^+/Ca^{2+} exchanger. An alternate possibility could be a direct modulatory effect of Na^+ on SOCE activation machinery (FONACIT G-2001000637).