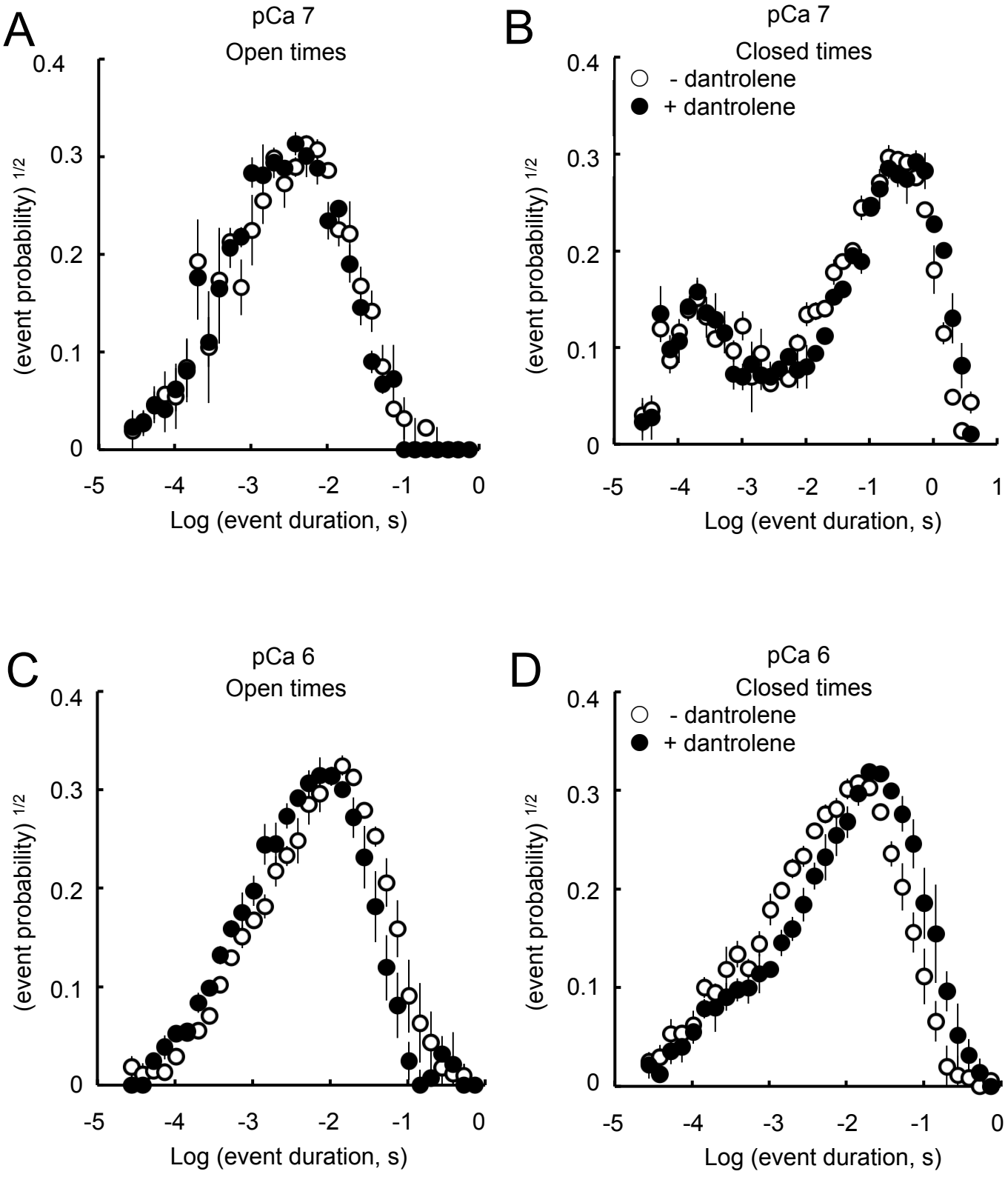
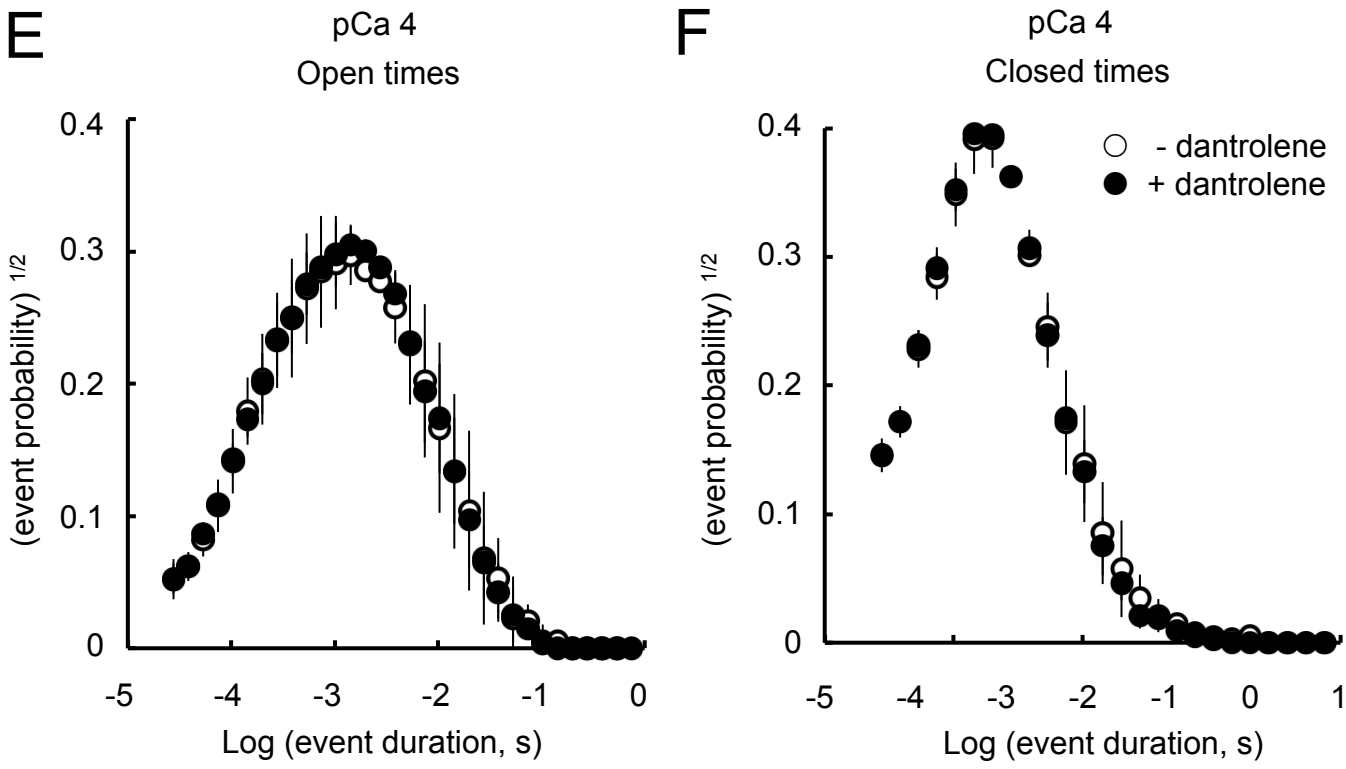
Essential role of Calmodulin in RyR inhibition by dantrolene
Y.W. Oo, N. Gomez-Hurtado, K. Walweel, D.F. van Helden, M. S. Imtiaz, B.C. Knollmann and D.R. Laver
Molecular Pharmacology



Supplementary 1 (part 1)



Supplementary figure 1. Effect of dantrolene on open and closed dwell-times of RyR2. (A,C,E) Open and **(B,D,F)** closed dwell-time histograms compiled using the log-bin method of Sigworth and Sine (1987). Histograms are averages of three experiments obtained in cytoplasmic [Ca^{2+}] (indicated by pCa in each pannel) in the absence (○) or presence (●) of 10 μM dantrolene. The constants of exponential constants fits to these dwell-time histograms are given in Supplementary Table 1. Figure 1C and D that the data from Figure 2A and B are re-plotted here for comparison purposes.

Supplementary 1 (part 2)

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	Fit to open dwell times				Fit to closed dwell times			
condition	A1 %	T1 ms	A2 %	T2 ms	A1 %	T1 ms	A2 %	T2 ms
pCa7	73 ± 16	3.8 ± 0.6	27 ± 16	22 ± 6	11 ± 3	0.77 ± 0.18	89 ± 3	500 ± 100
pCa7 + dan	81 ± 12	4.4 ± 1.0	19 ± 12	22 ± 5	8 ± 4	0.37 ± 0.04	92 ± 4	700 ± 150*
pCa6	37 ± 7	8 ± 2	63 ± 7	27 ± 9	31 ± 5	5 ± 2	69 ± 5	27 ± 6
pCa6 + dan	41 ± 17	5.2 ± 0.5	59 ± 18	16 ± 1	35 ± 10	15 ± 9	65 ± 10	50 ± 20
pCa4	68 ± 5	1.8 ± 0.4	32 ± 5	8 ± 2	93 ± 5	0.19 ± 0.01	7 ± 5	0.91 ± 0.09
pCa4 + dan	70 ± 10	1.7 ± 0.4	30 ± 10	7 ± 2	88 ± 3	0.18 ± 0.03	12 ± 3	0.61 ± 0.08

Table 1. Parameter values for multi exponential fits to RyR2 dwell-time histograms (***H(t)***). The conditions give the cytoplasmic [Ca^{2+}] in units of pCa in the absence and presence of 10 μM dantrolene. T1 and T2 are the exponential time constants and A1 and A2 give fraction of dwell times in each exponential where A1 + A2 = 100%. Asterisks indicate significant difference to absence of dantrolene in paired t-test (* $p<0.05$). The equation is: $H(t) = A1\ T1.exp(-t/T1) + A2\ T2.exp(-t/T2)$