Intracellular acidosis increases t-system excitability in depolarised muscle fibres of the rat in the presence but not in the absence of chloride

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This study was undertaken as part of an investigation into the mechanism responsible for the marked increase in the excitability of depolarised muscle upon intracellular acidification[1]. The preparation used in the study was the mechanically skinned fibre, where the surface membrane is removed by microdissection causing the t-system to seal off and polarize to different levels by placing it in carefully designed solutions. In this preparation all steps in the excitation-contraction coupling process are maintained fully functional[2] while allowing direct access to the intracellular environment, thus permitting direct control of intracellular pH and the level of polarization of the t-system.

The skinned fibre preparation was obtained from the extensor digitorum longus muscle of adult rats killed by halothane overdose as previously described[2] and the preparation was placed in a solution mimicking the myoplasmic environment. Action potential (AP) induced tetanic force responses were generated with square pulses of 2ms duration and field strength of 70V/cm at 25Hz for 1s [2]. Alternatively, the voltage sensors in the t-system were activated independently of APs, by replacing all K^+ in the bathing solutions with Na^+ [2]. Results obtained in carefully balanced solutions at pH 7.1 and pH 6.6. No pH dependence was observed in voltage-sensor activated force responses that were independent of APs in the presence or in the absence of Cl^- or in the AP-induced responses in the absence of Cl^- in solutions. However, in the presence of Cl^-, force responses to APs in the t-system were markedly greater at pH 6.6 than at pH 7.1 when the t-system was depolarized to the same level below about –70mV. These results indicate that Cl^- channels mediate the protective effect of intracellular acidosis on AP-induced force responses.

(1) Posterino et al, J Physiol 527, 131, 2000.
(2) Nielsen et al, J Physiol 536, 161, 2001.