Scientific Meeting
AuPS | ASB
HOBART · 2022

Abstract: 156P

Calcium release-activated channel activity in the uterus – CRAC-ing labour contractions

Jawaher H. Alfaidi, Harold A. Coleman, Helena C. Parkington

Department of Physiology, Monash University, Clayton, Vic, 3800.

Controlling uterine contractile activity is of great importance for successful labour. Increases in uterine contraction require intracellular free calcium, which occur as a consequence of calcium influx through voltage-gated calcium channels (VGCC), or calcium release from intracellular stores, the endoplasmic reticulum (ER). These mechanisms occur spontaneously and are used by contractants such as oxytocin (OT). Until now, no studies have described, in any species, the relative contributions of these mechanisms during labour. The aim of this project was to plug that gap.

Simultaneous recording were made of electrical activity and force in rat tissue strips obtained before and during labour. The blockers used were nifedipine for VGCCs, GSK-7975A for calcium release-activated channels (CRACs), and cyclopiazonic acid (CPA) for ER calcium.

Blocking CRACs induced a significant 8.5mV hyperpolarization of the membrane which abolished spontaneous activity. GSK-7975A also repolarized OT-induced depolarization and contraction. Before labour, calcium entry through VGCCs contributed to ~70% of OT-stimulated contraction, while VGCCs only contributed to 30% of tension during labour. CRAC channels accounted for 13% of the contraction before labour, but this significantly increased to 50% of tension during labour. Transient receptor-potential C channels (TRPCs) supported 26% and 15% of contraction before and during labour, respectively. Myosin light-chain phosphatase (MLCP) suppression contribution to contraction did not change with labour.

These findings reveal a hitherto unreported and unexpected role for CRAC in regulating uterine activity during labour. Clearly, further investigations are required to quantify the protein and gene changes involved. Also, human tissue needs to be studied. Preterm labour or failure to progress in labour are major clinical problems. OT does not always rescue failure to progress or postpartum haemorrhage, resulting in maternal death, especially in underdeveloped countries. Clearly, new therapeutic approaches are required and CRAC may be a novel consideration