Calcium signalling in glial cells: a potential role for TRP channels

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Glia possess specific receptors which allow these cells to respond to changes in neuronal activity. This neuron-glia cross-talk suggests that glia are integral modulatory components of neuronal excitability and synaptic transmission. Intra-glial Ca^{2+} signals, including Ca^{2+} oscillations, are important arbiters of glial activity but are poorly understood. Our aims were threefold: i) to establish the role of the endoplasmic reticulum (ER) in oscillations, ii) to determine if store-operated channels (SOCs) subserve this role, and finally iii) to explore links between, and possible co-identity of, SOC and transient receptor potential (TRP) channels. Standard recombinant DNA procedures were used to detect TRPC1 mRNA expression in primary hippocampal cultures (0-3 day neurons and glia). A modified calcium phosphate-based technique was used to transfect cells with either TRPC1 siRNA and/or D1ER cameleon (ER Ca^{2+} sensor) DNA. siRNA TRPC1 down-regulation was assessed with semi-quantitative PCR. Confocal microscopy techniques determined biosensor localisation and measured Ca^{2+} dynamics (fluo-4 and D1ER). Glia (confirmed by GFAP staining) but not neurons, expressed fully functional D1-ER. Glutamate (1μM-1mM) induced complex Ca^{2+} oscillations (n=6) that were significantly reduced by removal of extracellular Ca^{2+} (n=3), and caused reversible release from ER Ca^{2+} stores (n=6) independent of extracellular Ca^{2+}. Prior depletion of ER Ca^{2+} stores with thapsigargin (1μM) significantly reduced subsequent glutamate-induced Ca^{2+} responses (n=3) and triggered SOC function (n=3). TRPC1 mRNA was present in detectable levels in cell cultures (n=6). Low transfection efficiencies diluted overall siRNA TRPC1 down-regulation. ER function is clearly involved in glial calcium signaling and linked with activation of store-operated channels. Further assessment of the relationship between SOC and TRP channels requires improved siRNA delivery.