Sphingosine 1-phosphate induces Ca2+ transients and cytoskeletal rearrangement in C2C12 myoblastic cells

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Abstract:
In many cell systems, sphingosine 1-phosphate (SPP) increases cytosolic Ca2+ concentration ([Ca2+](i)) by acting as intracellular mediator and extracellular ligand. We recently demonstrated (Meacci E, Cencetti F, Formigli L, Squecco R, Donati C, Tiribilli B, Quercioli F, Zecchi-Orlandini S, Francini F, and Bruni P. Biochem J 362: 349-357, 2002) involvement of endothelial differentiation gene (Edg) receptors (Rs) specific for SPP in agonist-mediated Ca2+ response of a mouse skeletal myoblastic (C2C12) cell line. Here, we investigated the Ca2+ sources of SPP-mediated Ca2+ transients in C2C12 cells and the possible correlation of ion response to cytoskeletal rearrangement. Confocal fluorescence imaging of C2C12 cells preloaded with Ca2+ dye fluo 3 revealed that SPP elicited a transient Ca2+ increase propagating as a wave throughout the cell. This response required extracellular and intracellular Ca2+ pool mobilization. Indeed, it was significantly reduced by removal of external Ca2+, pretreatment with nifedipine (blocker of L-type plasma membrane Ca2+ channels), and inositol 1,4,5-trisphosphate [Ins(1,4,5)P-3]-mediated Ca2+ pathway inhibitors. Involvement of EdgRs was tested with suramin (specific inhibitor of Edg-3). Fluorescence associated with Ins(1,4,5)P(3)Rs and L-type Ca2+ channels was evident in C2C12 cells. SPP also induced C2C12 cell contraction. This event, however, was unrelated to [Ca2+](i) increase, because the two phenomena were temporally shifted. We propose that SPP may promote C2C12 cell contraction through Ca2+ independent mechanisms.