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The roles of G_q and G_{12} families of G-proteins in the regulation of neurite morphology.

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Growth cone collapse and neurite retraction are involved in developmental and regenerative processes in the nervous system. Ligands of G-proteins coupled receptors, such as the blood-borne factors thrombin and lysophosphatidic acid (LPA), have been shown to induce these morphological changes in neural cell lines and primary neurons. However, the specific roles of G-protein mediated signalling cascades leading to the induction of growth cone collapse and neurite retraction remained unclear. We used here primary neurons isolated from $G\alpha_q/G\alpha_{11}$- and $G\alpha_{12}/G\alpha_{13}$-deficient mouse brains to test distinct roles of G_q/G_{11}- and G_{12}/G_{13}-mediated signalling pathways in the process of thrombin and LPA-mediated neurite retraction. We showed that G_{12}/G_{13}-mediated signalling was absolutely essential for the effects of thrombin and LPA on neurite morphology. Interestingly, the action of LPA was predominantly mediated by G_{13}, while thrombin appeared to act preferably via G_{12}. Surprisingly, the absence of $G\alpha_q/G\alpha_{11}$ lead to a substantially enhanced response to both stimuli, indicating the novel role of G_q/G_{11}-mediated pathway as an antagonistic regulator of G_{12}/G_{13}-signalling. Provided evidence suggested that G_q/G_{11}-dependent inhibition of G_{12}/G_{13}-RhoA-mediated neurite retraction and growth cone collapse occurs most likely via calcium-dependent activation of Rac. Our data suggest that the G_q/G_{11}-mediated signalling pathway is a potential target for stimulating neuronal outgrowth and repair after nervous system injury.