Lysophosphatidic acid signaling in neural functions

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Since lysophosphatidic acid (LPA) was implicated as an intercellular mediator in 1989, accumulating evidence has indicated that LPA regulates many biological and pathological functions through stimulation of G protein-coupled LPA receptors (LPA_1~LPA_6). LPA_1-mediated LPA signaling has been shown to play an important role in neuropathic pain through enhancement of demyelination and reorganization of Aβ fibers. Furthermore, nerve injury is demonstrated to enhance LPA production via lysophospholipase D to cause neuropathic pain. These studies strongly suggest that LPA is an endogenous pain modulator. By contrast, the fundamental basis of LPA actions mediated by other LPA receptors in neuronal cells remains to be clarified. Recently, we have found that LPA stimulates neurite branch formation through LPA_3 in neuronal cells, including pheochromocytoma12 cells, B103 neuroblastoma cells, and hippocampal neurons. This effect is contrast to transient neurite retraction produced by activation of all other LPA receptor subtypes. In this symposium, I will discuss the molecular mechanisms of LPA_3-dependent neurite branch formation and its biological significance.