The absence of LPA1 receptor results in lipidome dysregulation and Neuropeptide-Y underexpression

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Abstract

LPA1 receptor is one of the six characterized G protein-coupled receptors (LPA_{1-6}) through which lysophosphatidic acid acts as an intercellular signaling molecule. It has been shown that the LPA1 receptor is involved in emotional regulation and, when depleted, has a key role in vulnerability to stress. In this sense, maLPA1-null mice, a knockout model for LPA1 receptor has been recently proposed as a model of anxious depression. Here, we sought to elucidate the effect of the genetic depletion of this receptor of LPA_1 receptor in both lipidome and Neuropeptide-Y (NPY) signaling, two factors associated with adaptive stress regulation. For that purpose, we measured the lipidomic profile of wild-type mice and maLPA1-null mice in both hippocampus and serum. In addition, through immunohistochemical procedures we quantified NPY+ cells in hippocampus, basolateral amygdala (BLA) and central amygdala (CeA). Interestingly, the comparative lipidomics analysis revealed differences in certain subspecies which are related to LPA1 receptor functionality. Regarding NPY, we found a reduction in BLA, but

not in hippocampus. Overall, both lipid abnormalities and amygdalar dysfunction of NPY can be related to lower resources in stress coping and, in turn, higher vulnerability to the noxious effect of stress that might lead to anxiety and depressive-like states.

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