Stress, depression and the hippocampus: modulatory effects of continuous LPA treatment

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The LPA_1, one of the six characterized G protein-coupled receptors (LPA_{1-6}) through which lysophosphatidic acid acts may be involved in promoting normal emotional behaviors. Evidence also imply a role for the LPA_1 receptor in mediating the consequences of stress on the hippocampus. However, to date, there is not available information regarding the mechanisms whereby the LPA_1 receptor mediates this adaptation. Changes in glutamate/GABA cycling could be one possible mechanism. To gain further insight into how LPA-LPA_1 may prevent the negative consequences of chronic stress, we assessed the effects of chronic ICV administration of LPA on depressive-like behaviours induced by a chronic restraint stress protocol. Then, gene expression for molecular markers for excitatory and inhibitory neurotransmission was determined. In addition, the hippocampal expression of mineralocorticoid receptor and glucocorticoid receptor genes and proteins were determined, as well as plasma corticosterone levels. Contrary to expectations, the continuous delivery of LPA in chronically stressed animals instead of inhibiting, potentiated some, though not all, negative effects of stress. Furthermore, this treatment induced as well altered the excitatory/inhibitory balance in the ventral hippocampus. In conclusion, the results of this study reinforce the assumption that LPA, mainly through the LPA_1 receptor, regulates hippocampal-dependent behaviour and functions.

Key words: lysophosphatidic acid, LPA, chronic stress, animal models of depression, hippocampus

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