Implications of Chronic Treatment with Ethanol on Some Parameters of the Inflammatory Response Induced by Lysophosphatidic Acid

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Neuroinflammation is a defense mechanism against insults such as infection, injury or disease. Many studies suggest a role for ethanol (EtOH) modulating inflammatory processes in rat brain, although cellular and molecular mechanisms by which alcohol causes brain damage are not fully understood. In the present study we used C6 cells to establish the implications of chronic treatment with EtOH on some parameters of the inflammatory response induced by bacterial LPS. We found that EtOH prevented the LPS-induced production of tumor necrosis factor α (TNF-α) without decreasing cell viability. Either LPS treated or EtOH plus LPS treated cells presented upregulated glial fibrillary acidic protein (GFAP) and downregulated vimentin levels characterizing a program of reactive astrogliosis. Also, EtOH plus LPS stimulation greatly increased the levels of reactive oxygen species (ROS) evaluated by DCF-DA measurement. Western blot analysis indicated that either EtOH, LPS or EtOH plus LPS treatments are unable to affect Akt/GSK3β signaling pathway. However, LPS alone and EtOH plus LPS co-treatment inhibited Erk phosphorylation. Furthermore, cells co-incubated with LPS and EtOH presented reversion of the dramatic loss of stress fibers provoked by EtOH. Interestingly, EtOH suppresses the inflammatory cascade (TNF-α production) in response to LPS. Concomitantly it sustains Erk inhibition, increases ROS production and induces reactive astrogliosis in the presence of LPS, conditions associated with neurotoxicity. The effects observed were not supported by actin reorganization. Altogether, these findings could mean that EtOH elicits a dual action in glial cell and probably Erk signaling takes part of the signaling pathways leading to cellular injury.

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