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Involvement of Inflammation in the Pathophysiology and Treatment of Mood Disorders

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Introduction: Accumulating data suggests that inflammation plays a role in the pathogenesis and treatment of mood disorders. Consistently, classic anti-inflammatory drugs exerted beneficial effects in randomized clinical trials of mood disorders patients. Moreover, psychotropic drugs possess anti-inflammatory effects. However, despite these supporting findings, many contradicting results have also been reported.

Aims: (1) We investigated the effects of chronic treatment with psychotropic drugs on bacterial lipopolysaccharide (LPS)-induced inflammation in rats; (2) we tested the efficacy of mechanistically-different anti-inflammatory compounds in behavioral models in rats.

Materials and Methods: (1) Rats were treated with psychotropic drugs (carbamazepine, lithium, haloperidol, and imipramine) for 4 weeks through a daily intraperitoneal (ip) injection. On day 29, rats were injected with vehicle or LPS. At 2 hours later, rats were sacrificed, blood was collected and different brain regions were excised. Levels of inflammatory constituents in plasma and brain were examined by ELISA. (2) Rats were treated (ip) for 2 weeks with one of the following anti-inflammatory compounds: dexamethasone, a potent corticosteroid; nimesulide, a selective cyclooxygenase-2 inhibitor; montelukast, a leukotrienes receptors antagonist; pentoxifylline, a tumor necrosis factor-a inhibitor; and, JSH-23, a selective inhibitor of nuclear factor-k B. At the end of drug treatment, animals were subjected to a battery of behavioral tests.

Results: Psychotropic drugs treatment resulted in both anti- and pro-inflammatory effects. Some of the drugs prominently affected the levels of particular inflammatory mediators in the plasma and specific brain regions. Similarly, the various anti-inflammatory compounds differently affected the behavioral phenotypes of rats, showing both therapeutic and negative effects.

Conclusions: Our results add to the ambiguity regarding the role of anti-inflammation as a therapeutic strategy for mood disorders. It is important to elucidate the therapeutic potential of mediator/pathway-specific anti-inflammatory compounds in randomized clinical trials.

Biography:

Dr. Azab completed his Ph.D. in pharmacology in the Department of Clinical Pharmacology in Ben-Gurion University of the Negev (Israel), focusing on the study of anti-inflammatory drugs. Subsequently, as a post-doctoral fellow in Wayne State University (Michigan), Dr. Azab investigated the mechanisms of mood-stabilizing drugs, focusing on the role of GSK-3 in inositol biosynthesis. Currently, Dr. Azab is an assistant professor in Ben-Gurion University of the Negev. Major research projects in his lab: 1) Studying the role of inflammation in the pathophysiology and treatment of mood disorders; 2) searching for novel therapeutic strategies for mood disorders.