Prozac and Celexa exhibit anti-inflammatory effects

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A new study found that fluoxetine (Prozac) and citalopram (Celexa) treatment significantly inhibited disease progression of collagen-induced arthritis (CIA) in mice. Research led by Sandra Sacre, Ph.D. from the Brighton and Sussex Medical School (BSMS) in the UK studied the anti-arthritic potential of these drugs, known as selective serotonin reuptake inhibitors (SSRIs), most commonly used to treat depression. Both SSRIs exhibited anti-inflammatory effects and may provide drug development opportunities for arthritic conditions such as rheumatoid arthritis (RA). Full findings of this study are published in the March issue of *Arthritis & Rheumatism*, a journal of the American College of Rheumatology.

RA is an autoimmune disease that causes inflammation in the lining of the joints. Typically, RA first affects hand and foot joints and later the disease spreads to larger joints. Inflammation eventually erodes the cartilage between the joints (articular cartilage) causing pain, stiffness, joint deformity, and physical disability. According to the 2000 Global Disease Burden study by the World Health Organization (WHO), RA affects approximately 1% of the world population.

To understand the anti-inflammatory properties of SSRIs, the research team at The Kennedy Institute of Rheumatology investigated the use of fluoxetine and citalopram in mouse and human models of RA. Dr Sacre, a lecturer in molecular cell biology at BSMS, a partnership between the universities of Brighton and Sussex, said: "We were interested in SSRIs because of their reported anti-inflammatory effects." "Prior studies have shown that patients with depression who respond to treatment with

SSRIs display a reduction in cytokine levels (signals that can induce inflammation), suggesting a connection between SSRIs and the immune system."

In the current study, researchers used a CIA mouse model due to the similarities to human RA, including synovitis, bone erosion and pannus formation. At the onset of arthritis, mice were treated daily for 7 days with a dose of 10 or 25 mg/kg of fluoxetine and 25 mg/kg of citalopram. At the lower dose of fluoxetine the mice showed a small reduction in the clinical score (a combined measure of redness, swelling and joint mobility/deformity) and a slower increase in paw swelling. At a dose of 25 mg/kg, fluoxetine halted disease progression and no further elevation was noted in the clinical score or paw swelling. "We observed reduced inflammation, reduced cartilage and bone erosion, and a preservation of the joint structure in the mice treated with a higher dose of fluoxetine," commented Dr. Sacre. Citalopram was not as effective as fluoxetine at inhibiting disease progression in this model.

Researchers also observed a decrease in cytokine production from cultures of human RA synovial joint tissues that were treated with SSRIs. Toll-like receptors (TLRs) are strong activators of immune cells leading to the production of cytokines that can induce inflammation. Fluoxetine was found to inhibit the activation of TLRs more effectively than citalopram.

"While the SSRIs effectively target TLRs contributing to inflammation and could provide therapeutic benefit in RA, they are not ideal candidates to progress into clinical trials," concluded Dr. Sacre. The levels of the SSRIs required to halt disease progression are higher than normally prescribed for standard treatment (depression in humans). "Our data suggests that effective inhibition of RA would require levels of the drugs higher than the safe therapeutic dosages." The authors suggest further study of the role of TLRs in chronic inflammation may uncover

drugs that offer an effective treatment of RA in the future.

More information: "Fluoxetine and Citalopram Exhibit Potent Antiinflammatory Activity in Human and Murine Models of Rheumatoid Arthritis and Inhibit Toll-like Receptors." Sandra Sacre, Mino Medghalchi, Bernard Gregory, Fionula Brennan, and Richard Williams. Arthritis & Rheumatism; Published Online: February 25, 2010 (DOI: 10.1002/art.23704); Print Issue Date: March 2010.

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