Antidepressant bone loss could be prevented with beta-blockers

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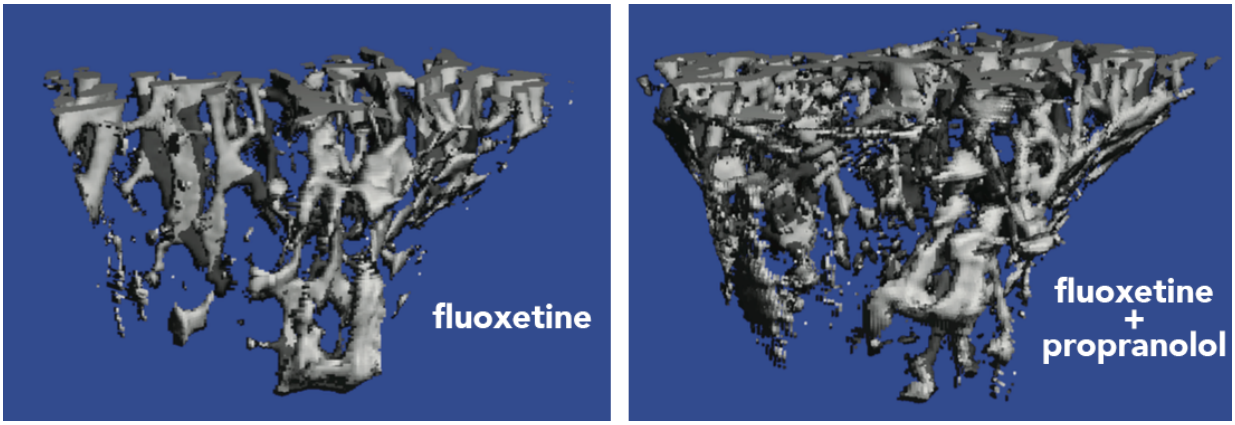

Bone scans of mice after treatment with the antidepressant fluoxetine show that adding the beta-blocker propranolol prevents bone loss. Credit: Patricia Ducy, Ph.D., CUMC

The antidepressant fluoxetine causes bone loss by instructing the brain to send out signals that increase bone breakdown, but a beta-blocker can intercept the signals, a new study in mice has found.

The study was published Sept. 5 in *Nature Medicine*.

The use of selective serotonin-reuptake inhibitors (SSRIs), a class of drugs broadly prescribed for mood disorders as well as for nonpsychiatric conditions, previously has been associated with an

increased risk of bone fracture.

The new study—by Patricia Ducy, PhD, and colleagues at Columbia University Medical Center—revealed that fluoxetine, one of the most-prescribed SSRIs, acts on bone physiology through two distinct mechanisms. Initially, fluoxetine protects bone by inhibiting the cells in the skeleton (osteoclasts) that constantly break down and resorb bone. But after a few weeks of treatment, fluoxetine triggers a brain-mediated signal that not only counteracts this effect but also impairs bone formation, thus leading to bone loss.

The brain signals cause bone loss by increasing the amount of epinephrine in the bloodstream, and the researchers found that they could neutralize these signals by co-treating the mice with a low dose of the beta-blocker propranolol. In these animals, bone loss was no longer observed with long-term fluoxetine treatment. The behavior of the mice did not change with co-treatment, suggesting that fluoxetine's effect on the brain and mood was not impaired.

Adding low-dose propranolol to depression treatment could potentially block an SSRI's deleterious effect on bone mass, Dr. Ducy says, and may be particularly important for peri- and postmenopausal women since they are already at risk of developing osteoporosis.

More information: María José Ortuño et al. Serotonin-reuptake inhibitors act centrally to cause bone loss in mice by counteracting a local anti-resorptive effect, *Nature Medicine* (2016). DOI: 10.1038/nm.4166

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