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Selective serotonin reuptake inhibitors anti-depressants act as endocrine disruptors of the feto-placental unit

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Selective serotonin-reuptake inhibitors (SSRIs) are prescribed to up to 6.2% of pregnant women. SSRIs have been associated with adverse effects on pregnancy and fetal development. However, the action of SSRIs onthe endocrine function of the feto-placental unit has not been studied. Our objective was to characterize the effect of fluoxetine, the most commonly prescribed SSRI during pregnancy, and its active metabolite, norfluoxetine, on placental aromatase (CYP19) and feto-placental steroidogenesis. A co-culture of BeWo (human villous trophoblast-like) and H295R (human fetal-like adrenocortical) cells, which we established as a representative model of feto-placental steroidogenesis, was treated with physiologically relevant concentrations (0.3, 1 and 3μM) of fluoxetine or norfluoxetine for 24 h. Fluoxetine did not affect β-human chorionic gonadotropin, progesterone, dehydroepiandrosterone, androstenedione, estrone, estradiol or estriol production. Norfluoxetine concentration-dependently reduced the production of estrone up to 62% and estradiol by 70% at 3 μM. In BeWo cells, fluoxetine induced CYP19 activity by 1.6- and 2.3-fold at 1 and 3 μM, respectively, whereas norfluoxetine decreased it by 54% at3 μM. In H295R cells, fluoxetine (1 μM) and norfluoxetine (3 μM) increased CYP19 activity 1.3 and 1.4-fold, respectively. The effect of citalopram, sertraline, paroxetine and venlafaxineon CYP19 activity in BeWo cells was also determined. Paroxetine induced CYP19 activity by 1.7-and 1.9-fold at 1 and 3 μM, respectively; sertraline by 2.7-fold at 1 μM; venlafaxine and citalopram had no effect. Our results indicate that SSRIs may disrupt estrogen biosynthesis in the feto-placental unit, which could have adverse effects on pregnancy and fetal development.

Biography

JThomas Sanderson and Cathy Vaillancourt are experts insteroidogenesis and placental endocrine function, respectively. Their doctoral student, Andree-Anne Hudon Thibeault, has established a co-culture model representing human feto-placental steroidogenesis, which provides a unique tool for the studyof endocrine disruption by exposures to environmental contaminant or medications, such as SSRIs. The ultimate goal of Drs Sanderson and Vaillancourt's research teams is to generate scientific knowledge that will improve the quality of life of mother andfetus, and of the newborn as it growsinto adulthood. This study was funded by the March of Dimes Foundation (12-FY12-179).

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