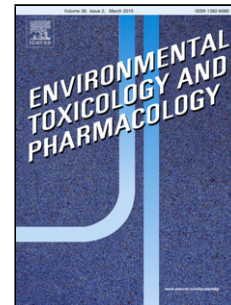


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# Combined oral contraceptive and nitric oxide synthesis inhibition synergistically causes cardiac hypertrophy and exacerbates insulin resistance in female rats

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**Running Title:** COC with NO inhibition synergistically causes cardiac hypertrophy

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## Research highlights

- COC treatment or NO deficiency induces high blood pressure and cardiometabolic disturbances.
- COC treatment or NO deficiency does not result in increased cardiac mass
- COC treatment and NO deficiency synergistically causes cardiac hypertrophy
- COC treatment during NO deficiency exacerbates cardiometabolic disturbances

## Abstract

Combined oral contraceptive (COC) use or inhibition of nitric oxide (NO) synthesis has been shown to cause hypertension and insulin resistance. However, the concomitant effects of COC and NO deficiency on the heart and glucose regulation are not well known. We therefore hypothesized that COC treatment during NO deficiency would lead to the development of cardiac hypertrophy that is associated with aggravated glucose deregulation, pro-inflammatory and pro-fibrotic biomarkers. Eight-week-old female Wistar rats were randomly allotted into control, NO deficient (*N*<sup>G</sup>-nitro-L-arginine methyl ester: L-NAME; 20.0mg/kg *b.w.*), COC-

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