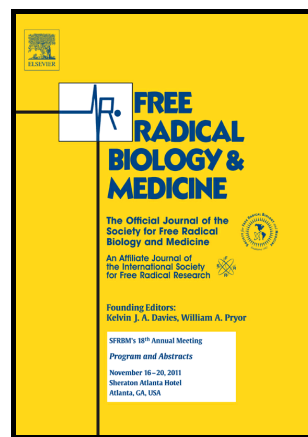


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Sex differences in the nitrate-nitrite-NO[•] pathway:
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ACCEPTED MANUSCRIPT

Sex differences in the nitrate-nitrite-NO[•] pathway: role of oral nitrate-reducing bacteria

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Abstract

Oral reduction of nitrate to nitrite is dependent on the oral microbiome and is the first step of an alternative mammalian pathway to produce nitric oxide in humans. Preliminary evidence suggests important sex differences in this pathway. We prospectively investigated sex-differences following inorganic nitrate supplementation on nitrate/nitrite levels and vascular function, and separately examined sex differences in oral nitrate reduction, and oral microbiota by 16S rRNA profiling. At baseline, females exhibit higher nitrite levels in all biological matrices despite similar nitrate levels to males. Following inorganic nitrate supplementation, plasma nitrite was increased to a significantly greater extent in females than in males and pulse wave velocity was only reduced in females. Females exhibited higher oral bacterial nitrate-reducing activity at baseline and after nitrate supplementation. Despite these differences, there were no differences in the composition of either the total salivary microbiota or those oral taxa with nitrate reductase genes. Our results demonstrate that females have augmented oral nitrate reduction that contributes to higher nitrite levels at baseline and also after inorganic nitrate supplementation, however this was not associated with differences in microbial composition (clinicaltrials.gov: NCT01583803).

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