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Oral Communication Abstract
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Duloxetine reduces lithium-induced polyuria by increasing aquaporin-2 transcription

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Objectives: Selective serotonin reuptake inhibitors (SSRIs) and serotonin and norepinephrine reuptake inhibitors (SNRIs) are two different types of antidepressants, and hyponatremia can occur with both SSRIs and SNRIs. We recently reported that SSRIs such as sertraline upregulate aquaporin-2 (AQP2) via accelerated AQP2 transcription, but how SNRIs such as duloxetine retain water in the kidney is unknown. This study was undertaken to test whether duloxetine may exert antidiuresis by upregulating AQP2 in lithium-induced nephrogenic diabetes insipidus (Li-NDI).

Methods: Sprague-Dawley rats were randomly divided into four groups: controls (n=6), lithium treatment (n=6), duloxetine treatment (n=6), and lithium + duloxetine cotreatment (n=6). Li-NDI was induced by offering lithium chloride (40 mmol lithium/kg dry food) for 2 weeks, and duloxetine (50 mg/kg/d) was additionally administered in food to the treated group for the same period. At the end of the animal experiment, kidneys were harvested to perform immunoblot and qPCR analysis.

Results: Urine output was increased by lithium treatment and decreased by duloxetine cotreatment. Urine osmolality was decreased by lithium treatment and increased by duloxetine cotreatment. The abundances of AQP2 protein and mRNA were reduced by lithium treatment and reversed by duloxetine cotreatment. Consistently, CREB phosphorylation was decreased by lithium treatment and restored by duloxetine cotreatment. Glycogen synthase kinase-3b (GSK3b) phosphorylation was increased by lithium treatment and reversed by duloxetine cotreatment. Interestingly, vasopressin-2 receptor (V2R) mRNA expression was decreased by lithium treatment and restored by duloxetine cotreatment.

Conclusions: In Li-NDI, duloxetine exerts antidiuresis by increasing AQP2 transcription. Recovery of V2R mRNA and GSK3b activity may underlie the duloxetine-induced AQP2 upregulation.