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**Lurasidone-Induced Rabbit Syndrome:  
A Case Report**

**To the Editor:** Rabbit syndrome is an uncommon extrapyramidal symptom occurring in 1.5%–4.4% of patients receiving antipsychotics, characterized by fine, rapid, rhythmic perioral muscle movements along the vertical axis that resemble the chewing motions of a rabbit.<sup>1</sup> First described by Villeneuve in 1972,<sup>2</sup> it is traditionally associated with first-generation antipsychotic use. However, case reports have also attributed this syndrome to second-generation antipsychotics including risperidone<sup>1</sup> and aripiprazole.<sup>3</sup> Here, we describe rabbit syndrome in a patient receiving lurasidone.

**Case report.** Ms A, a 31-year-old white woman with a history of DSM-5–defined major depressive disorder, attention-deficit/hyperactivity disorder, developmental delay, and epilepsy, was admitted psychiatrically for worsening depression and suicidality.

Six months prior to admission, lurasidone was started at 40 mg/d and titrated to 80 mg/d for mood stabilization. One month prior to admission, the dose was increased to 120 mg/d, and Ms A developed intermittent fine, rhythmic, vertical movements of her lips, bilateral resting hand tremor, and akathisia. The dose was tapered down from 120 to 20 mg/d over 1 month prior to admission to address these side effects. However, per clinical assessment during inpatient admission, these aforementioned movements persisted. There was no involvement of her tongue except for passive, lip-associated secondary movements. Other medications included lamotrigine 100 mg bid, venlafaxine 150 mg/d, ergocalciferol 50,000 IU/wk, and omeprazole 40 mg/d. Prior antipsychotic trials included quetiapine and risperidone in the year prior to admission with no recorded history of movement disorders.

To reduce these movements and address the exacerbation of Ms A's mood symptoms, lurasidone was replaced with olanzapine 2.5 mg bid. Her movement symptoms improved in 4–5 days.

This case demonstrates rabbit syndrome attributable to lurasidone, a second-generation antipsychotic previously not reported to be associated with this reaction. Rabbit syndrome is a form of drug-induced parkinsonism; risk for such side effects increases once 80% of nigrostriatal D<sub>2</sub> receptors are occupied.<sup>4</sup> In the case described above, this cumulative threshold of D<sub>2</sub> receptor occupancy was most likely crossed during the lurasidone dose titration that took place in the month prior to hospital admission, as this was the point when the abnormal movements

emerged. Rabbit syndrome is clinically differentiated from tardive dyskinesia by its rhythmicity, sparing of the tongue, and lack of irregular choreoathetotic extrabuccal muscle movements.<sup>5</sup> Additionally, rabbit syndrome is distinct from other forms of drug-induced parkinsonism in that it is exacerbated by physostigmine, a cholinesterase inhibitor, while tardive dyskinesia improves with physostigmine.<sup>6</sup> This is consistent with the observation that rabbit syndrome improves in response to agents with high anticholinergic activity including benztropine, clozapine, and olanzapine.<sup>1</sup> Lurasidone has relatively low anticholinergic activity,<sup>7</sup> which may have contributed to the risk for developing rabbit syndrome during treatment.

This case serves as an important reminder that uncommon extrapyramidal side effects can occur even with the use of newer second-generation antipsychotic agents such as lurasidone.

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