## t is illega to post this copyright ed PDF on any website. Withdrawal-Emergent Dyskinesia Following Abrupt Discontinuation of Desvenlafaxine Discontinuation of Desvenlafaxine

**To the Editor:** Tardive dyskinesia (TD) is defined by the *DSM-5* as athetoid or choreiform movements of the tongue, lower face, jaw, and extremities.<sup>1,2</sup> Withdrawal-emergent dyskinesia (WED) is a subtype of TD that appears after discontinuation or reduction in dosage of a medication and is generally limited to 4–8 weeks.<sup>2</sup> WED has been reported with antipsychotics, but despite an extensive literature search of PubMed with keywords, we found no published cases of WED associated with discontinuation of serotonergic-noradrenergic reuptake inhibitors (SNRIs). Here we describe, to our knowledge, the first case of WED after abrupt discontinuation of desvenlafaxine and subsequent improvement after restarting the medication.

*Case report.* An 84-year-old white man with treatmentrefractory depression and generalized anxiety disorder, as well as multiple medical comorbidities, was started on desvenlafaxine after failing a year-long trial of venlafaxine. He stayed on desvenlafaxine consistently for a year; however, he discontinued it when he happened to run out of the prescription and presented to the emergency department (ED) 1 week later with complaints of mouth pain.

On examination, the patient exhibited repetitive perioral movements including lip smacking, tongue protrusion, involuntary biting of his cheeks, and bruxism. Results of computed tomography head imaging and basic laboratory studies were within normal limits and unrevealing for an etiology of his movements. He was instructed not to restart desvenlafaxine out of concern that he was experiencing medication-induced TD. However, a few days later, he presented to the Psychiatric Emergency Clinic with no relief in his symptoms. Given the temporal relationship between the onset of oral movements consistent with TD and the abrupt discontinuation of desvenlafaxine, as well as normal laboratory workup and normal recent imaging, WED was considered to be the most likely diagnosis. He was restarted on oral desvenlafaxine 50 mg daily.

He returned to the ED a week later without improvement in his symptoms, and he was admitted to inpatient psychiatry. Approximately 2 weeks after his initial presentation, desvenlafaxine was increased to his original dose of oral 100 mg daily due a lack of improvement at the lower dose. At this higher dose, he gradually experienced a complete resolution of his repetitive oral movements.

A widely accepted pathophysiologic explanation of TD involves chronic continuous dopamine receptor blockade leading to up-regulation and supersensitivity of postsynaptic dopamine receptors.<sup>1,3</sup> Serotonin-2A (5-HT<sub>2A</sub>) receptor blockade may also play a role in the pathophysiology of TD, as the high 5-HT<sub>2A</sub> blocking activity of atypical antipsychotics has been shown to be protective.<sup>4</sup> Venlafaxine has binding affinity for 5-HT receptors,<sup>5</sup> though it's unclear what the interactions may be between venlafaxine and specific receptor subtypes such as 5-HT<sub>2A</sub>.

was recently approved by the US Food and Drug Administration for the treatment of major depressive disorder. Similarly to venlafaxine, desvenlafaxine has been demonstrated to have actions on 5-HT and norepinephrine and weak dopaminergic reuptake.<sup>6</sup> It is possible that the serotonergic and dopaminergic actions of desvenlafaxine contributed to the WED experienced by our patient.

The differential diagnosis for TD includes abnormal movements secondary to a neurodegenerative disorder, a particular concern in our elderly patient. His laboratory testing was normal, and the imaging results and extensive history ruled out other potential causes of his movement disorder, including Lewy-Body dementia, Parkinson's disease, and Huntington's chorea. In addition, the temporal relationship between the onset of his symptoms with the cessation of desvenlafaxine and improvement after restarting the medication suggests that WED was a more likely explanation.

While withdrawal-emergent dyskinesia associated with antidepressants is rare, this case suggests that it is a side effect that should be considered when starting and discontinuing desvenlafaxine in an elderly patient.

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