A Kind of D-Amino Acid Oxidase Inhibitor, Sodium Benzoate, Might Relieve Panic Symptoms in a First-Episode, Drug-Naïve Panic-Disorder Patient

To the Editor: It is unusual to discuss a glutamate-related mechanism in the treatment of panic disorder (PD). Here, I want to share a case of PD, who had significant improvement of panic symptoms within 6 weeks after receiving a kind of D-amino acid (DAA) oxidase inhibitor, sodium benzoate (SB).

Case Report

"Mrs. L" is a 58-year-old, female, first-episode, drug-naïve PD patient with the following panic symptoms for 6 months: unexplained abdominal pain, gastrointestinal upset, dyspepsia, chest tightness, palpitations, dizziness, and limb numbness. These symptoms occurred suddenly and exacerbated progressively within 10 minutes. She had significant anticipatory worry about additional attacks, and these attacks had already caused significant disturbances of her social and occupational role. She received many kinds of physical or laboratory examinations, such as electrocardiogram, chest X-ray, computed tomography of chest, and magnetic resonance imaging of brain and spine, but all these examinations failed to find any medical reason for these somatic symptoms. She also refused to take antidepressant or benzodiazepine treatment for fear of side effects and only received nonpharmacologic treatment. After signing informed consent, she started to take sodium benzoate (SB) for her panic symptoms. No concurrent psychotherapies were performed in this patient during SB treatment. After 2 weeks of SB, she had mild improvement of PD (PDSS score: 18 → 13), with less severity of abdominal discomforts, chest tightness, palpitations, and anticipatory anxiety. However, during the first 2 weeks, she still had limb numbness, dizziness, and headache. At the 6th week, she experienced subsequent response in PD symptoms (PDSS score: 13 → 7). She also had less dizziness, less anticipatory anxiety, and more improvement in abdominal discomfort, chest tightness, and palpitations. Residual PD symptoms, such as limb numbness and headache, were still noted in the 6th week. No significant side effects of SB treatment during this 6-week period were mentioned.

Discussion

Several antidepressants have been reported to act via glutamate receptors, and glutamate is a target for the development of novel antidepressants.[1] Glutamate receptor-related agents also can relieve symptoms of posttraumatic stress disorder, one kind of anxiety disorder.[2] In this case, she received SB, which increases the level of DAA because of inhibition of DAA oxidase. DAA genotype has been reported to be associated with anxiety.[3] D-serine, one kind of DAA, can enhance fear extinction through glutamate receptor-induced phosphorylation signaling in hippocampus and amygdala. It also suggests DAA's potential role in the treatment of anxiety disorders.[4]

A pilot study of D-serine in the treatment of posttraumatic stress disorder also suggests that D-serine can reduce anxiety through its glutamate receptor glycine-based mechanism.[5] DAA also can enhance adaptive learning to changing environments, extinguish contextual fear memory, and improve cognitive flexibility and inhibitory learning in the face of significant stress. These DAA-related actions might provide a role for DAA in treating anxiety disorders.[6] Hofmann et al. found that D-cycloserine, another kind of DAA, reduces social distress and anxiety in social-phobia patients.[7] Another randomized, controlled trial of D-cycloserine with exposure therapy also replicates their findings.[8] Behavioral therapy augmentation with D-cycloserine or sarcosine (with similar mechanism to D-cycloserine) can also reduce anxiety symptoms of obsessive-compulsive disorder patients.[9,10] To my knowledge, this is the first case of clinical response to SB treatment in PD. Further well-controlled study will be needed to clarify SB's role in PD therapy.[11–14]

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