reports suggest that the 5-HT1A agonists buspirone and tandospirone are efficacious in the treatment of SSRI-induced abnormal movements, especially bruxism.[2,3]

Aripiprazole is a partial agonist/antagonist at dopamine D2 and D3 and serotonin 5-HT1A receptors and antagonist at the 5-HT2A receptors. We hypothesize that its beneficial effect on a patient's orofacial and buccal dystonia is attributable to its partial-agonist activity on dopamine receptors and above all to its partial-antagonist action on 5-HT1A receptors, jointly overwhelming its antagonism of the 5-HT2A receptors. Although anecdotal, our case suggests that low-dose aripiprazole might be a promising new treatment modality of sub-acute SSRI-induced abnormal movements.

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What is a rational antidepressant treatment for major depression in patients with Parkinson's disease?

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ABOUT 50% OF PARKINSON'S disease (PD) patients suffer from depression.[1] As the quality of life (QOL) impairment in PD patients is partly caused by psychiatric symptomatology, the treatment for depression in PD is clinically important. Although a meta-analysis raises questions about the efficacy of selective serotonin reuptake inhibitors (SSRI) for treatment of depression in PD patients,[2] SSRI are often the first choice for treatment of these patients. A recent study suggested that the efficacy of SSRI may be inferior to that of tricyclic antidepressants (TCA) for depression in PD. SSRI have the potential to worsen parkinsonian motor function and TCA have a strong anticholinergic effect and impair cardiac conduction, causing poor tolerability. Here, we describe a PD patient with depression successfully treated with mirtazapine and consider the optimal treatment strategy for depression comorbid with PD, which remains a matter of debate.

The patient is a 62-year-old woman with mild dilated cardiomyopathy. At age 61, she was diagnosed with major depression based on the symptoms of psychomotor retardation and prescribed milnacipran 75 mg/day without improvement of the symptoms. Four months later, she was diagnosed with PD by a neurologist after developing motor symptoms, including resting tremor, rigidity, and gait disturbance. Although parkinsonian symptoms were well controlled with levodopa 300 mg/day and pramipexole 1.5 mg/day during 6 months, she had gradually developed insomnia, severe appetite and weight loss, loss of interest and suicidal ideation. She was sent by a neurologist to our outpatient department of psychiatric service, diagnosed as having major depression comorbid with PD, and subsequently hospitalized. Milnacipran 75 mg/day was switched to mirtazapine 30 mg/day over 2 weeks while keeping her anti-parkinsonian medication unchanged. After fixing mirtazapine 30 mg/day, her depressive symptoms were improved without the exacerbation of parkinsonian symptoms. She was discharged home and remained in remission at 1 month after hospitalization.

Dopamine agonists (DA) are first-line therapy for motor symptoms and effective for depression in PD as well. DA can cause nausea and appetite loss by stimulating dopamine D_2 receptor in the chemoreceptor trigger zone, thus DA are not suitable for patients who have digestive symptoms. The blockade of serotonin $(5\text{-HT})_3$ receptor in the same region (e.g. by mirtazapine), can reduce DA-induced digestive symptoms. Furthermore, the worsening of extrapyramidal symptoms involving SSRI is attributed to an agonistic effect on the 5-HT_{2A} receptor at the dopaminergic nerve terminal in the *substantia nigra* and inhibition of dopamine release.[3] The blockade of 5-HT_{2A} receptor with mirtazapine might reduce this risk. According to these pharmacological profiles, mirtazapine appears to be a rational treatment option for depression in PD patients. Randomized clinical trials are warranted to confirm the effectiveness of mirtazapine in PD patients with depression.

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Valproic acid augmentation in clozapine-associated hand-washing compulsion

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OBSESSIVE–COMPULSIVE SYMPTOMS (OCS) are frequent in patients with schizophrenia.[1] This association

has become prominent since the introduction of atypical antipsychotics for the treatment of schizophrenia, mainly clozapine.[2] Although clozapine has been reported to induce or exacerbate OCS, there is not enough data on the management of these symptoms.

We report the case of a schizophrenia patient without a history of OCS who developed clozapine-induced OCS that responded to valproic acid augmentation.

Mr S, a 51-year-old male patient, first developed paranoid delusions and auditory and visual hallucinations at the age of 23, fulfilling the diagnostic criteria of DSM-IV for schizophrenia. He had been in remission with clozapine 500 mg/day for approximately 1 year before relapse occurred as a result of treatment non-compliance. In April 2011, he was admitted with exacerbation of positive symptoms and was hospitalized. He was started on clozapine 50 mg/day and titrated up to 500 mg/day. A significant improvement was observed in positive symptoms. However, Mr S developed compulsive hand-washing behavior in the 3rd week of the treatment. He had been spending 5–8 h/day washing his hands. He did not have a history of obsessive–compulsive disorder. We assumed clozapine-induced OCS (meeting DSM-IV criteria) and gradually decreased the dosage of clozapine which resulted in aggravation of positive symptoms and elevated mood. Therefore, valproic acid 1000 mg/day was added to the regimen of clozapine 500 mg/day. Two weeks after starting valproic acid (serum level 77.8 mg/L), Mr S's positive symptoms and elevated mood were significantly reduced and his compulsive hand-washing had disappeared. During 3 months of follow up, he remained well under a combined treatment with clozapine (500 mg/day) and valproic acid (1000 mg/day) and there was no reemergence of his compulsion.

Our patient developed hand-washing compulsion during treatment with clozapine which disappeared after augmentation of valproic acid. Although the exact mechanism is not known, the development of OCS associated with clozapine use has been explained by the central serotonergic receptor blocking effects of this drug.[1]

Although a few case reports have mentioned the efficacy of valproic acid in the treatment of OCD in the literature,[3] there is only one case report showing alleviation of clozapine-induced OCD symptoms with valproic acid augmentation in a patient with schizophrenia.[4]

We suggest that valproic acid may be a choice when treating OCS, which may appear as the adverse effect of atypical antipsychotics in patients with schizophrenia. Randomized controlled trials are required to establish the efficacy of valproic acid in the treatment of antipsychotic-induced OCS before definitive conclusions can be reached.

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Risperidone augmentation with amisulpride: The blue-tongue sign

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THE BLUE-TONGUE SIGN is a strikingly blue tongue due to selective D2 dopamine antagonism. The blue-tongue sign occurs rarely in young women treated with metoclopramide; blue tongues have been anecdotally associated with haloperidol therapy.[1] We would like to report an uncommon and disturbing side-effect of risperidone augmentation with amisulpride. Our case is at variance with the traditional view that abnormal skin pigmentation is irreversible or only partially reversible.[2,3]

A 23-year-old man was admitted to a psychiatric closed ward because of aggravated psychotic symptoms. His chief complaints were auditory hallucination and paranoid delusions. Brain magnetic resonance imaging, electroencephalography, and laboratory examination were done to evaluate organic causes. He was diagnosed with schizophrenia after mental status examination. Medication for him was started with risperidone 6 mg and increased to 8 mg. On 6 weeks of admission, risperidone was augmented with amisulpride 200 mg for relieving the persisting nominal psychotic symptoms. From 7 weeks of admission, his psychotic symptoms were relieved with risperidone 6 mg augmentation with amisulpride 600 mg. During the follow up in the outpatient clinic, he complained of abnormal tongue pigmentation at 3 weeks of discharge. His tongue resumed its normal color after a 2-week observation without antipsychotics discontinuation or replacement of other neuroleptics.

This case indicates that risperidone augmentation with amisulpride-induced abnormal tongue pigmentation would be completely reversible without antipsychotics discontinuation or replacement of other neuroleptics. Also the blue-tongue sign could be the crossroad for understanding the pathophysiological mechanism of dopamine pathway in which most neuroleptics are involved for treating psychotic symptoms.

L-3,4-dihydroxyphenylalanine (L-DOPA) from tyrosine is converted to dopamine by the dopa decarboxylase enzyme. Simultaneously, DOPA from tyrosine will be changed to dopaquinone. This dopaquinone is sequentially converted to three kinds of melanin (pheomelanin, eumelanin, and neuromelanin). An explanatory hypothesis for the abnormal