

Diminished pain perception in schizophrenia

In their Case Report (March 6, p 864),¹ Hiroshi Murakami and colleagues describe administration of quetiapine to a patient with diabetes mellitus. I would like to ask why they did so, given that quetiapine has been contraindicated for diabetes mellitus in Japan since 2004,² when a death occurred due to its side-effect of exacerbating diabetes mellitus.

Additionally, Murakami and colleagues insist that the hypoalgesia of their schizophrenic patient with diabetes mellitus, who had neither abdominal pain nor guarding despite severe bacterial peritonitis, was attributable to hypoperception related to schizophrenia, and that such findings were unlikely to have resulted from diabetic neuropathy because there were no signs of obvious peripheral neuropathy. However, impaired pain perception cannot explain the lack of abdominal guarding, which is a type of visceral-somatic spinal reflex. Because perception is an executive function controlled in the cerebral cortex, no matter how much pain perception is affected, the spinal reflex ought to be preserved. Therefore, peripheral neuropathy is more likely than hypoperception to be the explanation for both hypoalgesia and the disappearance of abdominal guarding.

Furthermore, I wonder whether Murakami and colleagues considered the possibility that inappropriate use of quetiapine exacerbated diabetic neuropathy via aggravation of diabetes mellitus? Although they saw no signs of obvious peripheral neuropathy, neuropathy can occur in parts of the body other than those examined—eg, visceral autonomic neurons—and damage to afferent visceral nerves might eliminate guarding and produce hypoalgesia.

We physicians have an obligation to provide unbiased care for patients

with schizophrenia, and not attribute inexplicable physical symptoms to their psychotic disorder.

I declare that I have no conflicts of interest.

Futoshi Shintani
shintani@cmdlab.co.jp

Department of Psychiatry, Tokyo Musashino Hospital,
Komone 4-11-11, Itabashi-ku, Tokyo, Japan

- 1 Murakami H, Tamasawa N, Yamashita M, et al. Altered pain perception in schizophrenia. *Lancet* 2010; **375**: 864.
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Hiroshi Murakami and colleagues¹ raise an old, albeit controversial, issue: do patients with schizophrenia have diminished pain sensitivity? And if they do, what is the mechanism?

Some earlier researchers defied its existence,² and numerous hypotheses have been proposed for the phenomenon: behavioural inability to react, disorders of consciousness, analgesic effect of antipsychotic drugs, negative symptoms of schizophrenia, and disturbed psychophysiological development.³ Some researchers argue that hypoalgesia is less a consequence of physiological derailment than a psychosocial inability to express emotion.⁴

I would like to point out one more contributor: diabetes, which is a common comorbid condition in patients with schizophrenia. An elevated threshold for pain perception is associated with diabetic neuropathy. Back to the case, could Murakami and colleagues exclude the possibility of early manifestation of diabetic neuropathy?

Future studies are recommended to consider diabetes as a confounding factor. Besides, decreased sensitivity to pain has been postulated as a screening method for vulnerability to schizophrenia.⁴ Both issues might be interesting.

I declare that I have no conflicts of interest.

Jie-Yu Chuang
simone@mail.ndmctsgh.edu.tw

Department of Psychiatry, Tri-Service General Hospital, National Defense Medical Center, Taipei 114, Taiwan

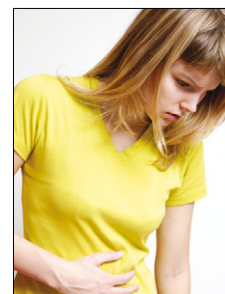
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Authors' reply

Exacerbation of diabetes mellitus is a possible side-effect of quetiapine, with published reports of associated diabetic ketoacidosis.¹ As noted by Futoshi Shintani, quetiapine is contraindicated in Japan for diabetic patients; unfortunately, the patient we discussed in our Case Report had been prescribed the drug by a psychiatrist before admission to our hospital. Needless to say, we discontinued this medication immediately.

On presentation the patient did not claim paraesthesia, hypaesthesia, or anaesthesia of her legs, and vibration perception on the legs with a 128-Hz tuning fork was normal at 15 s. Regarding Jie-Yu Chuang's question about an early manifestation of diabetic neuropathy, we did not do a nerve conduction study or peripheral nerve biopsies, so we did not exclude mild diabetic neuropathy as a complication of the patient's diabetes mellitus. There have been few reports of patients with diabetes mellitus and acute perforating appendicitis or pyoperitonitis without pain. Although severe bacterial peritonitis might have induced dysfunction of visceral autonomic neurons or afferent visceral nerves, which caused loss of abdominal guarding, it is difficult to test the validity of the hypothesis in a patient who recovered completely.

The mechanism of analgesia in the diabetic patient's case we presented remains to be defined. Such an event as reported might occur in schizophrenic patients with complicated diabetes mellitus, and physicians have an



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