to doses of less than 2.5 mg of olanzapine daily.

IH appear to result from disruption of corticobulbar and supraspinal reflex arcs regulating respiratory function, as well as the modulatory neurotransmitter inputs into these reflex arcs.[3] The principal CNS neurotransmitters responsible for both the generation and transmission of respiratory rhythm are glutamate, gamma-aminobutyric acid, and glycine.[5] Additionally, catecholaminergic and serotonergic afferents modulate the function of that reflex arc.[6] Successful treatment of IH may therefore employ agents that target one or more of these systems, whether at the level of the reflex arcs or at the level of their modulatory inputs.[3]

Although the pharmacology of olanzapine is complex,[7] among its major effects is antagonism of multiple types of postsynaptic serotonergic receptors.[8] The most consistently demonstrated effect of serotonin on the reflex arcs involved in the generation of hiccups is at the level of the spinal cord, where serotonergic input augments phrenic motoneuronal activity.[5,6] We propose that olanzapine, by antagonizing these postsynaptic serotonergic receptors, may decrease phrenic motoneuron excitability and thereby reduce hiccups. Further investigation of the therapeutic mechanisms and potential role of atypical antipsychotics, and in particular the activity of atypical antipsychotics at serotonergic receptors, in the treatment of IH is needed.

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Persistent Amnesia as a Sequel of Olanzapine-Induced Neuroleptic Malignant Syndrome

SIR: Persistent long-term cognitive sequelae of neuroleptic malignant syndrome (NMS) appear to be rare.[1] Memory problems as sequelae of NMS have been anecdotally reported with NMS associated with typical antipsychotics, but to our knowledge, there are no reports associating it with NMS due to atypical antipsychotics.[2,3] A case of persistent amnesia is described in a patient who developed NMS with olanzapine.

Case Report

"Mr. A," a 16-year-old adolescent, with a history of schizophreniform disorder of 6 week's duration, was initially treated with haloperidol (10 mg/day). However, this was discontinued within a week due to severe extrapyramidal symptoms (EPS). Mr. A did not receive any medication for the next 2 weeks and was then started on a regimen of olanzapine, 7.5 mg/day. A week later, he developed severe EPS again and olanzapine was stopped and the patient was treated with trihexyphenidyl (4 mg/day) and lorazepam (1 mg/day). Three days later, Mr. A developed a fever and worsening EPS. Over the next 3 days, this evolved into a full-blown NMS characterized by a fever of 102°F, marked rigidity, altered sensorium, urinary incontinence, labile blood pressure, tachycardia, and excessive sweating. Serum creatine phosphokinase (CPK) was 1,144 IU/liter (normal range, 0–200) and WBC count was 15 x10^9 (normal range, 4.5–11.0). Other blood work, including renal, hepatic, and electrolyte profiles were normal. He scored 5/30 on the Mini-Mental State Examination (MMSE). His computed tomography head scan did not reveal any acute changes. He was subsequently treated with norfloxacin for a urinary tract infection. Four days after Mr. A developed hyperpyrexia, he was treated with bromocriptine for the next 4 weeks. Ten days after starting treatment with bromocriptine, the patient no longer displayed any physical symptoms of NMS with the CPK and WBC count returning to normal. However, he continued to exhibit significant cognitive deficits and his MMSE score was only 14/30. He had intact attention, concentration, and calculation, but was only oriented to person and had impaired immediate and delayed recall. His mental status was remarkable for confabulation, perseveration, and echolalia. No fluctuation in consciousness or perceptual abnormalities suggestive of delirium were noted. His remote mem-

ory was relatively intact. On discharge, Mr. A continued to show improvement in his cognitive functions, and 2 months after the onset of NMS, his score on MMSE was 25/30 with persistent deficits in immediate and recent memory. He still had retrograde amnesia about the events surrounding the NMS and also had anterograde amnesia with deficits in learning new verbal information. Again, no deficits were noted in remote memory.

Comment

This patient met DSM-IV criteria for NMS. The cognitive deficits seen in this patient following NMS are reminiscent of an organic amnestic disorder, a rare entity described in patients recovering from NMS.[2,3] Of interest, among all the cognitive domains, memory impairment is the only one that has been consistently reported on recovery from NMS. Whether the concurrent urinary tract infection and the resultant delirium could have contributed to this presentation cannot be entirely ruled out. However, this seems less likely as this patient continued to exhibit cognitive deficits long after recovery from the urinary tract infection. Moreover, the Physicians' Desk Reference does not suggest any association of norfloxacin with cognitive deficits. Some investigators have speculated that these persistent deficits may be a consequence of complications of NMS, such as prolonged hypoxia and extreme hyperthermia.[1] This is supported by reports of memory deficit as a neuropsychological sequela of heat stroke.[4] In conclusion, more research is encouraged to explore why memory is preferentially involved in NMS. Excitotoxicity due to glutamate surge has been implicated in ECT-induced memory dysfunction,[5] and glutamate has also been hypothesized to play a role in NMS.[6] Thus, it would be interesting to decipher the role of this neurotransmitter in long-term cognitive sequelae of NMS.

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Nabilone Could Treat Chorea and Irritability in Huntington's Disease

SIR: Huntington's disease causes chorea and psychiatric abnormalities. Psychiatric symptoms were found in one study in 51 out of 52 patients.[1] Dysphoria, agitation, irritability, apathy, and anxiety were found in above 50% of the patients sampled.

Many sources postulate that cannabinoids could have a beneficial effect on the symptoms of Huntington's disease, especially on choreatic movements.[2–4] As well as providing possible symptomatic relief in Huntington's disease, there is also some evidence[5] that cannabinoids might have a neuroprotective effect which could delay the onset of symptoms by delaying or preventing the death of striatal neurons. This neuroprotective effect has also been postulated by other sources.[6–8]

To date there are only two reports on the use of cannabinoids in Huntington's disease in the literature. Cannabidiol, a nonpsychotropic cannabinoid, had no effect on chorea severity in 15 patients.[9] In one single patient, single dose, uncontrolled open clinical trial using nabilone, 1.5mg, the chorea increased significantly.[10] We present a case of a female patient with irritability, which improved after the introduction of cannabis. This improvement was maintained by treatment with nabilone.

Case Report

The patient was a 43-year-old female who died in December 2003. She developed symptoms of Huntington's disease at the age of 24 and her husband gave up paid employment to care for her in 1990 when she was 30 years old. In 1995, he reported difficulties in caring for his wife. These difficulties were related to personality changes due to her illness. She increasingly resisted help from professionals, especially care assistants, and refused any suggestion of short-term respite care. She became disinhibited and frequently undressed herself and walked around naked inside and occasionally outside the house. She exhibited a number of dangerous behaviors, such as leaving taps running and fires burning, and leaving burning cigarettes around. Her husband became concerned about the effect that the care for his chroni-