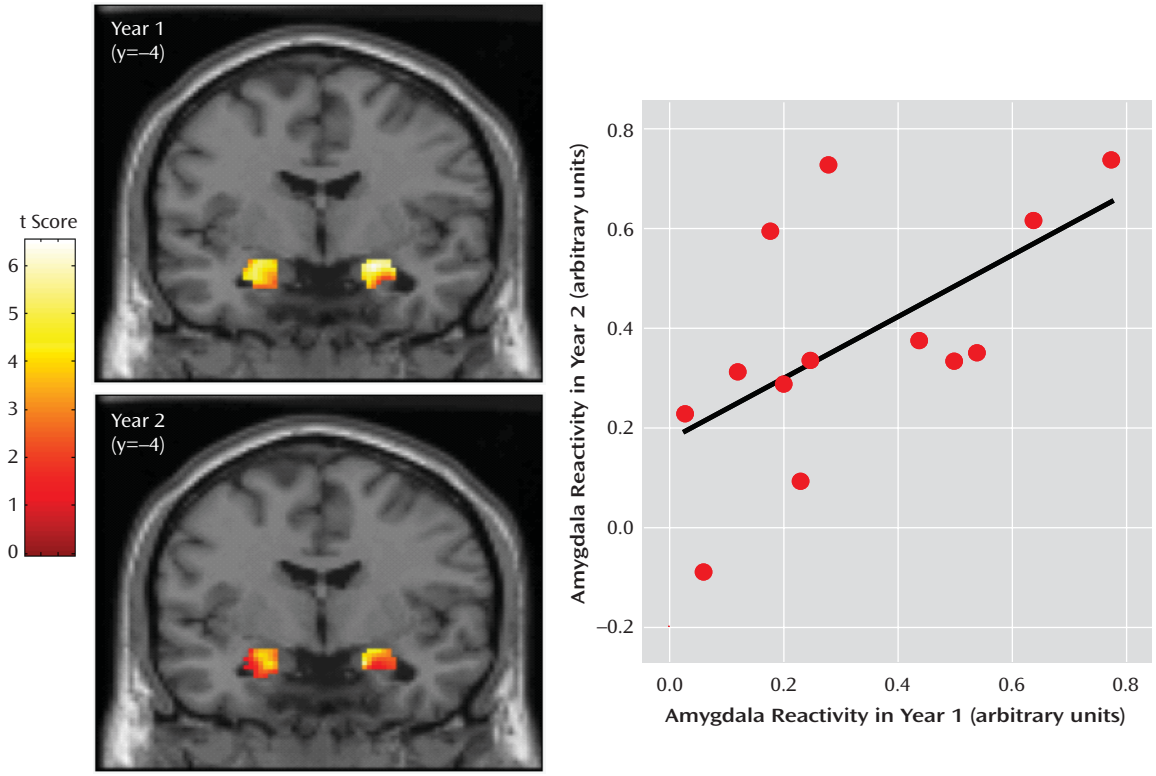
FIGURE 1. Amygdala Reactivity[a]



[a] The scans show mean bilateral amygdala reactivity to threat-related facial expressions for both sessions. Year 1: Right: 24, –4, –12, 154 voxels; t=4.59, p<0.001; Left: –20, –11, –16, 155 voxels; t=3.74, p<0.001. Year 2: Right: 22, –3, –12, 142 voxels; t=7.12, p<0.001; Left: –22, –8, –13, 150 voxels; t=6.63, p<0.001). Amygdala reactivity was calculated using random-effects analyses in SPM2 correcting for multiple comparisons (p<0.05) over the volume of the amygdala (for complete details of the fMRI challenge paradigm, blood-oxygen-level-dependent acquisition parameters, and statistical analyses, see [3]). The scatter plot of the bivariate correlation (r=0.59, p<0.035) shows mean right amygdala reactivity from the clusters for years 1 and 2.

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Severe Hyperlipidemia Associated With Olanzapine and Quetiapine Use

TO THE EDITOR: Atypical antipsychotics are associated with metabolic side effects, including weight gain, hyperlipidemia, and type II diabetes. We present a case of severe hyperglycemia, hypercholesterolemia, and hypertriglyceridemia during treatment with olanzapine and quetiapine. To our knowledge, this is the highest triglyceride level during antipsychotic treatment reported to date.

The patient was a 48-year-old, 6 feet tall, 230 lb Caucasian male presenting to an indigent care clinic. He was first hospitalized for depression three years before. Subsequently, he was diagnosed with mania and bipolar I disorder. His substance abuse history was negative. He was eventually stabilized receiving the following medications: olanzapine (40 mg every night), quetiapine (300 mg every night), sertraline (100 mg every morning), and zolpidem (10 mg every night).

The patient was psychiatrically stable and reported no history of chronic physical health problems. However, he reported diabetes symptoms, including thirst, frequent urination, and a 60 lb weight loss over the past year. He had generalized papular pruritic xanthomatous dermatitis and abdominal pain that was determined to be diverticulitis, both of which are associated with hypertriglyceridemia. Notable nonfasting laboratory results included the following: total cholesterol, 980 mg/dl; triglycerides, 9,450 mg/dl; and glucose, 507 mg/dl. High- and low-density lipoprotein were unobtainable because of severe lipemia of the blood sample. Metformin (500 mg bid) and gemfibrozil (600 mg bid) were initiated. Olanzapine and quetiapine were tapered and replaced with aripiprazole, which was then titrated to 30 mg. After 1 week, the patient's lipids were reexamined, with instruction to fast. His

total cholesterol level was 408 mg/dl, and his total triglyceride level was 2,796 mg/dl. Unfortunately, he developed depression and akathisia with the switch to aripiprazole. The aripiprazole dose was tapered to 15 mg, and a regimen, including enteric-coated valproic acid (1500 mg every night), sertraline (100 mg every morning), clonazepam (0.5 mg bid), and zolpidem (10 mg every night), appeared to be effective. One month later, the patient's total cholesterol level was 310 mg/dl and total triglyceride level was 1,313 mg/dl. After another month, the total cholesterol decreased to 260 mg/dl and the total triglycerides decreased to 400 mg/dl, respectively; high-density lipoprotein was 32 mg/dl, low-density lipoprotein was 48 mg/dl, and glucose was153 mg/dl.

After another month, the patient's total cholesterol level was 263 mg/dl, and his total triglyceride level increased to 527 mg/dl. He reported difficulty sleeping and receiving quetiapine at night (100–300 mg). After observing the lipid increase, the patient agreed to discontinue quetiapine. One month later, his total cholesterol level was 207 mg/dl and total triglyceride level was 300 mg/dl.

This case illustrates severe metabolic adverse effects associated with atypical antipsychotics, and one might question whether the combination of olanzapine and quetiapine increased these effects. The patient presented with severe hyperglycemia and hyperlipidemia, with extreme hypertriglyceridemia. Obesity and uncontrolled diabetes certainly contributed to the presentation. A Naranjo (1) score of 7 indicates a probable association with antipsychotics. Causal inference is limited, since no weights or laboratory values were available prior to olanzapine and quetiapine initiation. However, the increase in lipids after reinitiation of quetiapine supports a relationship of the metabolic presentation with antipsychotic treatment, even with relatively low doses of quetiapine as commonly used off-label for insomnia. Providers should recognize that these low doses may not be benign.

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Elevated Plasma Dopamine Metabolites in Cannabis Psychosis

To The Editor: Cannabis has received increasing attention as a risk factor for the development of psychotic states (1). There are relatively little data related to the biochemical profile in cannabis psychosis (2, 3). We report on five consecutive cases of first-admission psychosis associated with documented cannabis use. For comparison, we used a consecutive series of first-admission psychosis and a group of nonpsychotic inpatients treated during the same period. We collected plasma for homovanillic acid on the first morning after admission following an overnight fast.

The first-admission cannabis psychosis group (N=5) had a mean age of 21.2 years. Urine tests were positive for cannabis subjects on admission. The comparison groups had urine samples negative for cannabinoids on admission. The first-episode psychosis group (N=15) had a mean age of 20.4 years, and the nonpsychotic group (N=17) had a mean age of 32.0 years. The psychosis groups did not significantly differ in age, race, sex, or level of psychosis. The degree of psychosis was rated as moderate on the four positive symptom items of the Brief Psychiatric Rating Scale.

Plasma homovanillic acid was measured using gas chromatography mass spectrometry with deuterated internal standards. Homovanillic acid levels were compared using a Student's t test. Plasma homovanillic acid values were as follows: cannabis psychosis group, 24.8 ng/ml (SD=2.9); first-episode group, 15.1 ng/ml (SD=3.1); and nonpsychotic group, 9.6 ng/ml (SD=2.1). Homovanillic acid values for the cannabis group were significantly higher relative to the first-episode group ($p<0.001$) and the nonpsychotic group ($p<0.001$). Homovanillic acid values for the first-episode group were significantly higher when compared with the nonpsychotic group ($p<0.001$).

To our knowledge, this is the first report of elevated plasma homovanillic acid in cannabis-related psychosis, although we are aware of a report of elevated urinary homovanillic acid following cannabis administration to a volunteer population (2).

In this small case series of patients with first-episode psychosis associated with cannabis use, plasma homovanillic acid was significantly higher than values for each of the comparison groups. There are several possibilities for this result. First, plasma homovanillic acid is elevated in a number of newly admitted psychosis patients (4), which was the case in our first-episode psychosis group. However, plasma homovanillic acid was even higher in the cannabis group. Second, acute cannabis administration can produce increased dopamine activity in animals and humans (2, 3). Third, individuals with cannabis psychosis may also have a genetic vulnerability that can lead to increased dopaminergic activity (1).

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