

# A case of returning psychosis

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In the ER, Ms. Y is agitated, violent, and aggressive. She received care for psychotic symptoms 30 years ago, but had been healthy until she had a similar episode 6 months ago. What triggered her psychosis?

## CASE Agitated and violent

Police bring Ms. Y, age 42, to the emergency room (ER) after her boyfriend calls 911 because she is physically aggressive. The police note that the home is in disarray and several windows are broken. Ms. Y is threatening and violent—she bites and spits at her boyfriend and the police. The ER assessment reports that she is “agitated, confused, and not making sense.” She receives IV haloperidol, 5 mg, for agitation and aggressive behavior, but does not improve and receives a second dose of haloperidol approximately 1 hour later.

On examination she is afebrile. Laboratory results are notable for elevated blood urea nitrogen (27 mg/dL) and creatinine (2.3 mg/dL), suggesting renal failure. Her white blood cell (WBC) count is elevated at 14.7 K/ $\mu$ L with increased neutrophil count. Her creatine phosphokinase (CPK) also is elevated at 2,778 U/L. Other lab results, including liver function tests and a rapid plasma reagin, are within normal limits. Urinalysis reveals WBC >50 and leukocyte esterase 3+ WBC/ $\mu$ L. Urine drug screen is negative for barbiturates, benzodiazepines, opiates, and cocaine and her blood alcohol level is <10 mg/dL. She is overweight, but not obese. Ms. Y is admitted to the medical service for workup of rhabdomyolysis and altered mental status.

When the psychiatric consultation-liaison (CL) service evaluates Ms. Y 12 hours after presentation, she is disheveled, drowsy, and lying in bed, with multiple superficial lacerations on her

forearms. She is cooperative but claims to have no recollection of the events leading up to her admission. Her speech is soft with a lack of spontaneity, and she demonstrates substantial psychomotor retardation. Her mood is irritable and affect is restricted. She has a latency of thought and difficulty recalling basic historic information. Ms. Y appears confused and frequently responds to questions with “I don’t remember.” She seems frustrated and distressed by her inability to answer questions. She denies suicidal or homicidal ideation and auditory or visual hallucinations, although she appears to be responding to internal stimuli. We cannot complete a Mini-Mental State Exam because she becomes uncooperative. After 10 minutes, Ms. Y ends the interview, stating that too much is being “demanded” of her.

## What is the likely cause of Ms. Y’s agitation?

- psychotic disorder
- drug intoxication
- delirium
- personality disorder

## The authors’ observations

Ms. Y’s acute-onset agitation and confusion could be caused by an infection, such as a

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## How would you handle this case?

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## Clinical Point

Acute-onset agitation and confusion could be caused by a urinary tract infection, a frequent culprit in delirium or transient psychosis

### Box

## Carnitine: Supplementation usually isn't necessary

**C**arnitine is derived from an amino acid and found in nearly all cells of the body. "Carnitine" is used to refer to several compounds, including L-carnitine, acetyl-L-carnitine, and propionyl-L-carnitine. The natural form and the only one with biologic activity is the geometric isomer L-carnitine. Most endogenous L-carnitine is derived from diet—meat and dairy are the primary sources—and the remainder is synthesized.<sup>2-4</sup>

Carnitine transports long-chain fatty acids into the mitochondria so they can be oxidized to produce energy and transports toxic compounds out of the mitochondria to prevent them from accumulating. Carnitine is concentrated in tissues that use fatty acids as a dietary fuel, such as skeletal and cardiac muscle.<sup>2-4</sup> The body makes enough carnitine to meet most person's needs and supplementation typically is not required. Some drugs, such as

valproic acid and carbamazepine, can reduce carnitine blood concentrations.<sup>2</sup>

Because of its role in fatty acid oxidation, carnitine often is promoted as a weight loss aid. In addition, it is purported to improve exercise performance and enhance well-being.<sup>3,4</sup> However, there is no consistent evidence that carnitine supplements can improve physical performance in healthy individuals.<sup>5</sup>

At doses of approximately 3 g/d, carnitine supplements can cause nausea, vomiting, abdominal cramps, diarrhea, and a "fishy" body odor. Rare side effects include muscle weakness in uremic patients and seizures in those with a seizure disorder.<sup>2-4</sup>

In animal studies, carnitine persistently increases dopamine outflow in the nucleus accumbens.<sup>6</sup> Dopamine dysregulation in this pathway has been shown to cause psychotic symptoms.<sup>7</sup>

urinary tract infection, a frequent culprit in delirium or transient psychosis. Seizure activity with postictal confusion also has to be included in the differential, as well as an endogenous psychotic disorder such as schizophrenia or a manic bipolar episode. Ms. Y's boyfriend of 16 months indicated that Ms. Y uses alcohol but cannot quantify the amount or frequency. We considered and ruled out other intoxicant use as a potential cause of her transient psychosis. An extended drug screen was negative and her lab values did not suggest heavy alcohol use.

### HISTORY Past psychotic episodes

Ms. Y's boyfriend reports that she had 2 psychiatric hospitalizations approximately 30 years ago, which were precipitated by psychotic symptoms that she developed while abusing drugs. To the best of his knowledge Ms. Y had not used these agents recently. He stated that Ms. Y did not appear to have ongoing psychotic symptoms and had not received psychiatric treatment since she was a teenager until 6 months ago. He describes the current hospitalization as being "just like 6 months ago."

Medical records reveal that Ms. Y was admitted to our hospital 6 months ago because she was acting violently and combative. She was "talking out of context," "stated that she was God," and had auditory hallucinations. She was admitted to the medical service for rhabdomyolysis, which was thought to be caused by hyperactivity or exertion. Ms. Y indicated that she was taking food supplements, including L-carnitine, to help lose weight. Her psychotic symptoms cleared within 24 hours and she was discharged without any psychiatric medications. Her behavioral disturbance was attributed to ingesting excessive amounts of carnitine supplements, and Ms. Y was counseled to abstain from them.

### What is carnitine's purported mechanism for weight loss?

- increased energy expenditure
- increased satiety
- increased fat oxidation or reduced fat synthesis
- increased water elimination

### The authors' observations

Carnitine is a common dietary supplement that is advertised as being safe and effective.

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## Table

## Psychiatric effects of common weight loss supplements

Supplement	Psychiatric effects
Caffeine	Depression, anxiety, agitation, aggression, psychosis <sup>10-12</sup>
Ephedra*	Psychosis, severe depression, mania or agitation, hallucinations, sleep disturbance, suicidal ideation <sup>13</sup>
Panax (ginseng)	Euphoria, mania <sup>14</sup>
Amino acid-containing drinks (taurine and inositol)	Euphoria, hypervigilance, insomnia, verbal and physical aggression, impulsive behavior <sup>9,15</sup>
Hypericum (St. John's wort)	Mania, <sup>16</sup> psychosis <sup>17</sup>

\*FDA removed ephedra from the market in 2003 because of adverse events

## Clinical Point

Given Ms. Y's personal and family history of psychosis, we considered that she may have an endogenous psychotic disorder

tive.<sup>1</sup> It is purported to increase fat oxidation or reduce fat synthesis; however, no trials demonstrate that L-carnitine is effective for weight loss (*Box, page 52*).<sup>2-7</sup> Evidence from well-designed randomized, controlled clinical trials indicates that the safe upper limit of long-term intake is 2,000 mg/d of L-carnitine equivalents.<sup>8</sup> The data for doses >2,000 mg/d are not sufficient to make a confident conclusion on long-term safety.<sup>8</sup>

Further evaluation for possible causes of Ms. Y's symptoms include a chest radiography and blood and urine cultures, which are unremarkable. Results of a lumbar puncture are within normal limits. Computed tomography of the head reveals confluent periventricular hypodensities compatible with moderate to severe non-specific white matter disease.

## TREATMENT Rapid improvement

Ms. Y's renal dysfunction resolves within 24 hours with aggressive hydration and supportive therapy. Her WBC count normalizes and her CPK decreases.

When Ms. Y becomes more cooperative, the CL team pieces together more of her story with further interviews and collateral information from her cousin. Ms. Y's family history includes an aunt with schizophrenia. Three years ago Ms. Y moved from the Midwest to a large Southern city with her husband, from whom she is divorced. She has 2 children who were removed from her custody when she was a teenager for

unclear reasons. At admission, she lives with her boyfriend, whom she plans on marrying.

Ms. Y says she was taking carnitine to improve her energy and lose weight. She recalls that her physicians advised her to discontinue carnitine supplements, but she continued to take "4 or 5 a day" in an ongoing attempt to lose weight. When asked about other supplements, Ms. Y reports regularly consuming 16-ounce energy drinks, including the day before admission. The label on this drink lists L-carnitine and caffeine as main ingredients. She denies regularly drinking other caffeine-containing beverages, including coffee, tea, or soda.

## The authors' observations

Supplements for weight loss may appeal to people's desire for a "quick fix" that is less demanding than diets and increased physical activity. Supplements are available without a prescription and despite reports of adverse reactions generally are perceived as being safe and having few side effects. These supplements may be marketed as "natural," which can be misinterpreted as an assurance of safety and efficacy.

Given the similarities of the current admission to the one 6 months ago, we suspect Ms. Y is experiencing transient psychosis secondary to carnitine intoxication. Based on Ms. Y's boyfriend's report and the product labeling, we estimate that Ms. Y took approximately 4,000 mg of carnitine in the 24 hours before admission.

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Other causes of transient psychosis, such as infectious, metabolic, and neoplastic processes, were considered and ruled out. Seizures with postictal confusion also was ruled out because Ms. Y does not have a history of seizures and there is no evidence of convulsive activity, incontinence, or buccal lacerations. Given Ms. Y's family history of schizophrenia and reported history of psychotic symptoms as a teenager we considered that she may have an endogenous psychotic disorder. However, her psychotic symptoms were transient, and Ms. Y returned to her baseline level of functioning between episodes.

### Clinical Point

Patients predisposed to mania or psychosis may be more likely to respond adversely to nutritional supplements or energy drinks

### OUTCOME Advice to stop

We start Ms. Y on risperidone, 2 mg/d, at bedtime for her psychotic symptoms. Her psychotic symptoms quickly improve. She seems to return to her baseline state approximately 36 hours after admission and is medically

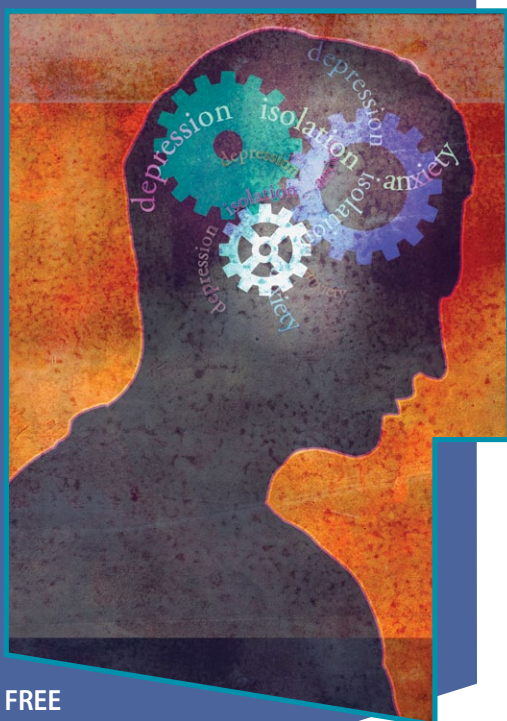
cleared for discharge. Risperidone is discontinued after only 1 dose.

Ms. Y is remorseful over her recent aggressive behavior, and fears that her boyfriend will leave her. She denies suicidal and homicidal ideation and does not require inpatient psychiatric hospitalization. We strongly advise her to discontinue carnitine supplements and energy drinks and to limit her caffeine intake. Because Ms. Y's had continued to use carnitine supplements despite adverse consequences and against medical advice, we refer her for substance abuse treatment.

### The authors' observations

Although temporal coincidence does not necessarily imply causality, in Ms. Y's case, the relationship between carnitine ingestion and psychiatric symptoms cannot be ignored. Individuals predisposed to mania or psychosis may be more likely to respond adversely after ingesting nutritional supplements or en-

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- George I. Papakostas, MD, Director, Treatment-Resistant Depression Studies, Massachusetts General Hospital; Associate Professor of Psychiatry, Harvard Medical School, Boston, Massachusetts

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ergy drinks.<sup>9</sup> Ms. Y's past psychotic episodes suggest that she could be vulnerable to future episodes. She also might have a biologic predisposition to psychosis because of her family history of schizophrenia.

The literature contains at least 1 other reported case of carnitine-induced psychosis. A patient with a history of bipolar disorder presented with auditory hallucinations, persecutory delusions, and verbally threatening and physically assaultive behavior 5 days after beginning nutritional supplements containing carnitine.<sup>1</sup> There also are reports of patients who experienced acute changes in mental status after consuming other nutritional weight loss supplements (*Table, page 54*).<sup>9-17</sup> Chelben et al<sup>9</sup> describe 3 patients with known psychiatric illness who showed clinical deterioration leading to psychiatric hospitalization after ingesting nutraceutical preparations. This may be a common but unrecognized cause of decompensation in psychiatric patients who take supplements.

This case highlights the importance of being aware of patients' use of alternative medications or nutritional supplements. Physicians should routinely inquire about the use of weight loss products, energy drinks, and supplements, and patients should be educated about the risks, including potential to exacerbate pre-existing psychiatric disorders.

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## Related Resources

- National Library of Medicine. Dietary supplements labels database. <http://dietarysupplements.nlm.nih.gov/dietary>.
- Grossberg G, Fox B. The essential herb-drug-vitamin interaction guide. New York, NY: Broadway Books; 2007.

#### Drug Brand Names

Carbamazepine • Tegretol	Risperidone • Risperdal
Haloperidol • Haldol	Valproic acid • Depakene

#### Disclosure

The authors report no financial relationship with any company whose products are mentioned in this article or with manufacturers of competing products.

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## Clinical Point

**Routinely ask patients about their use of weight loss products, energy drinks, and nutritional supplements**

## Bottom Line

Excessive use of weight loss supplements and energy drinks can precipitate changes in mental status, mania, or psychosis, especially in patients with a pre-existing psychiatric disorder. Symptoms often improve after discontinuing the supplement and with supportive medical treatment. Routinely inquire about patients' use of alternative medications and nutritional supplements, and educate patients about potential adverse effects.