The patient, a 49-year-old, successful businessman, was first diagnosed with bipolar disorder at the age of 35 years. He underwent trials of combination therapy including lithium, divalproex, venlafaxine, escitalopram, olanzapine, and quetiapine but never achieved full remission; symptoms of dysphoria, irritability, and impulsive behavior remained. However, he was able to continue working, and his marriage was stable.

At age 37 years, he and others noticed decrements in his ability to organize his work, and he became increasingly reliant on his assistant. By the age of 40 years, his organizational ability declined to the point that he required a second assistant while work demands remained stable. Over the course of 9 years, his symptoms changed from episodes of dysthymia and moderate hypomania to distinct episodes of depression with anhedonia and suicidal ideation, alternating with hyperthymia, grandiosity, and impulsivity while being maintained on divalproex, lamotrigine, and olanzapine. He eventually became volatile and had two separate altercations with the police leading to his hospitalization after the second event.

On admission, he appeared hypothyrmic and disinhibited. After a few days, these symptoms were rapidly replaced by profound sadness, psychomotor retardation, irritability, hopelessness, and suicidal ideation. Neuropsychological testing revealed deficits in executive function including profoundly impaired planning, execution, organization, set shifting, abstract rule inference, and control of impulsivity. However, his nonverbal reasoning, verbal abstraction skills, and sequencing skills were in the average range.

The patient’s divalproex was discontinued; and his olanzapine was replaced with asenapine 5 mg twice daily. Further, carbamazepine (plasma level 6.9 mcg/mL) was added to the regimen; his lamotrigine 200 mg daily was continued. These psycho-pharmacotherapeutic adjustments were made, along with counseling on a weight loss diet. This led to remission of the mixed mood symptoms, though some disinhibited behavior persisted. A neurological evaluation, including an EEG and an MRI, was within normal limits. He had no family history of neuropsychiatric disorders.
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Impaired executive function is well described in unipolar depression, and has a significant impact on the success of treatment.\textsuperscript{1,2} Further, there is a significant body of knowledge with respect to executive dysfunction in bipolar disorder across mood states.\textsuperscript{3-4} However, to our knowledge executive dysfunction has not been described in the rapid cycling subtype of bipolar disorder.

Distinguishing between executive dysfunction and mania as the etiology of behavioral dyscontrol is a diagnostic challenge. Identifying modifiable causes such as alcoholism, obesity, and psychopharmacotherapy can have implications on treatment. Tailoring medication to minimize weight gain and iatrogenic cognitive deficits may allow for overall improvement in the patient’s quality of life.

In this case, development of behavioral dyscontrol and disorganization was followed by an evolution in the course of bipolar disorder into a rapid cycling pattern. One potential explanation is that behavioral dyscontrol may arise from executive dysfunction, and the underlying neurobiological abnormalities of such a dysregulated state may exacerbate the course of bipolar disorder. This view is consistent with replicated findings implicating executive dysfunction and some of its underlyng frontolimbic abnormalities in the poor response of geriatric unipolar depression to antidepressants.\textsuperscript{2,5}

The etiology of behavioral dyscontrol and disorganization is often difficult to diagnose in a case such as this. Behavioral disinhibition originating from an underlying executive dysfunction may resemble disinhibition arising from a manic or mixed state. Failure to identify the components of behavioral dyscontrol that are not part of the manic syndrome may lead to overtreatment with antipsychotics, benzodiazepines, and mood stabilizers, some of which may further exacerbate disinhibition.\textsuperscript{5-8}

Observing the trajectory of the other manic symptoms in relation to behavioral dyscontrol and using targeted neuropsychological tests may be helpful in the determination of appropriate management of treatable symptoms. Further, identifying modifiable causes of executive dysfunction can have treatment implications.

High doses of benzodiazepines, antipsychotics, and perhaps divalproex may result in impairment of cognitive function and lead to behavioral dyscontrol.\textsuperscript{5-8} This patient abused alcohol periodically. Moreover, treatment with mood stabilizers and antipsychotics contributed to both his metabolic syndrome (body mass index: 37; increased abdominal girth; hypercholesterolemia; hypertension; impaired fasting glucose) and obstructive sleep apnea, both of which may have contributed to his behavioral dyscontrol. Obese individuals have decrements of executive function but the direction of causality is unclear as executive dysfunction may result in disinhibited eating.\textsuperscript{5} Moreover, the patient rarely adhered to positive airway pressure treatment of obstructive sleep apnea and remained exposed to chronic hypoxia during sleep.

Specific therapy to address each of these modifiable causes allowed for personalized treatment. The patient was counseled regarding alcohol use and a weight loss diet. Further, his medications were optimized to prevent weight gain. He was also advised to use an oral prosthesis to improve his sleep.

Some risk factors may not be modifiable. Behavioral disinhibition and impaired executive function previously have been documented in bipolar patients.\textsuperscript{3} First-degree relatives of bipolar patients have as much impairment in attention set shifting as bipolar patients, suggesting a genetic contribution to this deficit.\textsuperscript{10} The existence of impaired executive functioning is separate from the bipolar disorder that affects its course; this is suggestive of a baseline dysfunction. Thus, while it may be possible to manage many of the factors contributing to executive dysfunction, it is unlikely that it can be completely reversed.

To prevent overtreatment, it is important to determine whether behavioral dyscontrol in the rapid cycling patient with executive dysfunction is secondary to mania or executive dysfunction. Reduction of modifiable risk factors may allow for improved quality of life.

**REFERENCES**