

## Case Report

# Pathological gambling associated with cabergoline in a case of recurrent depression

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**ABSTRACT:** Pathological gambling has been described frequently in patients with Parkinson disease or other movement disorders who were treated with dopamine agonists. Here, we report a patient with recurrent depression who developed pathological gambling after administration of the dopamine agonist cabergoline. A 36-year-old male Japanese patient presented with his third episode of depression. His depressive symptoms responded minimally to fluvoxamine. Cabergoline was then added to augment the antidepressant's efficacy. Although this regimen resulted in dramatic improvement, he started to spend considerable money and time every day in pachinko parlors and go to the horse racing track every weekend. He spent more than twenty thousand US dollars in total. He tried to stop gambling many times but failed to control his urge. His gambling behavior did not stop even though he was experiencing a marital crisis. He had not displayed any manic symptoms during this entire period. This complication fulfilled the criteria for pathological gambling according to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* edition. The patient's perplexing behavior did not end until cabergoline was discontinued. Thus far, pathological gambling associated with cabergoline has rarely been reported while gambling associated with pramipexole and ropinirole, dopamine agonists, has frequently been documented. In addition, this is the first case of depression in which the patient developed pathological gambling during treatment with a dopamine agonist. In conclusion, clinicians should be aware of the potential for pathological gambling when prescribing cabergoline to patients with depression.

**Keywords:** Pathological gambling, cabergoline, dopamine agonist, depression

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## 1. Introduction

Pathological gambling has been described frequently in patients with Parkinson disease (1-6) or other movement disorders (7). This phenomenon is attributed to stimulation of dopamine receptors by dopamine replacement therapy and/or dopamine agonist administration. Dopamine agonists are occasionally used to treat antidepressant-resistant depression (8-10). However, pathological gambling has not been described in patients with depression treated with dopamine agonists. Reported here is the first case of recurrent depression in a patient who exhibited pathological gambling after administration of cabergoline.

## 2. Case Report

Mr. X is a 36-year-old government official. His younger brother has suffered from social anxiety disorder for several years. Mr. X has had no serious physical illness thus far. After graduating from university, he started to work in a government office and was transferred to this area at the age of 31. He had occasionally enjoyed pachinko (11), the most popular form of gambling in Japan, and horse racing earlier in his life but never had any problems. Three months after the transfer, he started to experience impaired concentration, decreased motivation, anxiety, depressive moods, malaise, and insomnia. He consulted a psychiatrist near his office and was treated for six months. At the age of 32, he started to experience similar symptoms and consulted another psychiatrist. His symptoms were treated successfully by administration of fluvoxamine 150 mg/d plus amoxapine 30 mg/d. At the age of 33, he had a recurrence of similar symptoms and consulted another psychiatrist. His depressive symptoms were not alleviated by combined treatment of paroxetine 30 mg/d and amoxapine 100 mg/d, so he was referred to this clinic for a consultation.

Fluvoxamine was initiated and was gradually increased to 150 mg/d. It was partially effective in that allowed the patient to work for brief periods of four hours a day. Since he lacked energy, fluvoxamine was increased to 200 mg/d and cabergoline 1 mg/d was

added. The course of the drug regimen and clinical response after introduction of cabergoline are shown in Figure 1. Six weeks after the addition of cabergoline, the dose was increased to 2 mg/d because lack of energy persisted. The patient's moods gradually returned to normal but his difficulty in sleeping was exacerbated. Quetiapine 25 mg was initiated for insomnia and was effective. Six months later, his sense of fatigue had almost disappeared, allowing him to be exercising at a local gym. At around the same time, he started to go to pachinko parlors and the horse racing track, although he lacked sufficient energy to work full-time. He spent considerable money and time every day in pachinko parlors and went to the horse racing track every weekend. Neither the patient nor his family was aware that his behavior was problematic, so he did not report it to his psychiatrist. Eight months later, his depressive symptoms had almost disappeared, so he was able to work for up to six hours. Nine months later, cabergoline was decreased to 1.5 mg/day because the patient exhibited no depressive symptoms except insomnia. However, his gambling behavior persisted. In the meantime, he exhibited no manic or hypomanic symptoms.

One year later, his wife finally noticed that his gambling behavior was excessive and that he had spent more than twenty thousand US dollars in total. He subsequently often quarreled with his wife over his gambling and always pledged to stop. Nevertheless, he could not refrain from going to pachinko parlors. He spent more money and time gambling. He sometimes went to a pachinko parlor to recover his losses on the same day he lost substantial money betting on horse racing. He and his wife visited this clinic together to discuss his gambling problem. His gambling behavior fulfilled criteria for pathological gambling according to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision edition* (DSM-IV-TR). Since pathological gambling might have been triggered by cabergoline administration, the dose was gradually decreased with close monitoring of the

patient's gambling behavior and moods. His gambling behavior continued until one week after cabergoline was discontinued, but depressive symptoms subsequently recurred.

### 3. Discussion

The current case involved a patient developing pathological gambling after the introduction of cabergoline, a dopamine agonist. This phenomenon did not disappear until the drug was discontinued. Thus far, four cases of pathological gambling associated with cabergoline have been reported (1,3,4,12). Three involved patients suffering from Parkinson disease who were taking cabergoline with L-dopa. Two were taking 4 mg/d of cabergoline. The other patient was taking cabergoline 0.25 mg weekly to treat pituitary prolactinoma. Like in the current case, gambling behavior stopped with the discontinuation of cabergoline except in one case where gambling stopped after reduction of L-dopa instead (1).

Other dopamine agonists which have been associated with pathological gambling include pramipexole, ropinirole, and pergolide (2,13-16). Two case series have implicated pramipexole as the agent most likely to cause pathological gambling in patients with Parkinson disease (2,16). However, more recent and larger-scale studies have not supported a differential association between specific dopamine agonists and pathological gambling (13-15). Instead, these recent studies have consistently indicated a higher prevalence of pathological gambling among patients treated with a dopamine agonist than those without (13-15). The lifetime prevalence of pathological gambling was 7.2% among patients with Parkinson disease on a dopamine agonist and 3.4% among those on any medication (14).

The mechanism by which dopamine agonists induce pathological gambling is not clear, but stimulation of dopamine D3 receptors has been repeatedly suggested (4). D3 receptors are distributed most abundantly in the limbic system, where the reward system is supposedly

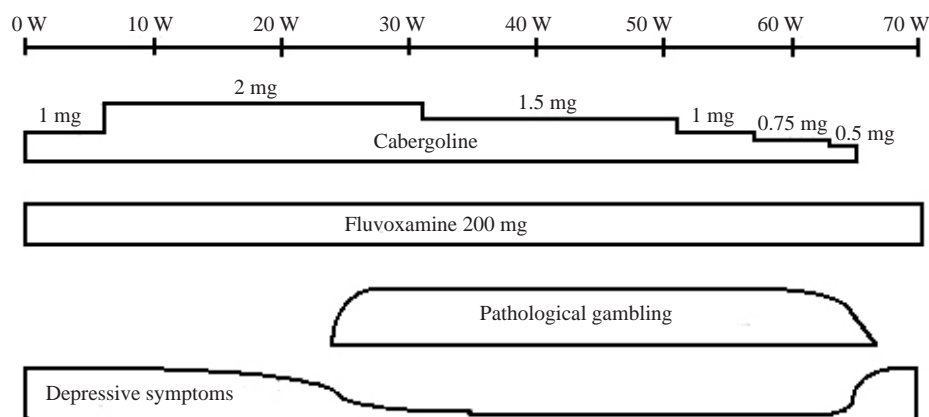


Figure 1. Schematic time-course of the cabergoline dose and severity of pathological gambling and depressive symptoms after introduction of cabergoline.

regulated (17). Pramipexole, ropinirole, and pergolide all show 10 to 100-fold greater selectivity for D3 receptors than for D2 receptors (18). Although cabergoline is not as selective, it is still slightly more selective for and fairly potent against D3 rather than D2 receptors. In contrast, bromocriptine, which is more selective for D2 receptors than for D3 receptors (18), has been linked with pathological gambling in only two cases (5,6).

In the current case, pathological gambling began after depression was partially alleviated and it persisted even after depression abated. Mood disorder itself has been associated with pathological gambling in many reports (19). Depression is prevalent in over half of the pathological gambling population, according to some studies. Depressive patients may start gambling to relieve their depressive mood while other patients may exhibit depression secondary to gambling behavior. Since the current patient did not exhibit pathological gambling in his preceding depressive episodes, his pathological gambling should not be attributed primarily to his depression. He did not show any manic symptoms, which must be ruled out according to the *DSM-IV-TR* criteria because clinical symptoms of pathological gambling and gambling as a symptom of mania share similarities.

Pathological gambling in the current case finally disappeared one week after cabergoline was discontinued. Most other reports have noted that pathological gambling had been successfully resolved by reducing or discontinuing the dopamine agonist prescribed. Some authors have suggested the efficacy of selective serotonin reuptake inhibitors (SSRIs) at curbing pathological gambling (3,19). Although the mechanism is not clear, research has suggested that the efficacy of SSRIs may be related to their anti-obsessional effect (19). However, the current patient developed pathological gambling while taking fluvoxamine, an SSRI, indicating that the prophylactic effect against pathological gambling by fluvoxamine is questionable.

In conclusion, physicians should be aware of the potential for the development of pathological gambling when prescribing cabergoline as well as pramipexole, ropinirole, and pergolide.

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