Hypersexuality and new sexual orientation following aripiprazole use

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Aripiprazole is a dopamine D2 receptor partial agonist infrequently associated with sexual side-effects. Here the authors present a case of hypersexuality and new-onset homosexual behaviour, following use of aripiprazole in a male patient, which resulted in discontinuation of aripiprazole and subsequent elimination of the side-effects. 

Sexual dysfunction constitutes a significant reason for non-adherence to antipsychotic treatment in patients with schizophrenia and other mental health disorders. Antipsychotic medication leads to dopamine levels decreasing and prolactin levels increasing, which reduces libido.1

Aripiprazole is a dopamine D2 receptor partial agonist that is infrequently associated with sexual side-effects and is frequently used to ease the side-effects that can arise from high prolactin levels.2 There are sporadic case reports associating aripiprazole partial dopaminergic agonistic effect with compulsive actions, including pathological gambling, excessive shopping and hypersexuality.3

Here the authors present a case of hypersexuality and new-onset homosexual behaviour, following aripiprazole use in a male patient, which resulted in discontinuation of aripiprazole and subsequent elimination of the side-effects.

Presentation
A 32-year-old heterosexual male patient was under the care of our specialist psychosis team with a diagnosis of paranoid schizophrenia with emotionally unstable personality disorder traits. He had regular outpatient follow-up appointments for almost six years. His persecutory delusions were generally well controlled with risperidone 4mg daily. He did not receive any other medication for mental or physical health issues. He was a social drinker and never used elicit substances throughout his life. The patient was complaining of decreased libido and erectile dysfunction and he requested a different antipsychotic medication. We decided to discontinue risperidone and we started him on aripiprazole, which is known to have fewer sexual side-effects. Aripiprazole was started at a 5mg daily and the dosage was titrated up to 20mg daily.

He presented to our clinic one month after the introduction of aripiprazole into his treatment regimen complaining of increased libido and erectile dysfunction and he requested a different antipsychotic medication. We decided to discontinue risperidone and we started him on aripiprazole, which is known to have fewer sexual side-effects. Aripiprazole was started at a 5mg daily and the dosage was titrated up to 20mg daily.

The increase in sexual behavior was related to commencement of aripiprazole, so it was discontinued and the patient switched to ziprasidone. The patient insisted and was adamant that aripiprazole was the reason for the hypersexuality. After four to six days of stopping aripiprazole the sexual behaviour started subsiding, with complete relief after approximately two weeks. The patient has been regularly followed up and remains well without any sexual side-effects.

Discussion
Antipsychotics, in general, cause a decrease in libido due to dopamine receptor antagonism and prolactin level increase.4 On the other hand, some medication such as amphetamines, pramipexole and L-dopa can increase libido.5

Aripiprazole is a D2 receptor partial agonist. Risperidone is another antipsychotic drug that causes a decrease in dopaminergic activity, and for this reason often causes sexual adverse reactions.6 As a consequence, aripiprazole could possibly raise dopaminergic transmission at the mesolimbic dopaminergic circuit, especially at the nucleus accumbens, which was earlier inhibited by risperidone.

Testosterone is known to be the basic mediator of sexual urge in
males and females, but serotonergic and dopaminergic pathways in the central nervous system have a significant role to play. More specifically, brain dopamine pathways that connect the limbic system and the hypothalamus seem to form the centre of the excitatory system.7

Classical receptor theory postulates that the density of the receptors directly affects the inherent activity of partial agonists. Hence, it can be predicted that former exposure to dopamine antagonists would boost the receptor responsiveness and support the partial agonism of aripiprazole.8

Aripiprazole is a partial agonist of 5HT1A serotonergic receptors and a 5HT2A serotoninergic receptor antagonist. It has been reported that 5HT2A antagonism and 5HT1A agonism enhance sexuality. Medications such as mirtazapine, which have 5HT1A agonistic and 5HT2A antagonistic effects, have hardly any sexual adverse reactions. Cyproheptadine, which is a 5HT2 antagonist, is considered an efficient medication in terms of reducing anorgasmia induced by antidepressants.10

The aforementioned receptor properties may be the aetiology of hypersexuality in our patient. Further studies and research are needed to explain the sexual effects of aripiprazole.

There are some case reports in the literature that describe increased libido and increased sexual appetite stemming from aripiprazole in both male and female patients.11,12 The US Food and Drug Administration has issued a warning related to impulse-control behaviours in patients receiving aripiprazole.13 One could say that the hypersexuality could be in the context or poor impulse control behaviours. In our case the patient did not display any impulse dysregulation nor did he display any manic or hypomanic symptoms.

We searched the literature and we found one more case report14 describing a patient who developed homosexual behaviour while being treated with aripiprazole. We assume that there may be more cases unreported due to social concerns.

In this case the patient presented with an addiction habit for gambling. Before aripiprazole commencement he was an exclusive heterosexual with poor sexual activity, while under aripiprazole he developed a homosexual behaviour with increased sexuality, sex without protection and sadomasochistic habits. The urge for gambling and compulsive sexual behaviour stopped two weeks after aripiprazole was discontinued and the patient was switched to amisulpride. After that he returned to heterosexual orientation. It is known that patients with Parkinson’s disease who receive dopamine agonists may develop compulsive behaviours, including hypersexuality, new sexual orientation and gambling.

In our case hypersexuality and homosexuality surfaced in an adult male who had no previous history of sexual indiscretion of either behaviour. One could hypothesise that this patient had homosexual drives that could have been suppressed during his life and that aripiprazole simply lowered the threshold for these thoughts to surface.

In this case the patient explicitly denied any pre-existing homosexual thoughts or physical attraction towards males throughout his life. These behaviours had never been exhibited prior to aripiprazole therapy and fully receded within two weeks of aripiprazole discontinuation. There were no similar symptoms reported by the patient at the one year follow up after aripiprazole discontinuation.

Conclusions

Aripiprazole is associated with fewer adverse reactions in comparison with other antipsychotic medication. We reported a patient who experienced hypersexuality and a new sexual orientation under treatment. The exact mechanism by which aripiprazole can cause these side-effects is unknown. It is frequently difficult for patients to report these phenomena due to social reasons and feelings of guilt.

Increased sexual desire should be considered in the spectrum of rare adverse reactions as a result of aripiprazole treatment, especially if aripiprazole is started after discontinuation of D2 antagonist antipsychotics, such as risperidone. If this unusual side-effect remains unrecognised it may cause embarrassment to patients and poor compliance with treatment.

More research is essential in order to comprehend the exact mechanism through which aripiprazole affects sexuality.

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Conflicts of interest
No conflicts of interest were declared.

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