

196 - Effects of antipsychotic drugs

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196 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 1 People with psychosis are less able to develop good psychosexual relationships and, for some, treatment with an antipsychotic can improve sexual functioning via an improvement in psychotic symptoms.¹⁸ Assessment of sexual functioning can clearly be difficult in someone who is psychotic. The Arizona Sexual Experience Scale may be useful in this respect.¹⁹ Effects of antipsychotic drugs Sexual dysfunction is an adverse effect of most antipsychotics. Individual susceptibility varies and effects are usually reversible. Psychosis, physical illness and drugs other than antipsychotics can also contribute to sexual dysfunction. Many studies do not control for these factors, making the prevalence of sexual dysfunction with different antipsychotics difficult to compare.²⁰ Antipsychotics decrease dopaminergic transmission, which in itself can decrease libido but may also increase prolactin levels via negative feedback. Hyperprolactinaemia is a key factor in sexual dysfunction^{21,22} but may only explain 40% of the sexual dysfunction that is associated with antipsychotic medication.²³ Hyperprolactinaemia can also cause amenorrhoea and infertility²⁴ in women, and breast enlargement and galactorrhoea in both men and women.²⁵ The overall propensity of an antipsychotic to cause sexual dysfunction is a function of the facility to raise prolactin (i.e. risperidone > haloperidol > olanzapine > quetiapine > aripiprazole).^{6,20,26} Aripiprazole is relatively free of sexual adverse effects when used as monotherapy²⁷ and may improve symptoms in combination with another antipsychotic.^{28,29} The same is probably true for brexpiprazole, and cariprazine is a theoretically appropriate alternative.³⁰ Anticholinergic effects of drugs can cause disorders of arousal³¹ and concomitant anticholinergics may thus contribute to sexual dysfunction.³² Drugs that block peripheral α_1 receptors cause particular problems with erection and ejaculation in men.⁹ Antipsychotic-induced sedation and weight gain may reduce sexual desire.³³ Table 1.45 gives details of the nature and frequency of sexual adverse effects caused by antipsychotics. Table 1.45 Sexual adverse effects of antipsychotics. Drug Type of problem

Drug	Type of problem
Aripiprazole	■ ■ No effect on prolactin or α_1 receptors. No reported adverse effects on sexual function. Improves sexual function in those switched from other antipsychotics ^{27,29,34-36} and when added as an adjunct. ³⁷ Case reports of aripiprazole-induced hypersexuality have been published. ^{38,39}
Asenapine	■ ■ Does not appear to significantly affect prolactin levels ⁴⁰ ■ ■ No

reported cases of sexual dysfunction Brexpiprazole ■ ■ Similar mechanism of action to aripiprazole (5-HT1A agonist, 5-HT2A antagonist and partial D2 agonist) ■ ■ Causes negligible increases in prolactin⁴¹ ■ ■ No problems with sexual dysfunction reported in clinical trials⁴² (Continued)

Schizophrenia and related psychoses CHAPTER 1 Table 1.45 (Continued) Drug Type of problem
Cariprazine ■ ■ Similar mechanism of action to aripiprazole (5-HT1A agonist, 5-HT2A antagonist and partial D2 agonist) ■ ■ Not associated with hyperprolactinaemia⁴³ ■ ■ Very low rates of sexual dysfunction reported in clinical trials⁴⁴
Clozapine ■ ■ Significant α 1 adrenergic blockade and anticholinergic effects.⁴⁵ No effect on prolactin.⁴⁶ ■ ■ Probably fewer problems than with typical antipsychotics⁴⁷
Haloperidol ■ ■ Similar problems to phenothiazines⁴⁸ but anticholinergic effects reduced⁴⁹ ■ ■ Prevalence of sexual dysfunction up to 70%⁵⁰
Lurasidone ■ ■ Does not appear to affect prolactin levels⁵¹ ■ ■ No reported cases of sexual dysfunction⁵²
Olanzapine ■ ■ Possibly less sexual dysfunction than drugs such as haloperidol owing to relative lack of prolactin-related effects⁴⁸ ■ ■ Priapism reported rarely^{53,54} ■ ■ Prevalence of sexual dysfunction >50%⁵⁰
Paliperidone ■ ■ Similar prolactin elevations to risperidone ■ ■ One small study⁵⁵ and one case report⁵⁶ showing reduction in sexual dysfunction following switching to paliperidone depot from risperidone oral or depot
Phenothiazines (e.g. chlorpromazine) ■ ■ Hyperprolactinaemia and anticholinergic effects. May cause delayed orgasm at lower doses followed by normal orgasm but without ejaculation at higher doses.⁵⁷ ■ ■ Priapism has been reported with thioridazine and chlorpromazine (probably due to α 1 blockade)^{49,58,59}
Quetiapine ■ ■ No effect on prolactin⁶⁰ ■ ■ Possibly associated with low risk of sexual dysfunction,⁶¹⁻⁶⁴ but studies are conflicting^{65,66}
Risperidone ■ ■ Potent elevator of serum prolactin ■ ■ Less anticholinergic than some other antipsychotics (olanzapine, quetiapine) ■ ■ Specific peripheral α 1 adrenergic blockade leads to a moderately high reported incidence of ejaculatory problems such as retrograde ejaculation^{67,68} ■ ■ Priapism reported rarely³³ ■ ■ Prevalence of sexual dysfunction 60-70%⁵⁰
Sulpiride/amisulpride ■ ■ Potent elevators of serum prolactin⁶⁹ but note that sulpiride was not associated with greater sexual dysfunction than SGAs in CUtLASS-118
Thioxanthenes (e.g. flupentixol) ■ ■ Arousal problems and anorgasmia⁷⁰
Lumateperone ■ ■ Does not appear to affect prolactin⁷¹ ■ ■ No sexual adverse effects reported in clinical trials⁷²
Pimavanserin ■ ■ Does not bind to dopamine receptors,⁷³ so has no effect on prolactin ■ ■ May improve sexual function in patients with depression⁷⁴
Iloperidone ■ ■ Does not usually affect prolactin⁷⁵ ■ ■ Some reports of sexual dysfunction in adverse event reporting databases,⁷⁶ case reports of retrograde ejaculation⁷⁷
CUtLASS-1, Cost Utility of the Latest Antipsychotic Drugs in Schizophrenia Study; SGA, second-generation antipsychotic.

Revision #1

Created 2026-01-04 20:13:07 UTC by Omar Ayman

Updated 2026-01-04 20:13:07 UTC by Omar Ayman