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Agomelatine and its reproduction effects

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Most of the pharmacological agents which are used in the treatment of depression are known to disrupt normal sexual function, which affects the patient's quality of life and represents the main side effect that leads to the discontinuation of treatment. Agomelatine has been reported not to cause sexual dysfunction requiring treatment. All dose regimens of agomelatine have been reported to be well tolerated and have no unexpected adverse event. Understanding that there is a strong interaction between circadian rhythm desynchronization and mood disorders is another reason, which has led to the development of agomelatine. Agomelatine is a melatonergic agonist for MT1 and MT2 receptors and a serotonin (5-HT)2C receptor antagonist. This compound was initially investigated as a chronobiotic; however, with the discovery of the 5-HT2C antagonist activity the emphasis shifted to its anxiolytic and antidepressant effects. The antidepressant-like activity of agomelatine has been suggested to depend on a combination of its melatonin agonist and 5-HT2C antagonist properties. There are a few studies on sexual side-effects of agomelatine in the treatment of depression in humans. Agomelatine is suggested to demonstrate favorable sexual acceptability in depressed patients and healthy volunteers and therefore to be a good option for the treatment of depression because it would not have adverse effects on sexual function. Abnormal sperm parameters have been found to be associated with treatment with the SSRI citalopram but no similar association with agomelatine. The effects of agomelatine on sexual response have not been studied sufficiently in animal models. In our study, chronic treatment with agomelatine has been found not to lead to adverse effects on sexual behavior and even exerts some putative pro-sexual effects in adult male rats. To our knowledge, this study provides the first evidence of lack of sexual dysfunction by chronic agomelatine treatment in rats. Our work also shows that agomelatine induces an antidepressant-like effect by means of enhancement of serotonergic and possible dopaminergic activity. Our studies suggest that the effects of chronic agomelatine administration on reproductive seem to be sex-dependent. Because agomelatine advanced vaginal opening in the female rats whereas it delayed puberty onset in the male rats, clinical use of agomelatine may lead to different side-effects on puberty in male and female. The understanding of the effects of agomelatine will not only contribute to the delineation of the combination of melatonergic and 5-HT2C receptor activation in the treatment of depression, but may also provide new therapeutic approaches to treat some reproductive disorders.

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