SEXUAL DYSFUNCTION

Central action of sildenafil on arousal and reward pathways

In addition to its peripheral effect on the corpus cavernosum, phosphodiesterase 5 (PDE5) inhibitor sildenafil also exerts effects on the central nervous system to modulate arousal, according to the findings of a new study.

A team of researchers from Athens, Greece, studied the effects of sildenafil administration on dopaminergic and serotonergic activity in the nucleus accumbens (NAcc) and the medial preoptic area (MPOA) of the brains of male rats during sexual arousal. Sildenafil was administered for either 2 days (to model acute administration) or 21 days (to simulate chronic treatment). 30 min after the last injection, rats were exposed to females in oestrus during a noncontact erection session. Half of the males had previous experience of a noncontact sexual encounter and the other half did not. After the encounter, levels of dopamine, serotonin and their metabolites were measured in the two brain areas using high-performance liquid chromatography. Turnover of dopamine

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and serotonin were also calculated as markers of neurotransmission.

In inexperienced males, acute and chronic sildenafil treatment increased both dopamine and serotonin turnover rates in the MPOA and in the NAcc. The same was true for acute treatment of experienced rats, but chronic treatment enhanced serotonin turnover only in the MPOA and dopamine turnover only in the NAcc. This discrepancy could be due to a

greater stress effect in experienced male rats, as copulation was prevented.

An effect of sildenafil on dopaminergic neurotransmission has been suggested in the past, but this is the first time that the MPOA has been implicated and that an effect on serotonergic activity has been demonstrated. The authors hypothesize that modification of the nitric oxide–cyclic guanosine monophosphate pathway, which is the target of action of PDE5 inhibitors, might be involved, as dopamine release in the MPOA before and during copulation is modulated by nitric oxide.

The effect of sildenafil on motivation and arousal pathways could help explain its clinical utility in treating psychogenic erectile dysfunction.

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