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THE ANTIDEPRESSANT AGOMELATINE REDUCES FEAR LONG TERM MEMORY BUT NOT ACQUISITION OR SHORT TERM EXPRESSION OF FEAR MEMORIES

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Alterations in fear learning processes may be implicated in mood disorders. Fear learning has been investigated with Pavlovian classical fear conditioning paradigms, consisting of pairing a neutral conditioned stimulus (CS), such as a tone, with an aversive unconditioned stimulus (US), such as a footshock. Upon subsequent exposure, the CS is perceived as aversive and provokes a fear response.The novel antidepressant agomelatine acts as a melatonergic receptor agonist and a 5-HT_{2C} receptor antagonist. Its antidepressant action was demonstrated in preclinical and clinical studies. Agomelatine has also anxiolytic properties. The aim of this study was to determine how acute agomelatine treatment might differentially alter fear circuits by using auditory fear conditioning in the rat.A single pre-training injection of agomelatine (40 mg/kg intraperitoneally) significantly reduced freezing to the fear arousing CS 24 hours after training but not during training or 3 hours after training. This pattern of results is consistent with an effect on the consolidation of the fear memory. A single pre-testing injection of agomelatine had no effect on conditioned fear expression. These effects of agomelatine should be considered in relation to its antidepressant action. Agomelatine achieved a reduction of fear conditioning in a single dose, while classical SSRIs only reduced fear conditioning after chronic treatment. This finding is consistent with clinical studies suggesting a faster onset of action of agomelatine than classical SSRI treatment.

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