In response to “The effect of agomelatine on 5HT_{2C} receptors in humans: a clinically relevant mechanism?”

by Trevor Norman

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We thank Dr. Norman for his interesting comments about the role of H1 receptors in the regulation of slow wave sleep. It is of course quite plausible that H1-receptor blockade could modify slow wave sleep (SWS) in humans; however, in a study with the selective H1 receptor antagonist, mepyramine, we saw no such effect (Solomon et al. 1989).

Regardless of whether or not H1-receptors play a role in SWS regulation in humans, the key issue in the case of agomelatine is whether selective 5-HT_{2C} receptor blockade is able by itself to increase SWS. In animals, there is good evidence that this is the case, and indeed, agomelatine, given in acute doses of 10 and 40 mg/kg, also increases SWS in rats, an effect mimicked by the selective 5-HT_{2C} receptor antagonist, S32006 (Descamps et al. 2009). This suggests that a dose of agomelatine sufficient to block 5-HT_{2C} receptors in humans should also increase SWS. However, we

agree with Dr. Norman that to resolve the question of whether agomelatine does block 5-HT_{2C} receptors in the human brain at clinically relevant doses, other models of 5-HT_{2C} receptor activity will be needed.

References

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