Effect of BD 1047, a sigma$_1$ receptor antagonist, in the animal models predictive of antipsychotic activity

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Abstract:
The sigma receptors were first classified as a subtype of opioid receptors but later they were found to be a distinct pharmacological entity. Many preclinical and clinical data have indicated that sigma receptor ligands have to be involved in neuropsychiatric disorders, including schizophrenia. Numerous data have suggested that potential antipsychotic activity of sigma ligands results from their „antagonistic“ activity. However, the subcellular mechanisms by which sigma ligands exert their effects have not been elucidated in detail, therefore, the terms „agonist“ or „antagonist“ and their functional implications are not entirely unequivocal. The aim of the present study was to find out if BD 1047, described recently as a selective functional antagonist of sigma receptors, shows antipsychotic activity in animal models predictive of efficacy in schizophrenia. In contrast to rimeczole and panamesine, two selective sigma ligands whose antipsychotic activity was confirmed clinically, BD 1047 did not decrease amphetamine-induced hyperactivity in mice in a statistically significant manner. Likewise, it did not modify the hypenactivity induced by NMDA receptor antagonists, phencyclidine, memantine or dizocilpine. On the other hand, BD 1047 attenuated apomorphine-induced climbing in mice and phencyclidine-induced head twitches in rats, like rimeczole and panamesine did. Summing up, BD 1047 shows a moderate activity in models used in this study suggesting that its usefulness as an antipsychotic drug is doubtful. However, more detailed studies are required for definitive confirmation of this conclusion.

Key words:
BD 1047, sigma$_1$ receptor antagonist, antipsychotic activity