ARE GLYCINE$_B$ SITES INVOLVED IN THE DEVELOPMENT OF MORPHINE TOLERANCE?

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Numerous data have indicated that competitive and non-competitive N-methyl-D-aspartate (NMDA) receptor antagonists attenuate the development of tolerance to the analgesic effect of morphine. This study extends these findings on the effects of glycine$_B$ site antagonist, L-701.324. Tolerance to the analgesic effect of morphine was measured in hot-plate test in Wistar rats. For 9 days, animals were first injected with vehicle or glycine$_B$ receptor antagonist, L-701.324 (2.5 and 5 mg/kg, po). The non-competitive NMDA receptor antagonist, MK-801 (0.05 or 0.1 mg/kg, ip) was used as a reference compound. The injection of L-701.324, MK-801 or saline was followed, 20 min later, by the injection of morphine (10 mg/kg, sc). Hot-plate latencies were determined 20 min after the second injection on odd-numbered days. The results indicated that chronic administration of glycine$_B$ site antagonist, L-701.324 decreased the analgesic effect of morphine and they may suggest that this substance at both used doses increased the development of morphine tolerance, whereas non-competitive NMDA antagonist, MK-801 at the dose of 0.1 mg/kg potentiated the analgesic effect of morphine and attenuated the development of morphine tolerance.

Key words: morphine, tolerance, NMDA antagonists, hot-plate test, rats

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