P02-286 - **METYRAPONE AND MIFEPRISTONE REVERSE MEMORY LOSS INDUCED BY SPONTANEOUS MORPHINE WITHDRAWAL IN MICE**

A. Mesripour[1], V. Hajhashemi[2], M. Rabbani[2]

[1]*Pharmacology, Pharmaceutical Sciences Research Center, Isfahan University of Medical Sciences,*
[2]*Pharmacology, Isfahan University of Medical Sciences, Isfahan, Iran*

Objectives: Morphine withdrawal leads to cognitive deficits and an increase in corticosterone concentrations in plasma. Evidently glucocorticoid hormones influence memory. Therefore the current study evaluated the effects of metyrapone and mifepristone on memory deficit following spontaneous morphine withdrawal.

Methods: To evaluate memory novel object recognition task was used, which comprised of three sections; habituation, first trial and the test trial. In this method, the difference in the exploration time between a familial (F) object and a novel (N) object is taken as an index of memory performance (recognition index, RI ={N - F/N + F} × 100). Male NMRI mice weighing 25-30 g were made dependent by increasing doses of morphine (30-90 mg/kg) subcutaneously twice daily for three days; RI was assessed 4 hour after the last dose of morphine on the third day. Mifepristone and metyrapone were used subcutaneously (40 min and 90 min, respectively) before the first trial.

Results: Memory performance was impaired in morphine dependent animals (RI= -14.8% ± 10.7, $P< 0.05$). Serum corticosterone concentration in 4 hr morphine withdrawn animals was 26.6 ± 0.9 ng/ml, which was 20% more than normal animals. Metyrapone 25 mg/kg, and mifepristone 50 mg/kg notably improved RI to 34.8% ± 10.8 and 25.4% ± 11.7 respectively, compared to vehicle group.

Conclusions: Therefore mifepristone and metyrapone by manipulating the corticosteroid function improves memory performance after withdrawal. These results show that increased glucocorticoid concentration is involved in memory deficit caused by morphine withdrawal.

Keywords: Morphine withdrawal; Memory; Corticosterone

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