

Effects of Repeated Administration of DL-Amphetamine and Methamphetamine on Tolerance to Hyperactivity

Studies have shown that the stimulating effect of DL-amphetamine on motor activity does not diminish with repeated treatment of the drug¹⁻³. Contrarily, repeated treatment with methamphetamine showed a progressive reduction in motor hyperactivity³⁻⁵. Reviewing the literature cited above, however, saline-controls were not included in the methamphetamine studies. It seemed, therefore, desirable to substantiate the presence of tolerance to hyperactivity in animals with methamphetamine.

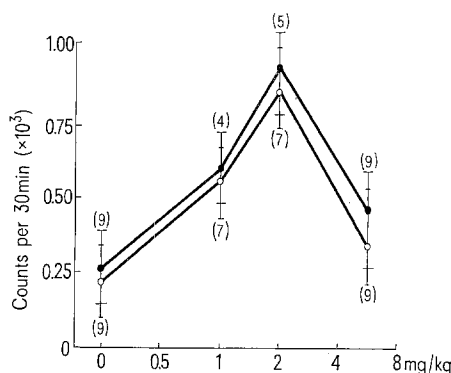
Male Sprague-Dawley rats weighing 230–300 g, or male Swiss-Albino mice weighing 20–25 g were used. They were fed with Wayne Laboratory Blox and water ad libitum. The rats were caged individually and the mice were group-

In the experiment with rats pretreated 2 weeks with a daily dose of 5 mg/kg methamphetamine or saline, injections of various test doses of methamphetamine, the compound produced dose-response curves shown in the Figure. Peak activity was obtained with 2 mg/kg of methamphetamine. There was no significant difference in responses to the final test dose of methamphetamine between the drug-pretreated and the saline-pretreated rats. In the other experiment, groups of 2 mice were pretreated daily with either 2 mg/kg of DL-amphetamine, 0.5 mg/kg of methamphetamine, or saline and motor activity was measured for 4 consecutive weeks. The results are given in the Table. Our data from the present study support the statement

Effect of chronic injections on motor activity in mouse

Treatments	No. in group	Weeks after treatment W0	W1	W2	W3	W4
Saline	10	1.28 (\pm 0.53)	1.21 (\pm 0.75)	1.29 (\pm 0.73)	1.21 (\pm 0.73)	1.26 (\pm 0.76)
DL-Amphetamine	10	1.71 (\pm 0.84)	1.76 (\pm 0.79)	1.80 (\pm 0.83)	2.08 (\pm 0.93)	2.10 (\pm 1.09)
Methamphetamine	8	2.19 (\pm 0.53)	2.51 (\pm 0.63)	2.54 (\pm 0.99)	2.74 (\pm 1.21)	2.86 (\pm 1.04)

Values represent total motor activities in thousand counts \pm 1 S.D. between 30 to 60 min after the injection.



Effect of methamphetamine on the motor activity of rats pretreated 2 weeks with a daily dose of 5 mg/kg of methamphetamine (○—○) and of control (●—●).

ed 2 in each group. The animals received daily between 16.00 and 16.30 h an i.p. injection of 1.0 ml/kg body weight of DL-amphetamine sulfate or methamphetamine hydrochloride dissolved in isotonic saline. The control group was injected with a corresponding volume of isotonic saline. Individuals rats or groups of 2 mice were placed in a photoelectric cage, for measurement of motor activity. All activity measurements were made in the afternoon and between 30 to 60 min after the injection. For statistical analysis of the data Students *t*-test or variance analysis, and a level of $p < 0.05$ was adopted to assess the significance of the difference of means.

that DL-amphetamine injections do not produce tolerance to hyperactivity. However, the lack of tolerance to motor activity in animals treated with methamphetamine is not in agreement with those works reported previously.

Résumé. Cette étude concerne le développement d'une accoutumance de l'activité motrice chez les animaux qui ont été traités avec de la méthamphetamine ou avec la DL-amphétamine. Nos résultats indiquent qu'il n'y a pas d'accoutumance chez les animaux qui ont été traités de DL-amphétamine ou de la méthamphetamine.

TZU-CHIAU LU, BENG T. HO and W. M. McISAAC⁶

Texas Research Institute of Mental Sciences,
1300 Moursund Avenue, Houston (Texas 77025, USA),
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