



Effect of prenatal methamphetamine exposure on sensitivity to other psychostimulants in adult male rats tested in Laboras apparatus

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INTRODUCTION

Methamphetamine (MA) is a psychostimulant drug with a high potential for addiction, which is often abused by drug addictive pregnant women. Psychostimulants have been shown to affect overall psychomotor activity by increasing locomotion and exploratory and decreasing comforting behavior in Open field test (*Bubenikova-Valesova et al., 2009; Shutova et al., 2010*). Previous studies have also shown that adult rats prenatally exposed to MA exhibit increased sensitivity to the same drug in adulthood (*Shutova et al. 2011*). This effect is known as sensitization (*Suzuki et al. 2004*). Once behavioral sensitization is established, it persists for several months (*Cornish and Kalivas 2001*).

There are studies showing that chronic application of one drug may induce higher sensitivity to another drug. This effect is called cross-sensitization (*Malanga and Kosofsky 2003*).

To validate our hypothesis that prenatal MA exposure induces cross-sensitization to challenge dose of other psychostimulants, adult male offsprings (prenatally MA- or saline-exposed) were divided into groups with challenge doses of drugs with similar mechanism of action as MA (1) amphetamine, (2) cocaine, (3) 3,4 methylenedioxymethamphetamine (MDMA), or saline.

Our hypothesis was tested in LABORAS (Metris B.V., Netherlands) to examine behavior in an unknown environment.

METHODS

- Maternal injection throughout the gestation period:
 - MA - methamphetamine (s.c. 5 mg/kg) 1x daily (E1-22)
 - Saline - physiological saline (0,9% NaCl solution)
- PD 1 - „Cross-fostering“ of pups
- PD 21 - Weaning of pups – two groups of male offsprings based on prenatal drug exposure:
 - MA groups
 - saline groups
- Immediately prior to testing (adult challenge) rats were injected with:
 - saline (1ml/kg)
 - amphetamine (5mg/kg)
 - cocaine (5mg/kg)
 - MDMA (5mg/kg)

- PD 70-90 - LABORAS (in LABORAS apparatus- Metris B.V., Netherlands)
The duration of each behavior was analyzed within six 10-minute intervals.
The following parameters were analyzed in all animals during the 1-hr period of testing:
 - the duration of locomotion [s];
 - the total distance traveled [m];
 - the duration of rearing [s];
 - the speed of locomotion [mm/s].



LABORAS APPARATUS

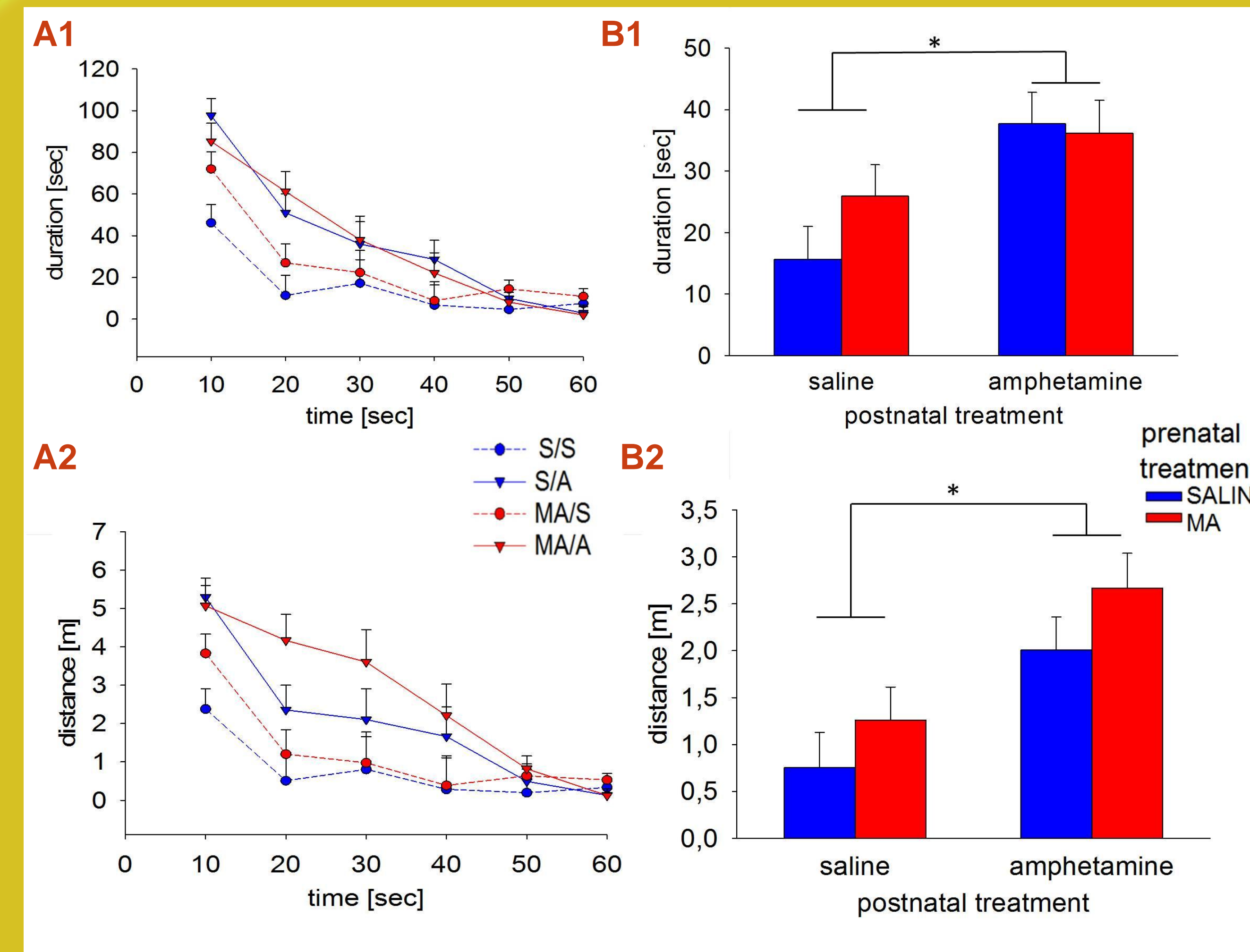


Fig. 1: The effect of prenatal MA exposure and adult challenge by amphetamine on duration of locomotion and total distance travelled in the LABORAS during a 1 hr. (A1) depicts duration of locomotion within the six 10-minute intervals for individual groups; (B1) mean duration of locomotion of individual groups; (A2) distance travelled within six 10-minutes intervals for individual groups; (B2) mean distance travelled for individual groups. Values presented as Mean + SEM; * p<0.05.

CONCLUSION

Prenatal MA exposure does not induce either cross-sensitization or tolerance to administration of amphetamine and MDMA in adulthood. Although, experiment results suggest that prenatal exposure to MA evokes tolerance to cocaine.

RESULTS

- ✓ Amphetamine challenge dose in adulthood increased locomotion and distance traveled in all animals regardless of prenatal drug exposure.
- ✓ Only rearing was increased in prenatally MA-exposed rats with challenge dose of amphetamine relative to prenatally saline-exposed rats with saline challenge. While amphetamine challenge increased the locomotion and distance traveled only in first 20 minutes of the session, their increase induced by MDMA challenge remained for the entire 1-hour period, regardless of prenatal treatment.
- ✓ Cocaine increased locomotion, distance traveled and rearing in prenatally saline exposed, but decreased it in prenatally MA-exposed rats.

SUPPORT

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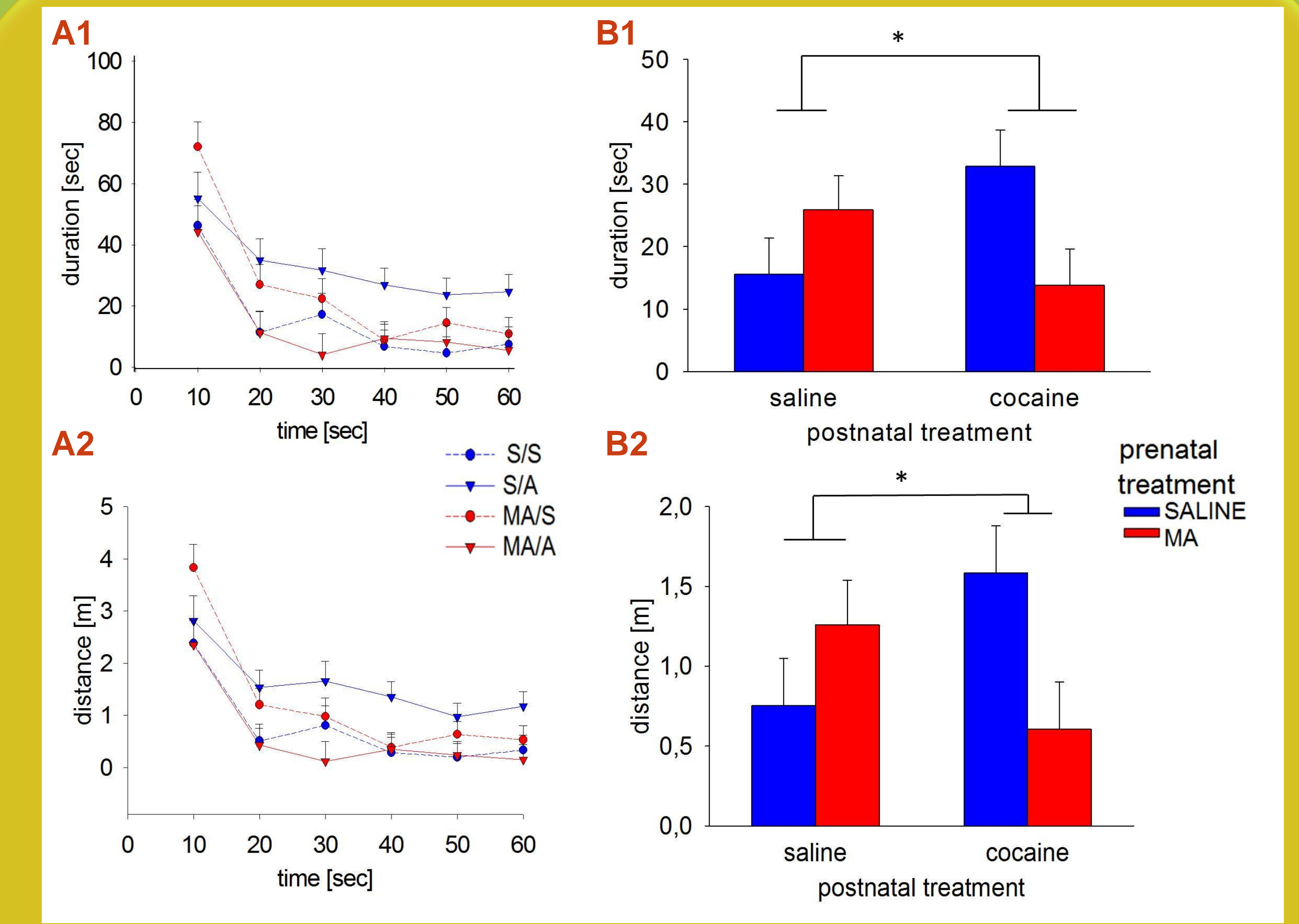


Fig. 2: The effect of prenatal MA exposure and adult challenge by cocaine on duration of locomotion and total distance travelled in the LABORAS during a 1 hr. (A1) depicts duration of locomotion within the six 10-minute intervals for individual groups; (B1) mean duration of locomotion of individual groups; (A2) distance travelled within six 10-minutes intervals for individual groups; (B2) mean distance travelled for individual groups. Values presented as Mean + SEM; * p<0.05.

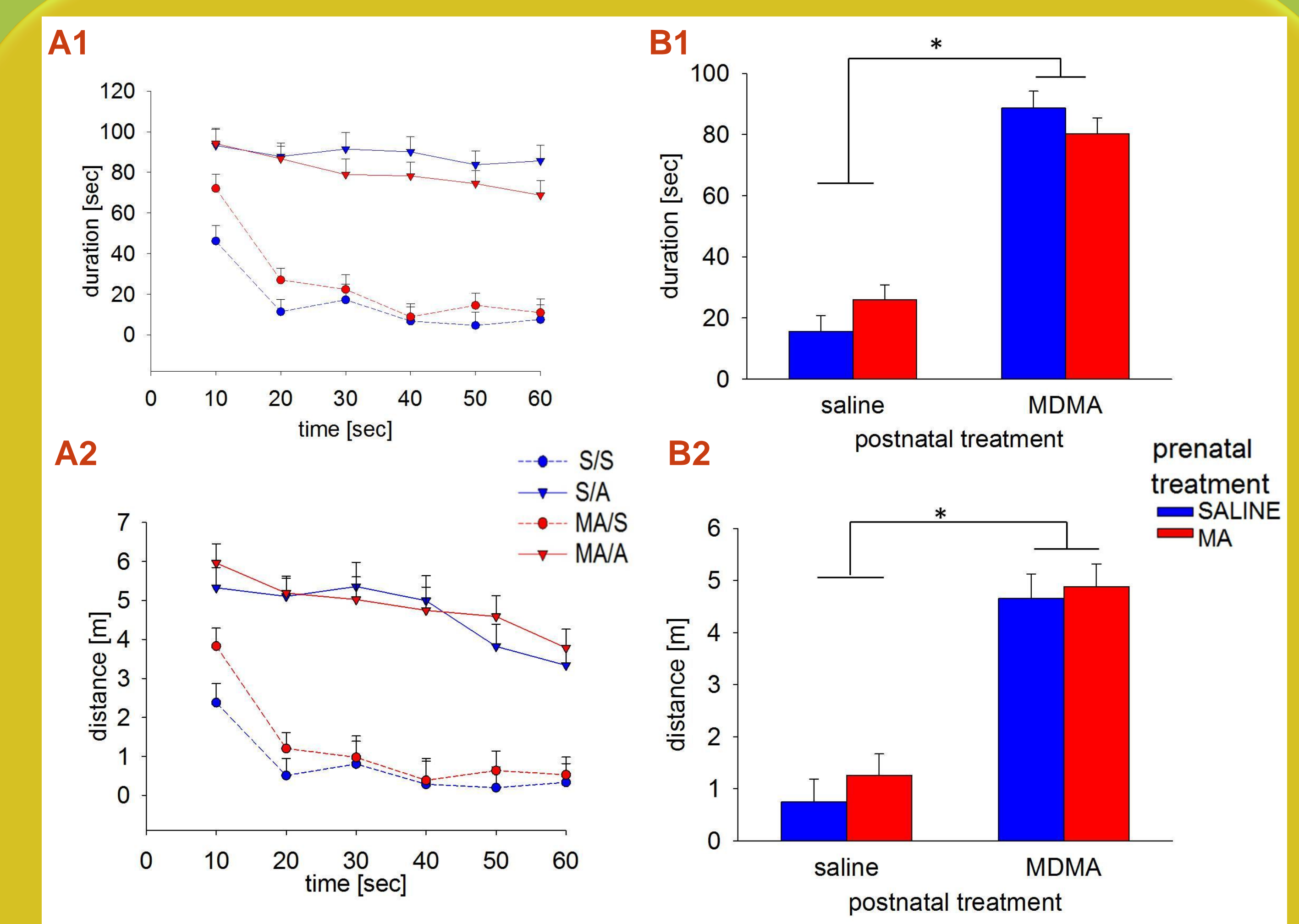


Fig. 3: The effect of prenatal MA exposure and adult challenge MDMA on duration of locomotion and total distance travelled in the LABORAS during a 1 hr. (A1) depicts duration of locomotion within the six 10-minute intervals for individual groups; (B1) mean duration of locomotion of individual groups; (A2) distance travelled within six 10-minutes intervals for individual groups; (B2) mean distance travelled for individual groups. Values presented as Mean + SEM; * p<0.05.