Maternal deprivation from the later infant stage to the early juvenile stage causes multiple abnormal behaviors related to autistic disorder only in male rats
Kenkichi Takase
(Department of Physiology, Himeji Dokkyo University)

Key words: Maternal deprivation; Sex difference; Comprehensive behavioral test battery

MATERIALS AND METHODS

The maternal deprivation was performed using the method of the modified version of 12-h separation protocol used by Garner et al. [1]. The Garner’s maternal deprivation procedure consisted of separating the entire litter from the dam at approximately 09:00 for a 12-h period on postnatal day 9 and 11. However, twice separations of the entire litter from the dam in the Garner’s procedure may alter the maternal behaviors, and subsequently influence the CNS development of the litter and their behavior in adult life. To minimize the influences in the present study, the half of litter was separated from the dam at 09:00 for a 12-h period on postnatal day 9 and 11. Maternally deprived litters removed from the dam were placed in plastic cages containing bedding from the home cage. Litters were then placed on a heat pad (35°C) in a separate room maintained at 25 ± 1°C. Neither food nor water was available during the deprivation period. At the end of the deprivation period, pups and the bedding were placed back with the dam. The pups were weaned at postnatal day 21 and two or three same-sex and same-reared rats were housed in a square plastic cage. Comprehensive behavioral tests were started at about 90 days of age. Before those, general health check and neurological screening tests were conducted at 27, 34, 41, 48, 55, 62, 69, 76, 83, and 90 days of age. Female rats were tested on the days of diestrus in the experiments except general health check and neurological screening tests. To minimize the handling effect followed by checking smears on the behavior of females, males were also handled for short time daily as well as females. All animal housing and experimental procedures were in accordance with the guidelines for animal experiment at Himeji Dokkyo University.

RESULTS AND DISCUSSION

The rats experiencing maternal deprivation on postnatal day 9 and 11 appeared grossly healthy and showed normal behaviors in neurological screening tests, 24-hour home cage activity monitoring, hanging wire test, vertical pole test, rotarod test, visual placing test, Preyer reflex test, two bottle choice test, painted odorant test, paintbrush stimulating test, PPI test, LI test, PA test, and novel object recognition test. The abnormal behaviors of the maternally deprived males were detected in only three tasks (i.e., open field test, social interaction test, and modified version of social interaction test). Males experiencing maternal deprivation significantly decreased the distance moved. Moreover, the percentage of the rat exhibiting the stereotyped behavior in the open field test was high in the maternally deprived males. Further, the total duration of interaction in two types of social interaction tests were significantly lower in the males experiencing maternal deprivation than that in the normal males. These abnormalities were not observed in females. In addition, factor analysis did not extract the common factor underlying the distance moved in the open field and the total duration of interaction in the social interaction tests, suggesting that the emotional status in the open field (i.e., anxiety for a novel place) did not influence the total duration of interaction in the social interaction tests. Further, this analysis extracted the common factor underlying two types of social interaction tests. Taken together, these results suggest that the maternal deprivation on postnatal days 9 and 11 enhances stereotypy, and specifically reduces sociability only in males. The enhancement of stereotyped behavior and the impairment of social interaction are the prominent features of autism in human. Based on these findings, we propose the potential animal model to reveal the cause of sex difference in the prevalence of autism in human.

REFERENCES


乳幼児期後期から幼若期初期の母性剥奪は雄性ラットにのみ自閉症に関連する複数の異常行動を惹起する

○高瀬堅吉
（姬路獨協大学薬学部生理学教室）
キーワード：母性剥奪、性差、自閉症

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