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Research Report

Sleep deprivation during late pregnancy produces hyperactivity and increased risk-taking behavior in offspring

*Arathi Radhakrishnan, B.S. Aswathy, Velayudhan Mohan Kumar, Kamalesh K. Gulia**

Sleep Disorders Research Laboratory, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum 695012, Kerala, India

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ABSTRACT

Sleep deprivation in women resulting from their modern lifestyle, especially during pregnancy, is a serious concern as it can affect the health of the newborn. Anxiety disorders and cognitive deficits in the offspring are also on the rise. However, experimental studies on the effects of sleep loss during pregnancy, on emotional development and cognitive function of the newborn, are scanty in literature. In the current study, female rats were sleep-deprived for 5 h by gentle handling, during the 6 days of the third trimester (days 14–19 of pregnancy). The effects of this sleep deprivation on anxiety-related behaviors of pups during their peri-adolescence age were studied using elevated plus maze (EPM). In addition to body weights of dams and offspring, the maternal behavior was also monitored. The weanlings of sleep-deprived dams showed heightened risk-taking behavior as they made increased explorations into the open arms of EPM. They also showed higher mobility in comparison to the control group. Though the body weights of sleep-deprived dams were comparable to those of the control group, their newborns had lower birth weight. Nevertheless, these pups gained weight and reached the control group values during the initial post-natal week. But after weaning, their rate of growth was lower than that of the control group. This is the first report providing evidences for the role of sleep during late pregnancy in shaping the neuropsychological development in offspring.

1. Introduction

Sleep restriction, necessitated by modern lifestyle, even during pregnancy, is an emerging health concern as there are reports of increased anxiety disorders and cognitive deficits in the offspring (Okun et al., 2009; Chang et al., 2010; Pires et al., 2010; Micheli et al., 2011). According to the World Health Organization, 10–20% of children and adolescents worldwide

*Corresponding author. Fax: +91 4712341814.
E-mail addresses: arathirad@gmail.com (A. Radhakrishnan), aswathybs25@gmail.com (B.S. Aswathy), wfsrs2005@rediffmail.com (V.M. Kumar), kkguliak@hotmail.com (K.K. Gulia).

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suffer from developmental disorders (http://www.who.int/mental_health/maternal-children). The most common among them are anxiety disorders, attention deficit hyperactivity disorder, autism, and attachment disorders that severely influence development, educational attainments and productive lives. However, the literature, which ascribes the cognitive deficits of the offspring to sleep deprivation during pregnancy, is limited. Sleep loss during pregnancy is a potential factor for pre-term birth (Micheli et al., 2011; Strange et al., 2009; Samaraweera and Abeysena, 2010; Abeysena et al., 2010; Okun et al., 2012). Impaired neural development during foetal life increases the chances for deranged emotional development of the newborn (Gale et al., 2004; O'Donnell et al., 2009). It was recently reported that the pups of the REM sleep-deprived dams have reduced vocalizations (Gulia et al., 2014). This clearly indicates the effects of sleep loss during pregnancy on emotional development and cognitive function of the newborn.

Human studies on sleep loss during pregnancy and the child's development would be difficult due to ethical and other issues. Therefore, the present study was designed to investigate in the rat model the effects of sleep deprivation of dams on the ontogenetic development of anxiety-related behavior in the offspring. The effects of maternal total sleep deprivation for 5 h (TSDX5h) for 6 days during the third trimester on the anxiety-related behavior in offspring during peri-adolescent period were evaluated using the elevated plus maze (EPM). In addition to the growth profile of pups, maternal body weight and behavior were also monitored.

2. Results

2.1. Maternal parameters

Gentle handling of the pregnant rats in the experimental group, at the onset of their sleep resulted in a reduction of sleep by 97.41±0.01% as compared to the control group of rats. The gestational duration was longer ($p<0.002$) in dams of the sleep-deprived group (22.50±0.19 days) in comparison to the control pups (21.43±0.20 days). No significant changes were observed in the number of pups born to them or in the male–female ratio (Table 1). No significant differences were observed in the body weights of mother rats of the control group and sleep-deprived group, during the entire study (Fig. 1).

The maternal behavioral scores (calculated for 5 h from 11 am to 3 pm) during post-parturition days in the sleep-deprived group were not significantly different from those of the control group (Table 2). Retrieval tests showed that the time taken to retrieve the pups by the sleep-deprived dams was not significantly different from that of the control group dams (Table 3).

Table 1 – Litter size at birth and male to female ratio in control and sleep deprived group.

S no	Litter size at birth	No. of males	No. of females
Control	9.85±0.26	5.00±0.53	4.85±0.46
TSDX5h	9.83±0.31	5.16±0.33	4.17±0.31

Values are presented as M±SEM. TSDX5h refers to the sleep deprivation group.

2.2. Growth profile of pups

The body weights of the newborns of sleep-deprived dams (6.33±0.1 g) were significantly lower ($p<0.05$; Fig. 2) than those of the control pups (7.10±0.2 g). But these pups of the sleep-deprived dams gained weight and reached the control group values during the initial post-natal week. Their rate of growth was similar to the control group until weaning. However, after weaning these pups had lower weights than the control pups ($p<0.001$; Fig. 2).

2.3. Elevated plus maze test study in pups

The pups of the sleep-deprived rats showed increased mobility. The percentage of the time spent in mobility was also higher ($p<0.001$) at all ages, in comparison to the pups of the control group (Fig. 3). In the control pups, the total time spent in mobility decreased from the pre-adolescent to the adolescent and post-adolescence stages, but it decreased ($p<0.05$) only during post-adolescence in the pups of sleep-deprived mothers.

The control pups travelled 9.14±0.2 m in 5 min in the EPM, whereas the pups of sleep-deprived dams covered longer distance, i.e. 14.9±0.4 m, during pre-adolescent stage ($p<0.001$; Fig. 4). Similar trends of higher locomotor activity were observed in these pups during adolescent ($p<0.001$) as well as post-adolescent stages ($p<0.001$; Fig. 4). In comparison to the pups of the control group, they traversed more in the open arm than in the closed arm and central zone ($p<0.01$; Fig. 4). The distance travelled by the control group pups in the different arms and the central zone decreased during adolescent and post-adolescent periods in comparison to the pre-adolescent values. However, these changes during adolescent and post-adolescent periods were mostly not significant in the sleep-deprived group (Fig. 4). Pups of sleep-deprived dams made higher number of entries in the open arm and lower number of entries in the central zone, whereas there was no increase in the entries in the closed arm, during all the stages of their growth ($p<0.001$; Fig. 5). They had also spent significantly more time in the open arm ($p<0.001$; Fig. 6).

Though there were no significant differences in head dipping counts between the two groups, the experimental group pups exhibited increased grooming and rearing during some of the peri-adolescence stages (Fig. 7).

3. Discussion

The body weights of pregnant rats that underwent sleep deprivation for 5 h during the third trimester were not different from those of the control group rats. The gestational duration was comparatively longer in the sleep-deprived rats. The pups born to them showed hyperactivity. They had spent more time in the open arm when compared to the control group pups. Though the pups born to sleep-deprived mothers