Effect of maternal occlusal stress on hippocampal neurogenesis in SAM mouse-pups

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Background

Learning-induced neurogenesis is blocked in pups obtained from dams whose bite was raised during pregnancy (bite-raised condition). Neurogenesis is regulated at several different levels, e.g., by cell proliferation, differentiation, and survival.

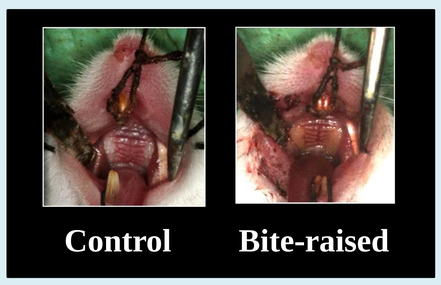
Aim

To determine the aspect of neurogenesis regulation influenced in the hippocampus of pups obtained from dams in the bite-raised condition during pregnancy, we examined the survival/differentiation and proliferation of newborn cells in the pup hippocampus.

Material and method

〈 Prenatal stress 〉

Pregnant senescence-accelerated prone (SAM)mice were anesthetized with soduim pentobarbital(35 mg/kg) .The vertical dimension of the bite was raised approximately 0.1mm by applying composite resin on the upper molars during the lost week of pregnancy.
Forty male SAM(4-mo-old) offspring of the bite-raised pregnant SAM mice(BR-group)were used.

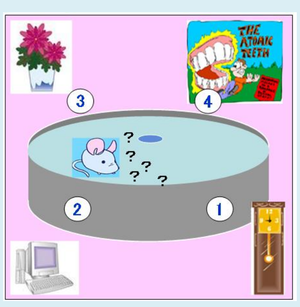


〈 Plasma corticosterone concentration 〉

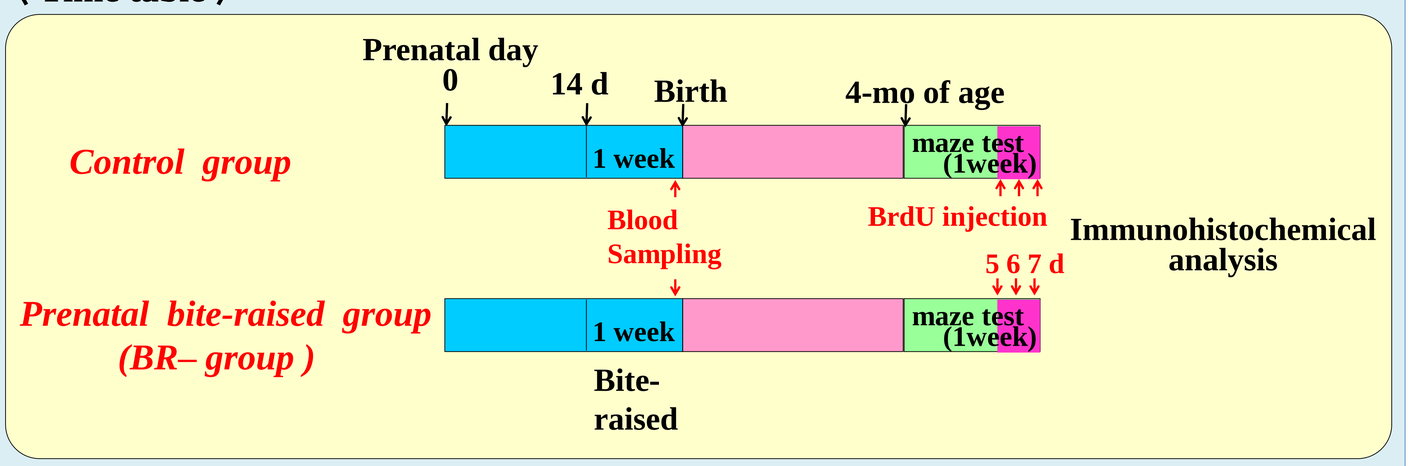
As a measure of stress of pregnant mice, plasma corticosterone (CO) concentration was determined by radioimmunoassay in the BR and control group (n=5/group).

〈 Behavioral analysis 〉

The Morris water maze test is a sensitive behavioral assay for hippocampal abnormalities. Four months after birth, all mice underwent Morris water maze test(4 trials/day for 7 days).



〈 Time table 〉

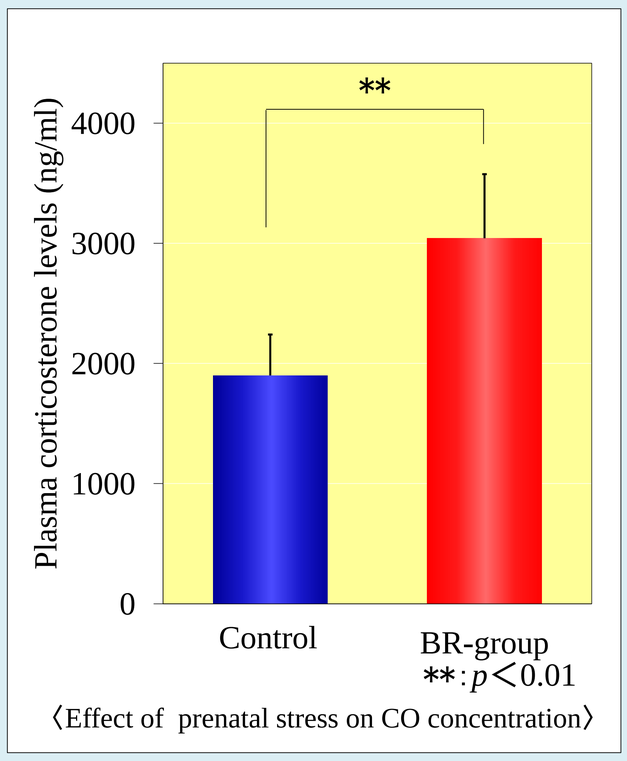


〈 Histologic analysis 〉

To determine the effect of prenatal stress on cell proliferation, bromodeoxyuridine (BrdU,50mg/kg) was injected intraperitoneally once a day , during days 5 though 7 of the water maze test. The day after the water maze test ended, the mice were anesthetized with pentobarbital sodium and transcardially perfused with 30 ml of saline at 37℃, followed by 100 ml of 4% paraformaldehyde in 0.1 M phosphate buffer. The brains were removed and placed in 2% paraformaldehyde fixative overnight at 4℃. Tissue sections were prepared on a microslicer. After denaturing the DNA, floating sections were processed through a standard immunohistochemical procedure using the ABC method.

Result

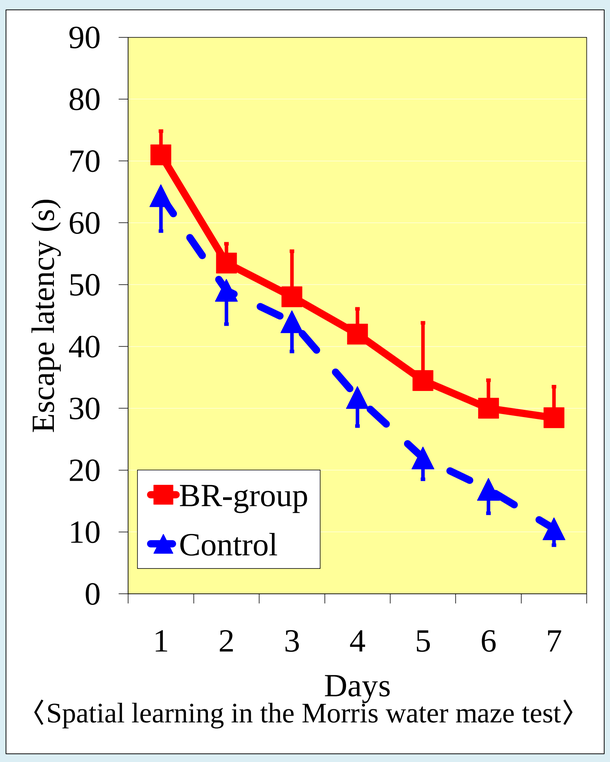
〈Plasma corticosterone concencetration 〉



〈Effect of prenatal stress on CO concentration〉

CO concentration was significantly higher in the BR-group compared to the control group ($p<0.01$).

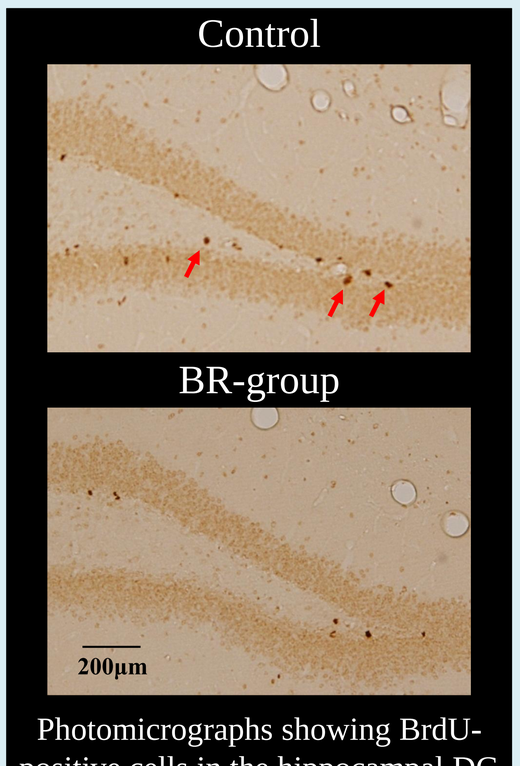
〈 Behavioral analysis 〉



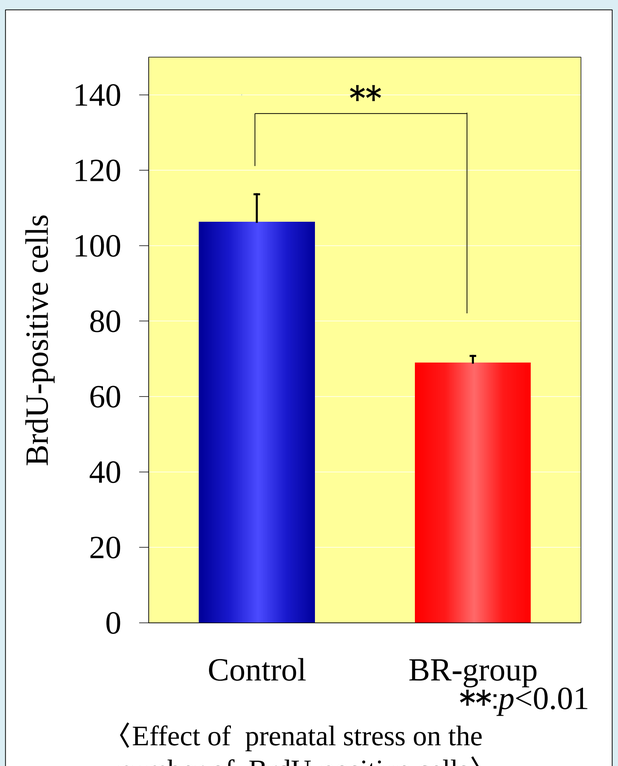
〈Spatial learning in the Morris water maze test〉

The results are expressed as the mean score of four trials per day. The BR-group required a significantly longer time to reach the platform than control group ($p<0.01$).

〈 Histologic analysis 〉



Photomicrographs showing BrdU-positive cells in the hippocampal DG



〈Effect of prenatal stress on the number of BrdU-positive cells〉

The number of BrdU-immunoreactive cells in the dentate gyrus (DG) subfields was greatly reduced in BR-group compared with control group ($p<0.01$).

Conclusion

1. The CO level in the bite-raised pregnant mice was increased by prenatal stress.
2. Prenatal stress, induced by a raised bite, impairs spatial learning ability in adult offspring mice.
3. Prenatal stress enhances the decrease in the number of proliferating cells in the hippocampal DG .

These findings suggest that learning deficits produced in association with occlusal disharmony during pregnancy result from altered neurogenesis in the hippocampal DG.

Reference

[1)]Kubo K, et al: Occlusal disharmony induces spatial memory impairment and hippocampal neuron degeneration via stress in SAMP8 mice: Neurosci Lett 414: 188-191, 2007.