Exposure to Enriched Environment May Act Epigenetically to Correct Defects due to Chronic Restraint Stress in Rats

Dear Editor,

I read with interest the article by Kumar *et al*.[1] in which they presented the results of their study of the effect of exposure to an enriched environment (EE) on defects in passive avoidance learning (PAL) and hippocampal cellular morphology in rats exposed to chronic restraint stress (CRS). The authors assigned male Wistar rats into three groups. One group comprised normal controls and remained undisturbed in their home cages (NC group). One group underwent CRS (6 h/day) for 21 days followed by housing in standard conditions (S group). Another group underwent similar CRS for 21 days followed by housing in an EE (S + EE group). After 21 days, the authors found that the PAL score in the S group was significantly lower than that of the NC group. However, compared to the S group, in the S + EE group, the PAL score was significantly higher. There also were significant neuroprotective effects of cornu ammonis-2 (CA2) and CA3 hippocampal neurons in the S + EE group compared to the CRS group. The authors inferred that exposure to an EE improved PAL and ameliorated hippocampal injury in the S + EE group. Hence, they suggested that an EE could be useful in patients with brain diseases due to its stress-reducing and neuroprotective effects. The authors suggested that the mechanism of action of an EE could be multifactorial, including N-methyl-D-aspartate receptor modulation, changes in hippocampal brain-derived neurotrophic factor (BDNF) expression, and changes in activities of nerve growth factors.

I wish to discuss the possible role of epigenetics in the results of Kumar *et al*.[1] Epigenetics, heritable changes in gene expression not involving changes in DNA sequence, involves molecular mechanisms such as DNA methylation, modifications of histones (DNA packaging proteins), and noncoding RNA-mediated regulation of gene expression. There is increasing evidence that epigenetic mechanisms of gene expression are abnormal in patients with brain disorders and that such disorders can be affected by environmental factors like psychosocial factors, diet, and chemicals due to changes in epigenetic mechanisms of gene expression.[2] CRS in rodents is thought to be an epigenetic animal model for mood and anxiety disorders.[2] Fischer *et al*.,[3] using a mouse model that allows temporally and spatially restricted induction of neuronal loss, showed that EE re-instated learning behavior and improved long-term memory after brain injury and neuronal loss had occurred. They found that EE correlated with increased histone acetylation. Babenko *et al*.[4] found that CRS in rats induced genetic and epigenetic changes in the cerebellum by altering the expression of 39 genes and 9 miRNAs (a type of noncoding RNA). Seo *et al*.[5] showed that CRS to rats resulted in epigenetic changes in the gene encoding BDNF, like a decrease in histone acetylation. They also found that administration of the antipsychotic olanzapine prevented the decrease in histone acetylation due to CRS in the rats. In the light of these data, I suggest that in the study of Kumar *et al*.,[1] exposure to an EE could have acted epigenetically to restore PAL and ameliorate hippocampal injury.

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Conflicts of interest

There are no conflicts of interest.

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