

Insights: Publications

Social defeat stress induces genome-wide 5mC and 5hmC alterations in the mouse brain

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Stress is adverse experience that require constant adaptation to reduce the emotional and physiological burden, or “allostatic load”, of an individual. Despite their everyday occurrence, a subpopulation of individuals is more susceptible to stressors, while others remain resilient with unknown molecular signatures. In this study, we investigated the contribution of the DNA modifications, 5-methylcytosine (5mC) and 5-hydroxymethylcytosine (5hmC), underlying the individual differences in stress susceptibility and resilience. Genome-wide 5mC and 5hmC profiles from 3- and 6-month adult male mice that underwent various durations of social defeat were generated. In 3-month animals, 5mC and 5hmC work in parallel and do not distinguish between stress-susceptible and resilient phenotypes, while in 6-month animals, 5mC and 5hmC show distinct enrichment patterns. Acute stress responses may epigenetically “prime” the animals to either increase or decrease their predisposition to depression susceptibility. In support of this, re-exposure studies reveal that the enduring effects of social defeat affect differential biological processes between susceptible and resilient animals. Finally, the stress-induced 5mC and 5hmC fluctuations across the acute-chronic-longitudinal time course demonstrate that the negative outcomes of chronic stress do not discriminate between susceptible and resilient animals. However, resilience is more associated with neuroprotective processes while susceptibility is linked to neurodegenerative processes. Furthermore, 5mC appears to be responsible for acute stress response, whereas 5hmC may function as a persistent and stable modification in response to stress. Our study broadens the scope of previous research offering a comprehensive analysis of the role of DNA modifications in stress-induced depression.

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