Higher- order chromatin architecture influences neuronal function.

The cell nucleus is a highly organized three-dimensional structure in which chromatin is partitioned into distinct chromosome territories with nonrandom distribution. The spatial organization of chromosome territories is flexible and permits many local and long-range contacts of genes and other sequence elements, which influence their function. To investigate neuronal chromatin organization and dynamics in vivo, we generated bitransgenic mice expressing GFP-tagged histone H2B in principal neurons of the forebrain. Surprisingly, the stable expression of this chimeric protein in mature neurons resulted in severe changes in nuclear architecture like chromocenter declustering and loss of peripheral heterochromatin. Such a phenomenon has never been observed in cultured cells. The change of aforementioned structures does not affect neuronal viability, yet it is associated with specific transcriptional and behavioral deficits related to serotonergic dysfunction. Our results demonstrate that higher- order chromatin organization of the neuronal nucleus supports an additional level of epigenetic regulation of gene expression and thereby neuronal function.