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Title:	Evolutionary Loss of Genomic Proximity to Conserved Noncoding Elements Impacted the Gene Expression Dynamics During Mammalian Brain Development
Authors:	Bagadia, Meenakshi (/jspui/browse?type=author&value=Bagadia%2C+Meenakshi) Chandradoss, K.R. (/jspui/browse?type=author&value=Chandradoss%2C+K.R.) Jain, Y. (/jspui/browse?type=author&value=Jain%2C+Y.) Singh, Harpreet (/jspui/browse?type=author&value=Singh%2C+Harpreet) Lal, Mohan (/jspui/browse?type=author&value=Lal%2C+Mohan) Sandhu, K.S. (/jspui/browse?type=author&value=Sandhu%2C+K.S.)
Keywords:	Conserved noncoding elements Loss of proximity CNE
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Abstract:	Conserved noncoding elements (CNEs) have a significant regulatory influence on their neighboring genes. Loss of proximity to CNEs through genomic rearrangements can, therefore, impact the transcriptional states of the cognate genes. Yet, the evolutionary implications of such chromosomal alterations have not been studied. Through genome-wide analysis of CNEs and the cognate genes of representative species from five different mammalian orders, we observed a significant loss of genes' linear proximity to CNEs in the rat lineage. The CNEs and the genes losing proximity had a significant association with fetal, but not postnatal, brain development as assessed through ontology terms, developmental gene expression, chromatin marks, and genetic mutations. The loss of proximity to CNEs correlated with the independent evolutionary loss of fetus-specific upregulation of nearby genes in the rat brain. DNA breakpoints implicated in brain abnormalities of germline origin had significant representation between a CNE and the gene that exhibited loss of proximity, signifying the underlying developmental tolerance of genomic rearrangements that allowed the evolutionary splits of CNEs and the cognate genes in the rodent lineage. Our observations highlighted a nontrivial impact of chromosomal rearrangements in shaping the evolutionary dynamics of mammalian brain development and might explain the loss of brain traits, like cerebral folding of the cortex, in the rodent lineage.
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