Computational Analysis of Neuronal Chromatin Structure and Nuclear PARP-1 and PAR Expression Provides Novel Marker for Detecting Learning Associated Changes in Mice

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Chromatin remodeling, modification of nuclear chromatin allowing for the regulation of gene expression, is believed to be an integral part of memory encoding. The enzyme PARP-1 and its product PAR catalyze PolyADP-ribosylation, a specific chromatin modification allowing for histone tail relaxation and regulation of gene expression. I obtained immunohistochemically stained confocal images of CA1 region hippocampal neurons (known to encode spatial information) of mice from a control group and mice trained in a spatial task. I created a novel NetLogo-based computer program to quantify and analyze the density of chromatin structure (relaxation indicating chromatin remodeling), and the expression of PARP-1 and PAR within the nuclei of the neurons. Threshold ranges were placed to compare PAR and PARP-1 expression in different degrees of condensed chromatin. The program implemented intensity difference and distribution methods in order to isolate learning-associated activity in the trained neurons. The program detected significant increases in PARP-1 activity in specific regions of decondensed chromatin, indicating an active recruitment of PARP-1 to these areas in trained neurons and suggesting that learning-associated epigenetic changes occur during memory encoding. Learning-associated PARP-1 activity was then traced back to the images and the program identified 20-25% of neurons within trained networks believed to be involved in memory encoding. Using PARP-1 as a novel marker to isolate memory encoding neurons with this program, it is possible to uncover the molecular pathways by which stronger synaptic connections are formed. Inducing these changes may reverse the loss of cognitive function in certain neurological disorders.

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