Neuroepigenetics and alcoholism

Epigenetic mechanisms, such as histone acetylation and DNA methylation induced changes in gene expression play an important role in brain maturation and synaptic plasticity. The effects of adolescent intermittent ethanol (AIE) treatment on epigenetically regulated synaptic plasticity associated events in the amygdala and on anxiety-like and alcohol-drinking behaviors at adulthood were investigated. Adolescent (Sprague-Dawley) rats were exposed with intermittent n-saline or ethanol [2 g/kg, intraperitoneal (IP); 2-days on/2-days off, 4 cycles (8 injections) from postnatal days 28-41]. The behavioral and epigenetic measures were performed at adulthood (postnatal day 92). It was found that histone deacetylase (HDAC) activity was increased in the amygdala of AIE adult rats as compared with adolescent intermittent saline (AIS) adult rats. This was due to increase in HDAC2, but not HDAC4, protein levels in the central (CeA) and medial nucleus of the amygdala (MeA) of AIE adult rats compared with AIS adult rats. The global histone H3-K9 acetylation was correspondingly decreased in the CeA and MeA of AIE adult rats compared with AIS adult rats. It was also found that mRNA levels of activity-regulated cytoskeleton-associated (Arc) protein and brain-derived neurotrophic factor (BDNF) exons (I & IV) and protein levels of Arc and BDNF were significantly decreased in the CeA and MeA of AIE adult rats compared with AIS adult rats. Interestingly, decreased expression of BDNF and Arc was associated with lower histone H3 acetylation levels in the promoters of these genes in the amygdala. AIE produced a reduction in dendritic spine density in the CeA and MeA of rats at adulthood. AIE also induced anxiety-like and alcohol-drinking behaviors at adulthood which were attenuated by treatment with the HDAC inhibitor, trichostatin A (TSA). Using, different model alcohol preferring and non-preferring genetic rats it was demonstrated that innately higher expression of HDAC2 in the CeA produced deficits in synaptic plasticity associated events and regulated anxiety-like and alcohol drinking behaviors. These results suggest that innately or ethanol exposure-induced abnormal chromatin architecture due to HDAC2-mediated histone modifications in the amygdala may play a crucial role in anxiety and alcoholism (Supported by the grants from NIH-NIAAA and VA Merit grant from department of Veterans Affairs).

Biography

Subhash C Pandey received his PhD in 1987 from the Pharmacology division of the Central Drug Research Institute in Lucknow, India and then received his postdoctoral training in neuropsychopharmacology in the Department of Psychiatry, University of Illinois at Chicago. He is currently a Professor of Psychiatry, Anatomy and Cell Biology and the Director of Neuroscience Alcoholism Research at the University of Illinois at Chicago. He also holds a position as a VA Career Scientist at the Jesse Brown VA Medical Center, Chicago. He is well known for his scientific contributions towards the molecular and cellular neuroscience of alcoholism. He received Bowles Lectureship from the Alcohol Research Center located at University of North Carolina, Chapel Hill in 2010 and 6th SN Pradhan Lectureship from the department of pharmacology, Howard University, Washington DC in 2011 and distinguished scientist award in 2014 from the association of scientists of Indian origin in America for his outstanding contributions in the field of alcoholism research. He is serving as a Field Editor of Alcoholism: Clinical and Experimental Research Journal since 2011.