

Addiction Therapy-2014

Chicago, USA

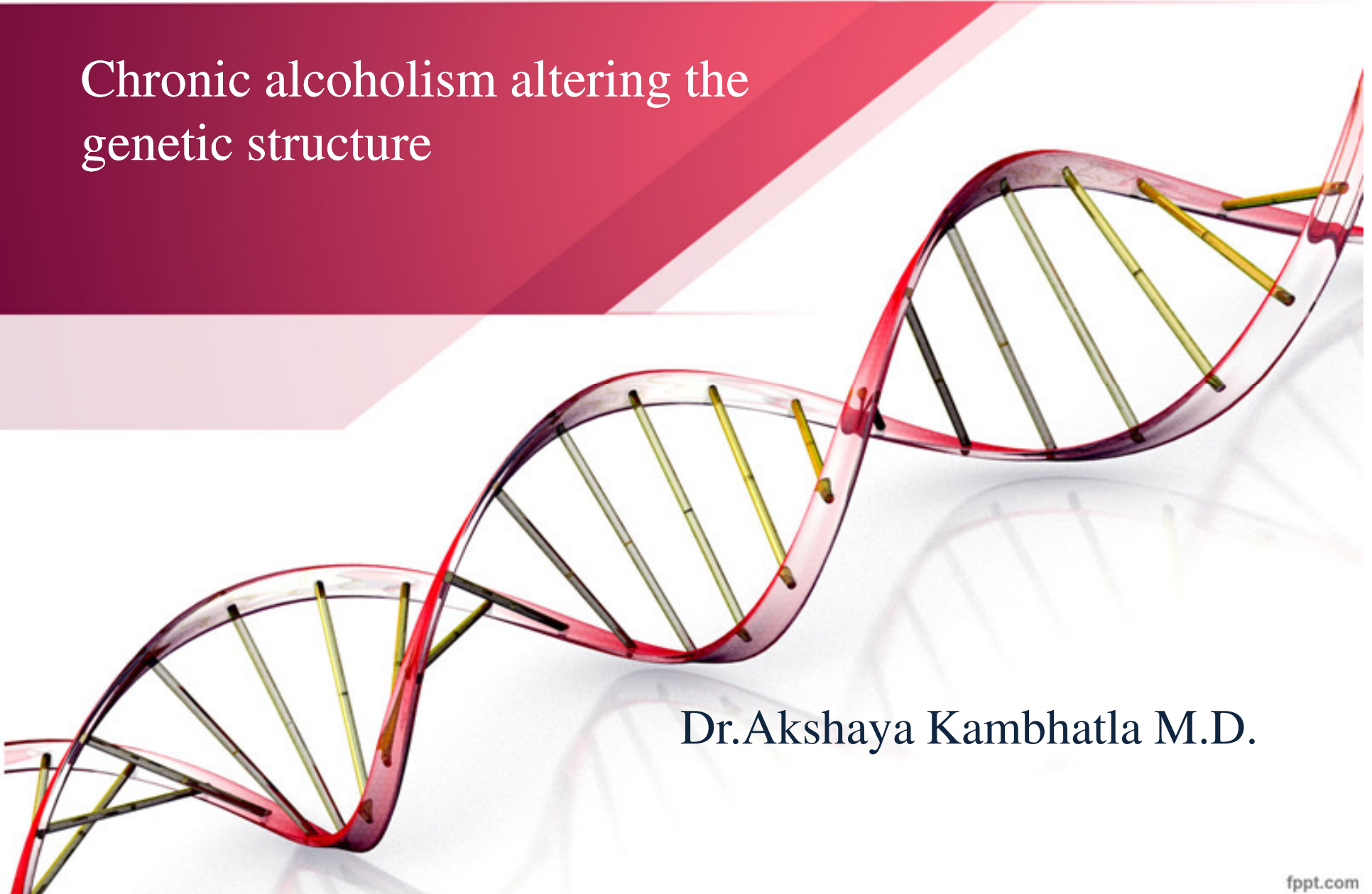
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Chronic alcoholism altering the genetic structure

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Some Facts about the influence on genes related to hippocampus



- 639 genes studied in the post mortem hippocampal tissue in 20 alcoholics and 19 controls.
- False Discovery Rate less than or equal to 0.20
- Glucocorticoid receptor and related gene FK506 Binding protein 5 (FKBP5), UDP Glycosyltransferase 8 (UGT8), urea transporter (SLC14A1), zinc transporter (SLC39A10), Interleukin 1 receptor type 1 (IL1R1), thioredoxin interacting protein (TXNIP), and many metallothioneins.
- Inappropriate activation of inflammation through the mediation of NF- KB pathway
- Decline in neurogenesis and myelination pathways.

Metallothioneins



- Four isoforms of Zinc binding proteins made of cysteine .
- Zinc is predominantly found in retina, pineal gland and hippocampus.
- Altered levels of Zinc levels in the neurons in several CNS disorders including Alcoholism.
- Help in sequestering Zinc in the synaptic vesicles and thereby maintaining the redox potentials at the nerve endings in the hippocampus, pineal gland and retina.

Pro-Opio Melano Cortin Neurons



- In chronic alcoholism, there is reduced function in POMC neurons due to gene methylation of several CpG dinucleotides .
- Associated with altered histone modifying proteins and DNA methyltransferases in the POMC neurons.
- Fetal alcohol exposed male and female rat offspring showed hyper methylation of POMC gene but was transmitted only through male offspring.

C- fos gene activity



- Increased expression of c-fos gene in the cerebral cortex in offspring of chronically alcohol exposed rats when treated with alcohol .
- Altered content of biogenic amines which in turn lead to behavioral disturbances.
- Genetically derived alcoholic motivation.

Effects on Pancreas



- Activation of Transcription factor 3, Heat Shock Protein 70, Heat Shock Protein 27 and Methotrypsiogen.
- Decreased Pancreatitis Associated Protein, Folate Carrier and Metallothianein.
- Animals wre fed Alcohol containing Leiber De Carle and control diet for 8 weeks and Pancreas RNA was analyzed later .
- CRITERIA – changes being nore than 3-fold and $P < 0.05$
- Likely reason for Pancreas injury after long term alcohol ingestion.

Effects on Lung Alveoli



- Altered dynamic balance between GM-CSF and TGF Beta 1 factors both being increased.
- Decreased expression of KLF4 and PIF4 genes.
- Decreased Zinc in the alveoli
- Cellular dysfunction in the ‘Alcohol lung’ phenotype.
- Studies were done on rat alveolar macrophage lineage under ethanol exposure for 4 weeks.

References – Pubmed

2008-2014



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