Addiction is defined as a chronic, relapsing brain disease that is characterized by compulsive drug seeking and use, despite harmful consequences. The addictive phenotype can persist for the length of an individual’s life, suggesting that drugs of abuse may induce long-lasting changes in the brain.

**NEUROBIOLOGY OF ADDICTION**

The activation of the mesolimbic dopaminergic system produces a reward signal, related with learning mechanisms to beneficial actions. Drugs of abuse can activate this circuit far more intensively than natural rewards, being able to hijack these learning mechanisms. Besides, they can induce molecular adaptations, that translate into neuroplastic changes in the mesolimbic system.

- **Acute cocaine**
  - Histone acetylation
    - Fos
    - Cdk5
    - BDNF
  - Early behavioral response to the drug
  - Overexpression of these factors is related with increases in dendritic spine density in nucleus accumbens (NAC), altering synaptic plasticity.

- **Chronic cocaine**
  - Histone acetylation
  - Histone methylation
  - DNA methylation
  - miRNAs

**EPIGENETIC REGULATION OF COCAINE ADDICTION**

Cocaine-induced downregulation of G9a increases dendritic spine density in NAc as well as expression of genes implicated in synaptic activity.

**DNA methylation**

- Increases dendritic spine density
- Binding
- MeCP2
- miR-134
- BDNF
- CREB
- Specific Kinases
- cAMP
- Adenylyl cyclase
- Raf1
- Pathway that protects against addiction
- miR-212
- SYNAPTIC PLASTICITY
- Pathway that contributes to addiction
- Lim Kinase 1
- MeCP2
- BDNF
- miR-134
- SPREAD1
- SYNAPTIC PLASTICITY

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