Autism Spectrum Disorders & Epigenetic

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What is Autism Spectrum Disorder?

- Autism spectrum disorders (ASDs), refer to a group of heterogeneous neurodevelopmental disorders with polygenic heritability.

- The word autism derived from Greek word(autos) was first used by Kanner and the words “spectrum disorder” it means a wide range of symptoms that range from mild to severe.

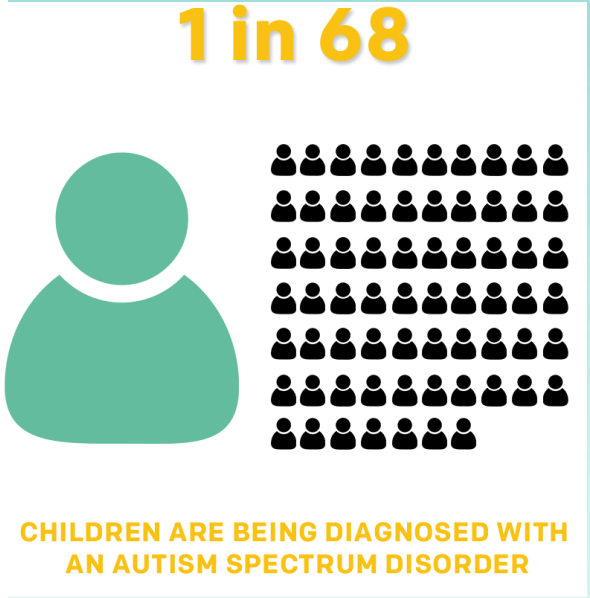
- Characterized by impaired social interaction ,communication and by restricted and repetitive behaviors.

What is Autism Spectrum Disorder?

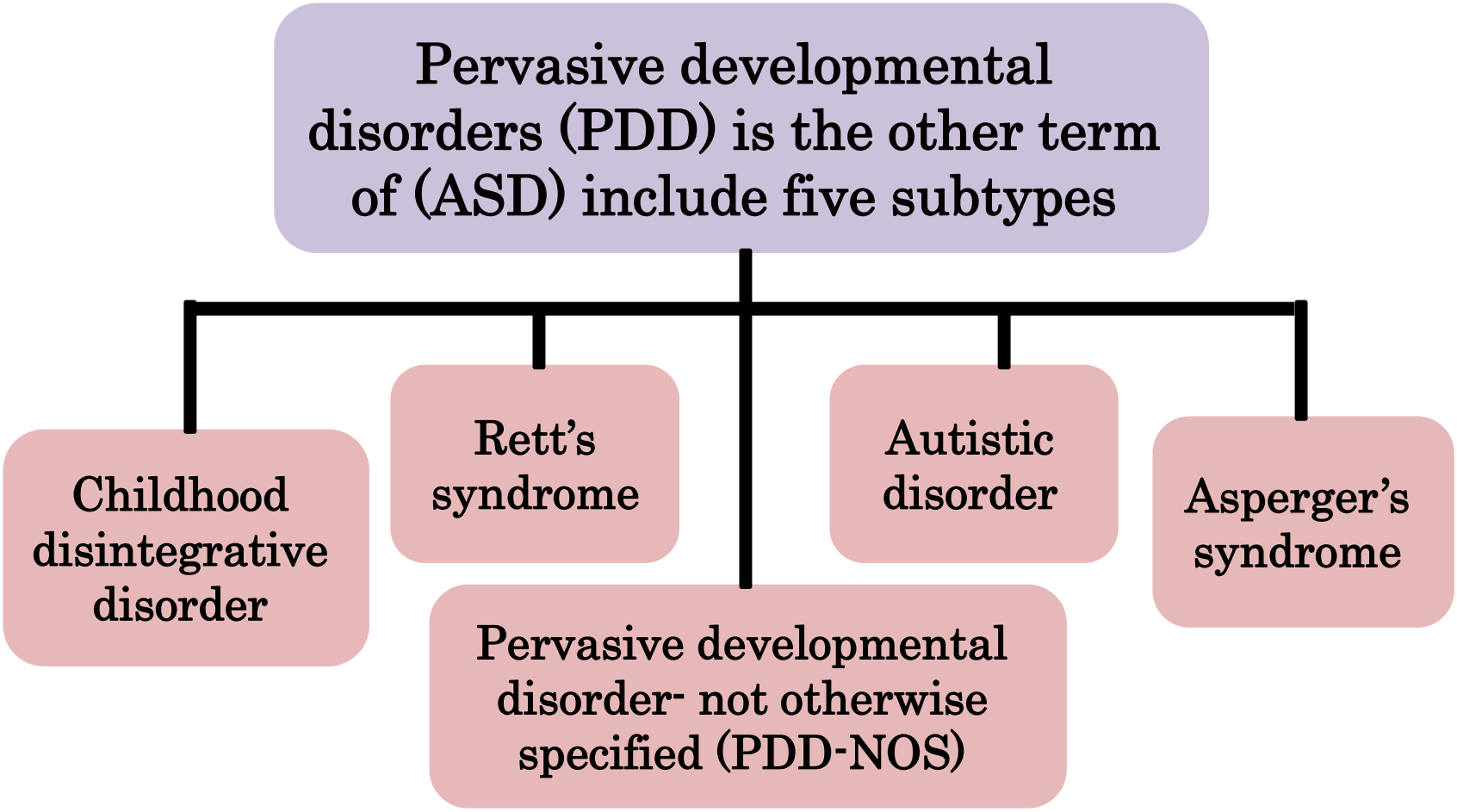
- ASD is rapidly becoming one of the most common developmental disabilities around the world.

- The Centers for Disease Control and Prevention (CDC), estimates the prevalence rate for ASD at 1 in 68.

- ASD is more prevalent in males than females, with a ratio of 4:1.



The Types of ASD



Diagnosis of ASD

- Diagnosing ASD is difficult because there is no medical test.

- Doctors look at the child's behavior and development to make a diagnosis.

- While ASD is considered a developmental disorder, a key category of its diagnostic criteria is that of deficits in social skills.

Diagnosis of ASD

- According to the CDC (2015) there are two steps to diagnosing autism:

1- The first step is the developmental screening done to ensure that children are hitting developmental milestones when they should.

2-The second step to diagnosing autism is a comprehensive diagnostic evaluation.

- Other testing may also be done such as hearing tests or neurological testing.

Causes of ASD

- Researchers have discovered many different areas of the brain that appear irregular in patients with ASD.

- It is likely that multiple genes are interacting with one or more environmental factors to produce autism

- Autism may be most accurately described as a multi-gene disorder with epigenetic influences.

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Causes of ASD

- Research has been indicating premature birth as a significant risk factor for ASD.

- There is evidence that in-utero exposure to valproic acid, thalidomide drugs during may increase the risk of ASD.

Treatment

- The goal of treatment is to teach skills and behaviors that will allow autistics to function within the confess of the disorder.

- For many people with autism, a regimen of vitamins and medication, as well as multiple therapies, are employed to reduce the symptoms of autism with early treatment.

Treatment

- Many autistics have higher functioning and can also learn skills that will help them cope with the disorder.
- The use of technology can aid a child with communication, social interactions, and can allow the child to observe more appropriate behaviors (such as use iPad).

Epigenetic

Epigenetic refers to the study of changes in the regulation of gene activity and expression that are not dependent on gene DNA sequence.

has been defined as the study of heritable changes in gene expression without any change in the underlying DNA sequence.

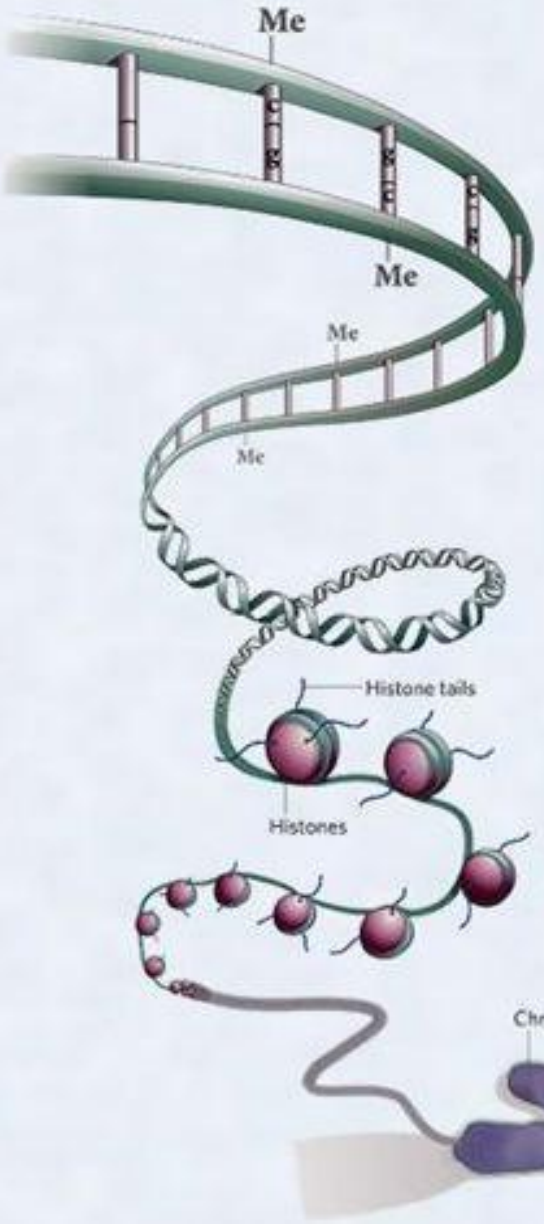
- All cells of a complex multicellular organism contain the same genetic information but during development ,each single cell differentiates into a specific phenotype With out any changes in DNA sequence.

Epigenetic

- Epigenetic mechanisms can be altered by environmental changes , are heritable and stably maintained following environmental exposures.

- Epigenetics refers to processes, notably the methylation of DNA and modification of histones.

The 'epigenetic' code

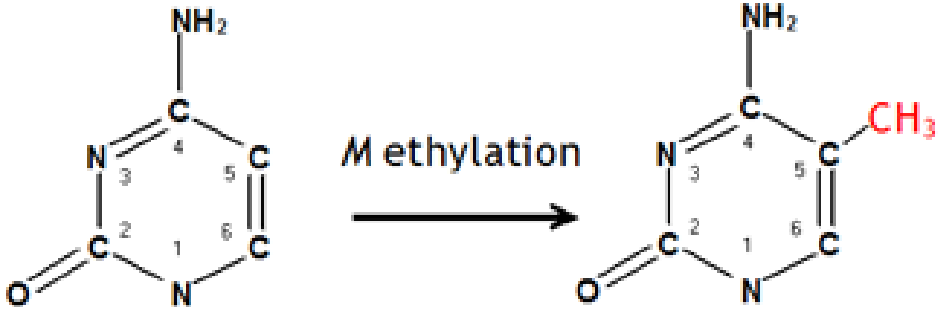


DNA methylation
Methyl marks added to certain DNA bases repress gene activity

Histone modification
A combination of different molecules can attach to the "tails" of proteins called histones, These alter the activity of the DNA wrapped around them

DNA methylation

- The term DNA methylation refers to cytosine that contain a methyl group on carbon 5, with the majority of DNA methylation occurring in CpG sites ("—C—phosphate—G—“).



- They are usually clustered in CpG islands located near approximately 40% of promoters of genes

DNA methylation

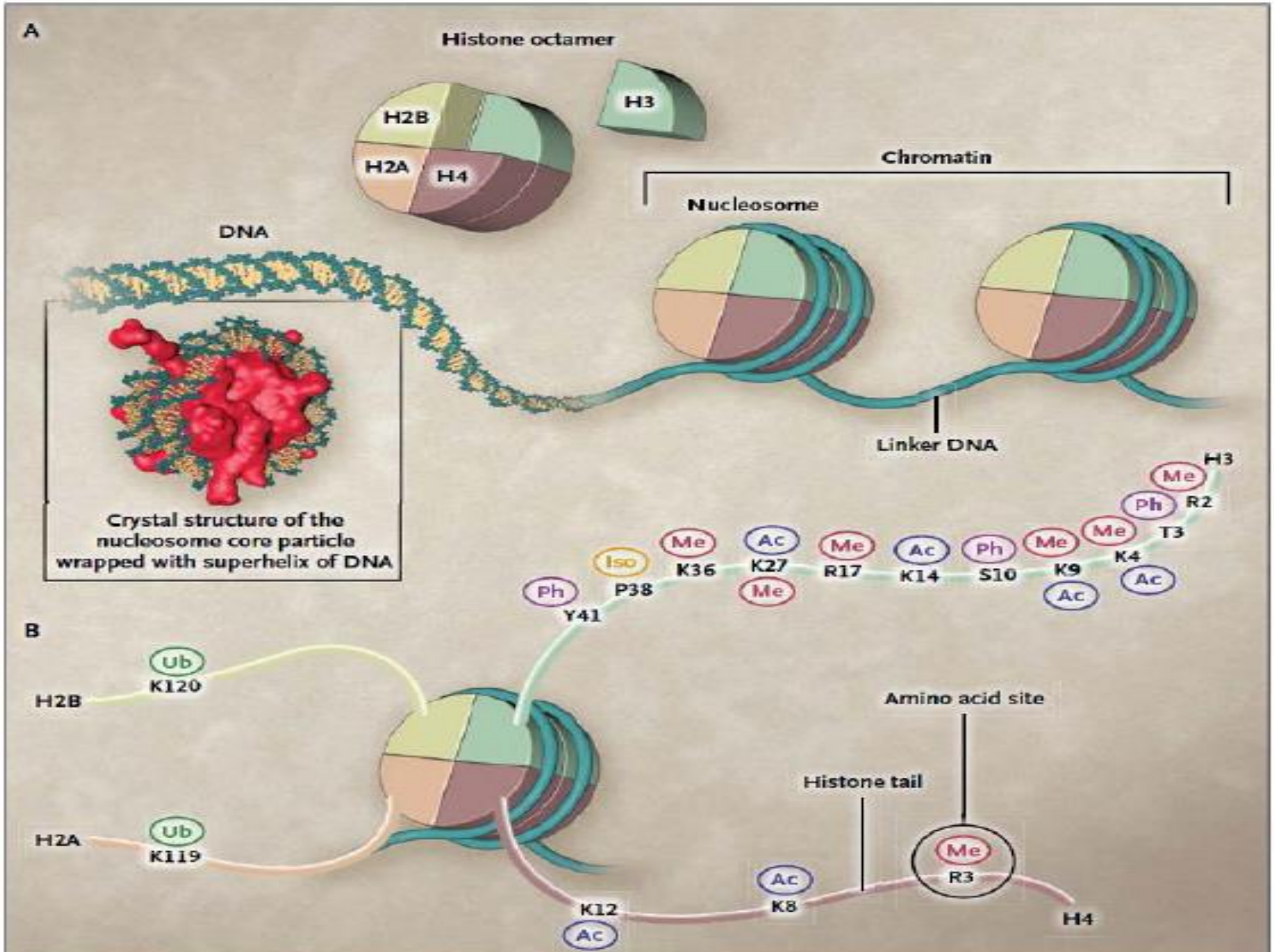
- DNA methyltransferases are enzymes involved in the process of DNA methylation.

Histone modification

- Histones are proteins with a positive charge, the main types of histones involved in compacting DNA are H1, H2A, H2B, H3, and H4.

- DNA is negatively charged and wrapped around histone proteins.

- Histone tails undergo a number of PTMs, including acetylation, methylation and phosphorylation.


A
Histone octamer
H2B
H3
H2A
H4
Chromatin
Nucleosome
DNA
Linker DNA
Crystal structure of the nucleosome core particle wrapped with superhelix of DNA
H3
Me
R2
Ph
T3
Me
K4
Ac
Me
K9
Ac
Ph
S10
Ac
K14
Me
R17
Ac
K27
Me
Me
K36
Iso
P38
Ph
Y41
B
Ub
K120
H2B
Amino acid site
Histone tail
Ub
K119
H2A
Me
R3
Ac
K8
K12
Ac
H4

DNA methylation & ASD

There are abnormalities of transcriptional regulation in Rett syndrome, caused by a mutation of methyl-CpGbinding protein 2 (MeCP2). Indeed, MeCP2 binds to methylated DNA and represses the transcription of target genes.

In several studies the *RELN* gene has been shown to be associated with ASD, and its expression is possibly regulated by epigenetic mechanisms which further highlight the importance of epigenetic factors in pathophysiology of ASD.

Epigenetic & ASD

Alterations in DNA methylation patters have also been observed in the gene (Related orphan receptor-alpha)*RORA* and the oxytocin receptor gene *OXTR* in cases with ASD but not contols.

- The developing human brain is also acutely sensitive to alterations in epigenetic pathways, as observed by the fact that mutations in epigenetic effectors can result in human neurodevelopmental disorders.

DNA methylation & ASD

- Therefore, the protective nature of folate and other B vitamins is likely at the epigenetic interface of DNA methylation where it may counteract the impact of environmental factors that reduce DNA methylation levels.

Thanks for listening