KING'S College LONDON

INSTITUTE OF PSYCHIATRY,
PSYCHOLOGY & NEUROSCIENCE

Module:

Biological Foundations of Mental Health

Week 4:

Biological basis of learning, memory and cognition

Dr Deepak Srivastava

Topic 2:

From the dynamic synapse to synaptopathies

Part 3 of 4

Topic list

This week, we will be looking at the following topics:

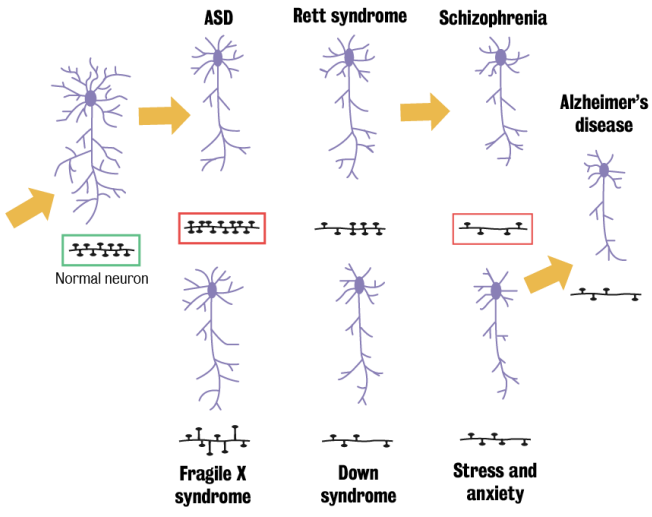
- Topic 1: Learning, memory and synaptic plasticity
- ***Topic 2: From the dynamic synapse to synaptopathies***
- Topic 3: The effects of activity, experience and deprivation on the nervous system

Click **Next** to continue

Part 3

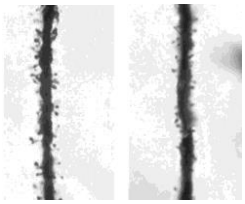
Part 3

Dendrites, dendritic spines and mental health (1)



Neurodevelopmental disorder – ASD

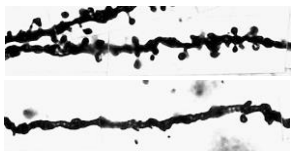
Autism Control



Glantz & Lewis 2000

Neuropsychiatric disorder – Schizophrenia

Pre-frontal cortex (PFC), layer 3

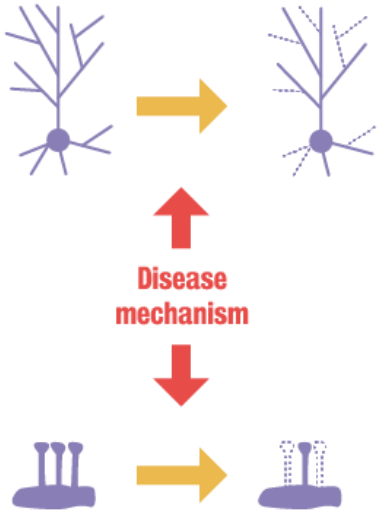


Control

Schizophrenia

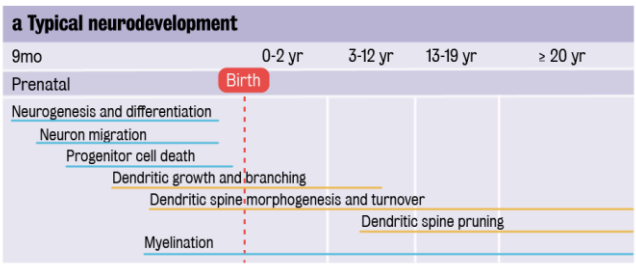
Kulkarni & Firestein (2012); Hutsler & Zhang, 2010

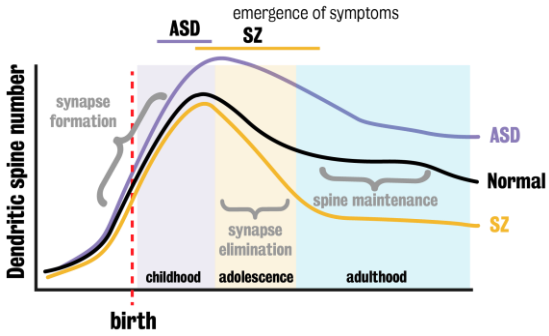
Dendrites, dendritic spines and mental health (2)



Linking dendritic spine pathology with the emergence of disease

The occurrence of specific disease symptoms coincide with critical periods of synapse formation.





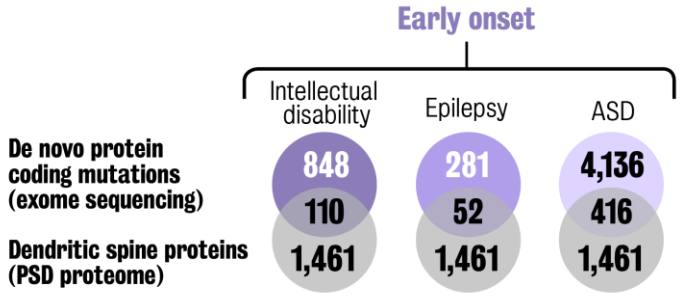
- symptoms of autism spectrum disorder emerge during early childhood, when there is increased spine and synapse formation
- symptoms of schizophrenia emerge during adolescence and early adulthood, during a period of synaptic connection refinement

Penzes et al., 2011; Forrest et al., 2018

Disease genetics

Studies of disease genetics indicate a critical role for synapses.

Large scale studies have identified an increasing number of genetic variants that can cause a change in the sequence of specific proteins associated with disease risk.

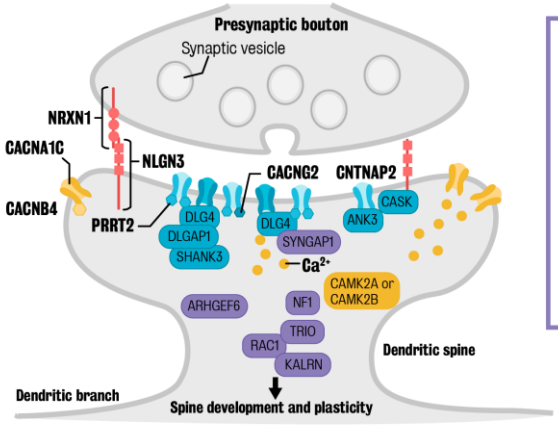


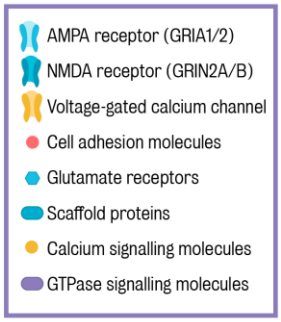
This indicates that many of the de novo protein coding mutations associated with neurodevelopmental and psychiatric disorders **occur in proteins that are found at synapses**.

Forrest et al., 2018

Molecular underpinnings of synaptic deficits in neuropsychiatric disorders

Genes implicated with disease encode for proteins that localise to dendritic spines, and also have critical roles in dendritic spine formation, maintenance and remodelling.





Alterations in the function of these proteins could result in dysfunction of dendritic spines, thus impacting synaptic communication and connectivity.

Forrest et al., 2018

References

[1] Forrest, M. P., Parnell, E. & Penzes, P. (2018). Dendritic structural plasticity and neuropsychiatric disease. *Nature Reviews Neuroscience*, 19(4): 215.

[2] Glantz, L. A., & Lewis, D. A. (2000). Decreased dendritic spine density on prefrontal cortical pyramidal neurons in schizophrenia. Archives of general psychiatry, 57(1), 65-73.

[3] Hutsler, J. J., & Zhang, H. (2010). Increased dendritic spine densities on cortical projection neurons in autism spectrum disorders. Brain research, 1309, 83-94.

[4] Kulkarni, V. A. & Firestein, B. L. (2012). The dentritic tree and brain disorders. *Mol Cell Neurosci*, 50(1): 10-20.

[5] Penzes, P., Cahill, M. E., Jones, K. A., VanLeeuwen, J., & Woolfrey, K. M. (2011). Dendritic spine pathology in neuropsychiatric disorders. *Nature neuroscience*, 14(3): 285.

End of part 3