

Module:

Biological foundations of mental health

Week 1:

Introduction to brain anatomy



Prof Sarah Guthrie

Topic 1
Overview of CNS development

Part 3 of 3

Neurodevelopmental disorders that affect mental health



Examples of human disorders which can be caused by defective developmental processes:

- Autistic spectrum disorder
- Schizophrenia
- Childhood onset epilepsy
- X-linked mental retardation

We now know some of the genes that are mutated in humans with these disorders. Developmental neuroscientists are trying to unravel how these mutations lead to the disorders. It appears that dendrite and synapse development are often affected by these gene mutations.

Case study: Synaptogenesis and autistic spectrum disorder (ASD)



- Studies in humans have shown that mutations in several genes including Neuroligin4 (NLGN4) are linked to autistic spectrum disorder
- NLGN4 is involved in synapse development and markers of inhibitory synapses are reduced in NLGN4 knockout (KO) mice
- NLGN4 knockout (KO) mice show behavioural changes reminiscent of ASD, such as impairments in social interactions and communication, repetitive behaviours and interests

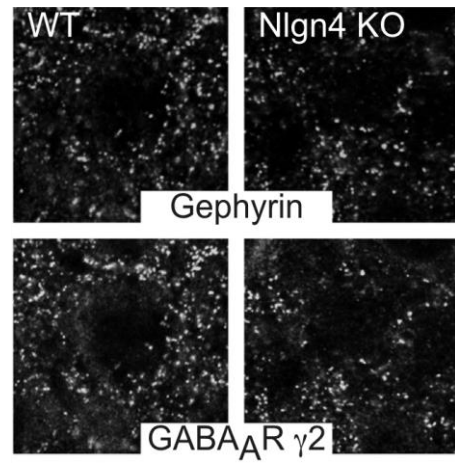


Figure 26: Defects in synaptogenesis play a role in ASD

Case study: Dendritic spine development and schizophrenia/ASD



Schizophrenia

- The number of dendritic spines is reduced in the dorsolateral prefrontal cortex of some schizophrenic subjects

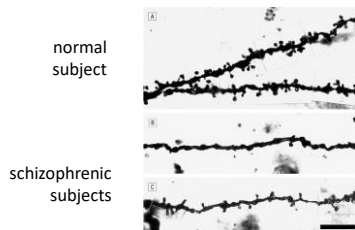


Figure 27: Decreased Dendritic Spine Density on Prefrontal Cortical Pyramidal Neurons in Schizophrenia

- The process of dendrite development and/or pruning is implicated in schizophrenia and ASD

Fragile X mental retardation syndrome

- Mice lacking the Fragile X mental retardation protein have more immature, thin spines

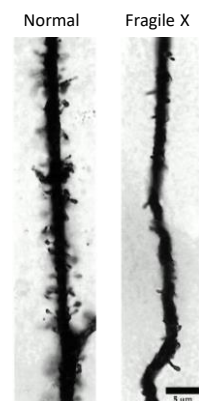


Figure 28: Dendritic Spine Structural Anomalies in Fragile-X Mental Retardation Syndrome

Neurodevelopmental disorders that affect mental health



Research in developmental neuroscience will help us understand neurodevelopmental disorders and mental health and vice versa

- Live imaging of development is scaling new heights
- Advanced behavioural tests can mimic some aspects of human behaviour in the mouse
- Identification of genes mutated in human populations can then lead to studies in animal models
- Identification of genes through developmental neurobiology can be screened for mutations in humans

Figure references (1)

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