Module:
Biological Foundations of Mental Health

Week 2
Building blocks of the brain

Topic 1
Neuron-glial interactions and mental health – part 1a

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Lecture transcript

Slide 1

My name is Isabella, and I'm going to talk to you today about neuronal-glia interaction in mental health, giving you what is probably going to be a slightly surprising new take on the causes of mental health issues.

Slide 2

The primary goal of neuroscience, is to understand the mind. That is, how we perceive, move, think, remember. Or, more generally, what are the biological basis of our behaviour and our mental wellbeing. So far, studies in the neurobiology of psychiatric and neurodevelopmental disorders have focused on the role of neurons, seen as the only determinent of behaviour, a concept that we called neurocentricsm.

Another subtopic is the introduction of a different perspective, which has been developing over the last ten to fifteen years, which sees glial cells in particular astrocytes as fundamental players in determining brain function, behaviour and, as a consequence, mental health.

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Astrocytes morphology and function were introduced in the previous subtopic. Here we should briefly revise two aspects of astrocyte function, which are important for the role in influencing behaviour. So initially, we are going to look at astrocyte networks, and then, we're going to move to their role in the modulation of synaptic function, the so-called 'tripartite synapse'

In part two, we are going to look at astrocytes in the pathology of the central nervous system, Studies carried out in the past few years have led to the discovery that astrocytes can modulate behaviour, and this has led to an increase in the interest in the potential causative on contributing roll in psychiatric disorder. We shall discuss this putative role of astrocytes in psychiatric disorder and the difficulties that have been encountered in demonstrating this role and the cellular and molecular mechanism involved, using studies on depression as an example.

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So in this first part, we shall look at how astrocytes may contribute to determine behaviour. This is an image of astrocytes visualised originally in the 19th century with techniques, such as the silver

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impregnation method, which was invented by Camillo Golgi in 1873.

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But first of all, I mention that we now think that astrocytes might have an influence on determining our behaviour, but do we actually have any evidence that astrocytes may indeed affect behaviour?

This image is a micrograph of human astrocytes from a study that Han and colleagues performed 2013. In an intriguing set of experiments, they transplanted human glial progenitor cells in immunosuppressed mice. These progenitors survived, they migrated long distances and that gave rise to astrocytes with typical features of human ones, which are the ones that we see in red in this picture.

Surprisingly, when Han and his colleagues examined the behaviour of these mice, they found mice with human astrocytes perform better in learning tasks and displayed and improved long-term potentiation, which is a strengthening of synaptic connection, which is thought to be the mechanism underlying learning and memory. Four astrocytes may be responsible for human cognitive abilities.

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But how can astrocytes affect behaviour? Well, astrocytes can obviously affect it indirectly, being, for example, involved in neuron and development and maintenance of a stable environment, which is their homeostatic role, which has been addressed in the previous subtopic. However, two function of astrocytes may potentially make them more directly responsible for behaviour in health and disease, and these are the ability to release neurotransmitter, the so-called glial transmission and their ability to form astrocytic networks. We shall now discuss these two features of astrocytes briefly.

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This is a schematic representation of the three tripartite synapse, that is a synapse composed of three elements. Two neuronal, the pre- and postsynaptic terminal belonging to two separate neurons and an astrocytic process.

During synaptic activity, neurons release neurotransmitters. An astrocyte responds to these neurotransmitters, which are represented in blue here. We have elevations of calcium, and in turn, they control neuronal excitability in synoptic transmission through calcium dependent release of glial transmitters, which are represented here in red. The glial transmitter that astrocytes can release are glutamate, GABA, ATP, adenosine, D-serine, et cetera. Probably every single transmitters that neurons can also release, and probably also express receptor transporter for all the major neurotransmitters.