Module:
Biological Foundations of Mental Health

Week 1
Introduction to brain anatomy

Topic 3
Microanatomy of the nervous system – Part 3 of 3

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In the final part of the topic, we're going to be talking about gene expression.

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Compared to other cells and organisms, neurons have a particularly high protein and lipid content due to their specialisation and elongated form. Renewing the protein content of a neuron is essential for maintaining neuronal cell health and plasticity, a key feature of neurons. By plasticity, we mean the ability of a neuron to adapt to stimuli, such as the growth of existing or new synapses during memory formation. Renewal of proteins can occur by protein synthesis or the recycling of existing proteins.

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Gene expression is the process by which a gene is used to synthesise the product it encodes. This is most commonly protein but can also include functional RNAs, such as transfer RNA and ribosomal RNA. Protein synthesis is how gene expression results in the generation of new proteins from the genetic code. For those of you that are already familiar with this process, I hope this serves as a succinct refresher course.

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Gene expression occurs via two key steps: transcription – the photocopying of DNA into messenger RNA. This is a clever evolutionary step that keeps the DNA in the nucleus where it can be protected from damage. The second step is translation – the literal translation of the genetic code on the mRNA photocopy into protein. These processes are highly regulated so that proteins are only made when they are needed.

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Transcription occurs by the enzyme RNA polymerase moving along the DNA, copying it from the DNA code ('A', 'G', 'C' and 'T') into messenger RNA ('A', 'G', 'C' and 'U'). Note the changing of 'T's to 'U's from DNA to RNA. DNA is normally kept in a condensed structure, which needs to be relaxed so that transcription factors can bind and initiate transcription. Epigenetic factors, such as DNA methylation, can control when the DNA structure can be relaxed.

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Before being ready for translation, RNA undergoes several processing steps, including RNA splicing. The splicing machinery chops out non-coding regions – 'introns' – of the messenger RNA, thus leading only protein-coding regions. Alternative splicing can chop out different regions, producing different mature RNA transcripts, which encode different proteins, which may have different functions within a cell. This is a way in which the genetic code can increase the number of potential proteins it makes. This mature RNA is then exported from the nucleus to the cytoplasm for translation into protein. Gene expression is often assessed at the mRNA level by 'RNA sequencing'. This informs which genes are being actively transcribed and how they are spliced.

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In the cytoplasm, ribosomes read mRNA code and translate this into protein. The ribosome recognises a 3 base-pair code on the mRNA and brings in a transfer RNA carrying the appropriate amino acid. It binds sequential amino acids together to form a polypeptide which, when folded into the correct structure, becomes a functional protein. Translation begins at the start code of an mRNA, which is AUG – or ATG on DNA – encoding the amino acid ‘methionine’. Translation normally occurs close to the nucleus, where the RNA is made, but in neurons this also occurs at sites with high protein demand, such as synapses. This is called local translation.

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Processing of proteins is essential for their correct folding and cellular targeting. Protein folding occurs as soon as a protein is made and then undergoes quality control to ensure it is correct. Thus, misfolded proteins can be targeted quickly and efficiently for degradation. Proteins also often have post-translational modifications that modulate their folding (such as phosphorylation), again, greatly increasing the diversity of protein functionality. This can allow different protein activity during different cellular activities. Protein misfolding is a major cause of disease, especially in neurodegenerative disorders. This can be due to genetic mutations, cellular stress or impairment of clearance mechanisms and often leads to a build-up of aggregated protein in the brain.

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In summary, I hope this topic has guided your understanding into the foundations of the complex microanatomy of the nervous system. In Part 1, we learned how the nervous system is comprised of neurons and glia which come in many different forms with specific functions. In Part 2, we explored how neurons and glia have specialised morphologies which enable them to carry out their function and that neurons share many substructures with a standard eukaryotic cell, but also have their unique features and demands. And, finally, in Part 3, we delved into the totally critical cellular process of protein expression.