# Neurophysiology: Neurons and Circuits (NEUR30002)

Study Notes

# Contents

# 1.1

## *Cellular components of the brain*

Types of glia: astrocytes, ependymal cells, microglia, oligodendrocytes & radial glia

**Classifying neurons**

- ➔ Chemical (neurotransmitter released)
  - ◆ Identified electrophysiologically or by observing the effect of exciting the neuron
- ➔ Function
  - ◆ Identified through direct labelling (immunohistochemistry), genetic markers or mRNA (in situ hybridisation)

Phenotype

- ➔ Location (brain area, layer of matter)
- ➔ Morphology/structure

**Regions of a neuron in order of info flow**

Dendrites  cell body/soma, axon

**Other features of neurons**

- ➔ Synaptic processes can be axo-dendritic or axo-synaptic
- ➔ Axons are covered in myelin, which has specialised properties for electrical conduction

**Glial cells in the CNS**

- ➔ Oligodendrocytes form myelin sheaths
- ➔ Astrocytes
- ➔ Microglia are modified immune cells that act as scavengers
- ➔ Ependymal cells create the BBB and are a source of neural stem cells
- ➔ Notes:
  - ◆ Ratio of astrocytes to neurons increases with complexity of nervous system
  - ◆ Glia > neurons

**Functions of astrocytes**

- ➔ Ensuring fidelity of neurotransmission
  - ◆ Eg. astrocytes (between neurons) have glutamate transporters that clear glutamate from the synapse, avoiding overstimulation
- ➔ Maintaining extracellular ion homeostasis
  - ◆ Eg. when neurons depolarise, they release $K^+$, which is taken up by astrocytes, maintaining extracellular composition of $K^+$
- ➔ Spatial buffering
  - ◆ Eg. if they take up too much $K^+$, astrocytes may suffer toxicity. Luckily, they are connected by gap junctions, so $K^+$ can distribute
- ➔ Regulating blood flow

# 5.3

*Viscerosensory processing in the NTS*

**Organisation of primary afferent input at NTS**

- ➔ Experiment (patch clamp electrophysiology)
    1. Insert recording electrode into NTS to record postsynaptic activity & compare to reference electrode
    2. If responses are consistent → monosynaptic connection
    3. If responses are inconsistent → NTS receives multiple inputs
- ➔ Distribution of inputs
    - ◆ 65% of NTS neurons receive 1 input
    - ◆ 20% of NTS neurons receive 2 inputs
    - ◆ 15% of NTS neurons receive 3 inputs

**Properties of solitary tract info to NTS**

- ➔ Relatively sparse, high fidelity & monosynaptic network
- ➔ Some tracts send specific info (baroreceptor/chemoreceptor) in labelled lines
- ➔ Sometimes different afferent converge onto solitary tract (polysynaptic info)

**Where does the info go?**

- ➔ Monosynaptic info → autonomic brain centres (sometimes hypothalamus)
- ➔ Convergent info → hypothalamus & amygdala

**Asynchronous glutamate release**

- ➔ Occurs after and depends on synchronous glutamate release
- ➔ Doubles glutamate release and extends postsynaptic period

**TPRV1 ion channel**

- ➔ Properties
    - ◆ Non-selective cation channel (allows $Na^+$ and $Ca^{2+}$ influx)
    - ◆ Responds to heat, acid & capsaicin (in chilli)
    - ◆ Expressed in C-fibres
- ➔ How we use it experimentally
    1. Capsaicin activates TPRVI channel, allowing cation influx
    2. Initial depolarisation and glutamate release
    3. Subsequent depolarisation block and glutamate staps being released
    4. Less activation of NTS second order neurons

# 9.2

*Neurogenesis 2*

**Neurogenesis in the neocortex of adult primates**

- ➔ Uses BrdU staining
- ➔ Results:
  - ◆ After 2 hours, cells living lateral ventricle were stained
  - ◆ After 1 week, some cells migrate
  - ◆ After 2 weeks, some cortical neurons are visible

**Where else does adult neurogenesis occur?**

- ➔ Hypothalamus: cells living 3rd ventricle may migrate to ARC
- ➔ Frontal cortex: amygdala, striatum & substantia nigra

**2 pathways from NTS**

- ➔ Nerves release excitatory amino acids onto nucleus ambiguus nerves, which exit via vagus nerve & slow HR
- ➔ Nerves release excitatory amino acids onto CVLM, which releases GABA onto RVLM. This suppresses excitatory projections to IML column, decreasing blood flow to heart

**A2 catecholaminergic neurons & BP**

- ➔ Results:
  - ◆ Control rat: stable BP with narrower range
  - ◆ Lesional rat: labile BP with broader range

**BrdU vs EdU**

- ➔ DNA denaturation is required for antibodies to reach BrdU
- ➔ EdU recognition only requires a chemical reaction
  - ◆ Since it is metabolised quickly, it can enter the brain through canals

**What does EdU staining show?**

- ➔ Neurogenesis in:
  - ◆ Dentate gyrus & SV
  - ◆ Central canal of NTS

**Checking that EdU-positive cells are actually neurons**

- ➔ Co-label with neuronal stains (eg. NeuN)

**Studying neurogenesis & hypertension**

- ➔ Method:
  1. 2 experimental groups: spontaneous hypertensive & renal artery clip rats
  2. Intracerebroventricular injection of EdU pump

2. APCs present antigen to T cells, causing a protective immune response

➔ In MS:
- ◆ Self cells (eg. myelin) are taken up, causing a maladaptive immune response

**Helper T subtypes**

Pathological subtypes:
- ➔ $T_H1$ → produces IFNγ & TNFα
- ➔ $T_H17$ → produces IL-17A & GM-CSF
- ➔ Functions:
  - ◆ Release pro-inflammatory cytokines
  - ◆ Stimulate macrophages/microglia
  - ◆ Recruit more inflammatory cells

Regulatory subtypes:
- ➔ $T_H2$ → produces IL-4
- ➔ $T_{regs}$ → produces IL-10
- ➔ Functions:
  - ◆ Release anti-flammatory cytokines
  - ◆ Regulatory macrophages/microglia
  - ◆ Tissue repairs
  - ◆ Inflammation resolution

**Pathogenesis**

➔ Key pathogenic cells
- ◆ T cells & B cells
- ◆ APCs: macrophages, microglia, monocytes & myeloid dendritic cells
  - Functions: activate/reactivate T cells, produce inflammatory mediators & phagocytose myelin

**Steps in pathogenesis**

1. In periphery, dendritic cells encounter self-antigens and migrate to lymph nodes to present antigens to T cells
2. Helper T cells cross BBB and cause inflammatory response after being reactivated by microglia
3. Demyelination of neurons & oligodendrocyte loss → neuron& axon loss

**Types of lesions**

| Active | Mixed active/inactive | Inactive |
|---|---|---|
| ➔ Early disease/RRMS<br>➔ Axon loss<br>➔ Hypercellular<br>➔ Demyelination/post-de myelination<br>➔ Inflammatory inflammation, including astrocytes | ➔ Axon loss<br>➔ Demyelination/post-de myelination<br>➔ Fewer active cells (some astrocytes & inflammatory cells)<br>➔ Ring of macrophages/microgli a at border | ➔ Glial scars<br>➔ Hypocellular<br>➔ Profound axon loss |