Pathology

Sheet

Lec No: 1

Subject: Introductions & patterns of injury in the nervous system

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Lecture 1:- Introduction to CNS pathology

This is our first lecture out of 11 lectures we will be taking to discuss the pathology of the central nervous system.

In this lecture we will discuss:

1. Introduction:
   A. quick review of the brain gross anatomy
   B. quick review of the brain histology
2. patterns of injury in the nervous system

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1. introduction

A. quick review of the brain gross anatomy:

The brain developmentally is composed of three parts:

- forebrain : cerebrum , thalamus ,and hypothalamus
- midbrain
- hindbrain: cerebellum, Pons ,and medulla oblongata

now we will briefly talk about some part of the brain:

The Cerebrum:

The cerebrum is composed of 2 cerebral hemispheres (right and left) connected together via corpus callosum (a group of neuronal axons joining the two cerebral hemispheres).

Each cerebral hemisphere is composed of:

- inner white matter which is histologically composed of neural axons surrounded by neuroglial cells (supporting cells)
- Outer grey matter (the cortex) which is thrown into folds or gyri separated by fissures or sulci. A number of the large sulci are used to subdivide the surface of each hemisphere into 4 lobes named according to the overlying cranial bone: - frontal, temporal, parietal, and occipital lobes. Please note that each lobe performs certain functions that will be discussed later on.
  Histologically the cortex is composed of neural cell bodies surrounded by neuroglial cells (supporting cells)

Note:

1. Usually each hemisphere controls the contra lateral (opposite) side of the body. for e.g. the left hemisphere controls the movement of the right hand.
2. Although the hemispheres are mirror image of each other, some functional areas (like speech production) are found only in one hemisphere (the dominant hemisphere) which is the left in the majority of people. Therefore, the same intensity of the same disease/lesion can have different consequences according to the affected side.
   The dominant hemisphere can be known by asking the patient "which foot do you use to kick the ball?" or noticing if the patient is right handed or left handed. If the patient writes or kicks with his right side (the usual case) then the dominant hemisphere is the left hemisphere.

Functions of the cerebral cortex lobes:-

1. Frontal lobe
   -controls movement
   -motor function of speech (specifically by: - **Broca's area** which is usually found in the left hemisphere)
   A stroke affecting the left hemisphere in a right handed person will cause loss the ability to talk (expressive *dysphasia*) and self-expression, whereas the same stroke affecting the right frontal lobe will not cause any symptoms.
   Therefore it is very important to know if your patient is right of left handed while taking history by asking the patient: -

   Note:-
   Generally, the anterior part of the brain is important for motor function while the posterior part is important for receiving sensory sensation from the environment)

   -Keep in mind, speech has two aspects: - talking which is controlled by Broca's area as we said and understanding or receiving speech controlled by **Wernicke's area** (part of the temporal lobe)

2. Temporal lobe
   -important for complex processing of sensory input
   -as we said, it contains **Wernicke's area** which is responsible for understanding received spoken or written language (if damaged => *receptive dysphasia*)
   -of course, there are associations between Broca's and Wernicke's area because there must be a connection between how we receive and express speech
   -the inferior part of the temporal lobe also contains centers for recognizing faces bilaterally. If affected (by a congenital disease for example) patients lose the ability to

recognize people by face unless they hear their voice or way of walk or so on, although they have no problem in sight or vision.

3. Parietal lobe
   -contains somatic sensory areas
   -contains area for naming objects
   -contains area for processing visual language (reading)

4. Occipital lobe
   -most importantly contains the visual cortex (how you see things)

The thalamus & hypothalamus:

The thalamus:

It is responsible of appropriate attention of sensory perception ,in other words it selects what reaches the cortex and what does not (even when we are sleeping) .

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The hypothalamus:

Responsible of regulating body functions or homeostasis (controls body temperature , hunger, electrolytes and water balance,….etc)

The cerebellum:

The cerebellum (المخيخ) is important for balance. If affected, person moves without balance.

The medulla oblongata:

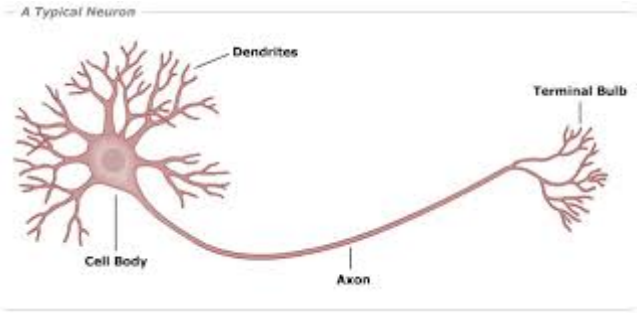
The medulla oblongata which is a part of the brain stem is important because it contains the respiratory and cardiac centres.

Note: the purpose of studying the exact functions of each part of the brain is to locate the disease depending on the signs and symptoms the patient presents with. Because the difference between a disease in any part of the body and the brain is not only the importance of the disease process but also the location which causes the signs and symptoms. For e.g. A minimal infarct in the brain stem can be lethal, where as a small infarct in the frontal lobe can have no signs and symptoms.

B. Quick review of the brain histology:

Brain cells are 2 types: **neurons** (parenchymal cells that do the function) and **glial cells** (supportive cells that give structural support)

1. Neurons
   - There are 100 billion neurons in the CNS
   - A neuron has a cell body with a nucleus, dendrites and an axon



   - Function :- receive and transmit information (moves along axon as impulses)
   - Some impulses moving along an axon must be insulated from the surrounding environment to speed them up (just like an electrical wire). This isolation is provided by myelin produced from oligodendrocytes.
   - Neural cells are permanent cells; i.e. If you lose a neural cell, you can NOT replace it (because neural cells cannot undergo mitosis) however, the brain , like any other organ in our body has stem cells known as **neural progenitors** and these can proliferate and replace most neural and glial cells but of course they have problems like all other stem cells as :
     - ✓ They are few in number and can multiply a limited number of times, therefore cannot completely replace the damaged tissue.
     - ✓ Differentiate into a limited repertoire of cell types.

     Expansion of these can help patients with CNS diseases allowing this to be an active area of research
   - clinical note: Zika virus infection is associated with microcephaly, through infecting neural progenitors causing their death and resulting in decreased brain growth in embryos (microcephaly)

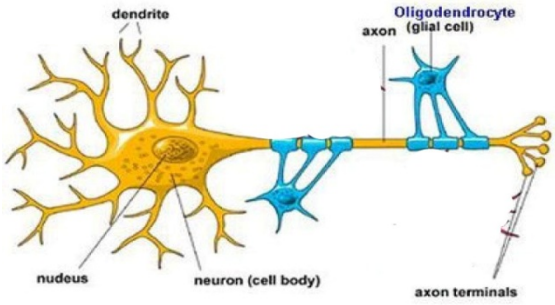
2. Glial cells
   - 10-50 times more than neural cells (1000 – 5000 billion)
   - We said they are supportive cells
   - 4 types :-
     a. Astrocytes
        - ✓ Most abundant

- ✓ Works like fibroblast in the rest of the body
- ✓ Main functions :-

1) Gives structural support to neurons
2) Important for controlling microenvironment of neural cell or neural biochemical environment
3) Its processes are associated with the blood vessels to form the blood brain barrier which is important in isolating neural cells and controlling what goes in and what goes out

b. oligodendrocytes

- ✓ cells forming layers of plasma membrane known as the myelin sheath around axon of neural cells in the brain , insulating it for faster transmission of action potential
- ✓ if lost, cause demyelinated CNS diseases (eg :- multiple sclerosis MS)



Modfied from:
http://science-naturalphenomena.blogspot.com/2009/04/oligodendrocytes.html

c. microglial cells

- ✓ mesoderm derived phagocytic cells that serve as resident macrophages of the CNS.
- ✓ phacytosing cell (blood derived macrophages)

d. ependymal cells

- ✓ Secrete CSF
- ✓ Line the ventricles forming choroid plexus

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2. patterns of injury in the nervous system “reaction of brain cells to injury”

Types of injury that affect the brain:- viral / ischemia / trauma / infections / necrosis / demyelination / hemorrhage / infarction and many more …

Brain cells respond to injury in a different way than the rest of the body

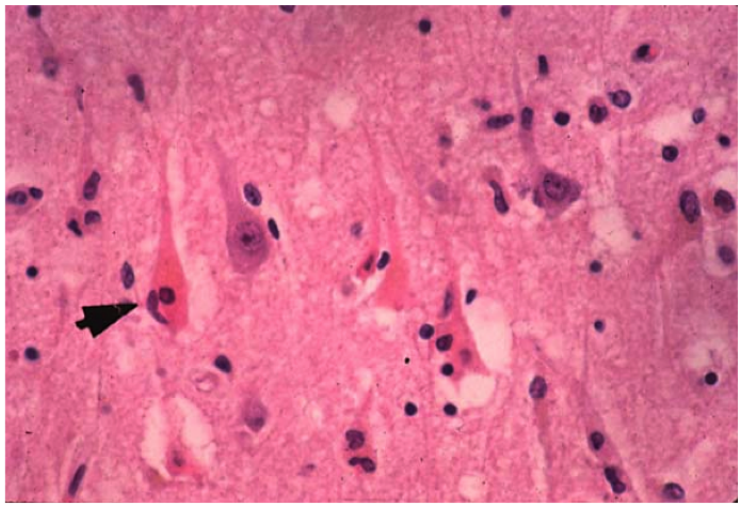
a. neurons:

I. Reaction of neural cells to acute injury:

- Acute injury occurs due to hypoxia or ischemic injury which causes neuronal cell death and apoptosis

> Note: Generally, any acute injury in the body causes acute inflammation However, if this happens in the brain it will cause a huge damage therefore the immune system in the CNS tries to create an anti inflammatory environment in order to minimize the damage, One of the factors helping in the restriction of inflammation is the BBB which limits the number of inflammatory cells reaching the site of injury.

- When the neurons die, the following events take place:
  Cell body shrinkage, pyknosis of the nucleus, disappearance of the nucleolus, and the cytoplasm becomes red (intense eosenophilia) due to the loss of Nissel substance forming **red neuron.**



II. Subacute and chronic neuronal injury

- Neuronal death due to a progressive disease (e.g. Alzheimer) which are neurodegenerative diseases
- Cell loss affecting functionally related neurons (not necessarily structurally related)

b. Glial cells (neuroglial cells)
Neuronal death usually is apoptotic death and is associated with reactive gliosis.

Generally, chronic injuries in other sites of the body usually cause fibrosis
In the CNS, we do not have fibrosis but we have gliosis!!!
Gliosis: a nonspecific reactive change of the glial cells in response to damage to CNS. In most cases, gliosis involves the proliferation and/or hypertrophy of several different types of glial cells, including astrocytes, microglia, and oligodendrocytes.
(So, glial cells unlike neural cells can proliferate and divide)

I. Reaction of astrocytes to injury:
- Astrocytes are the principle cells responsible for repair and scar formation.
- Reactive astrocytes try to repair the injury by undergoing changes and these astrocytes are termed gemistocytic astrocytes
  So injury causes:
  Increase in size (hypertrophy) and number (hyperplasia), nucleus enlarges (macronucleus with prominent nucleolus), cytoplasm becomes more pinkish (eosinophilic), and increased ramifying processes these changes cause the astrocyte to become a gemistocytic astrocytes.

II. Reaction of microglia to injury:
- They respond to injury by : proliferating , developing elongated nuclei (rod cells), aggregating around foci of tissue necrosis (microglial nodules), and congregate or aggregate around cell bodies of dying neurons (neuronophagia)
- In addition to resident microglia, blood derived macrophages may also be present at the inflammation site.

"Your dreams are all possible because of 3 pounds of grey matter."

Get up and catch them!

The future belongs to those who believe in the beauty of their dreams ☺

Good luck