**Neuroanatomy, development, & damage**

Nervous system – communication network consisting of nerve cells, both inside and outside of the brain and spinal cord

Central nervous system – brain and spinal cord

Peripheral nervous system

Somatic nervous system

Autonomic nervous system

Sympathetic nervous system

Parasympathetic nervous system

Neuroanatomical directions & terms

Neuraxis – Imaginary line through center of CNS

Rostral (or anterior) – Head end (toward front)

Caudal (or posterior) – Tail end (toward rear)

Ventral (or inferior) – Towards belly (underneath)

Dorsal (or superior) – Towards back (above)

Lateral – Toward side

Medial – Toward middle

Humans complicate things because we walk upright, meaning neuraxis bends at right angle

Affects directional labeling in brain

Ipsilateral – On same side

Contralateral – On opposite side

Sagittal – Plane parallel to neuroaxis and perpendicular to ground (midsagittal divides brain symmetrically)

Coronal or frontal – Plane parallel to forehead

Horizontal or axial – Plane parallel to ground

Major divisions of brain

Forebrain

Midbrain

Hindbrain

Hindbrain critical for:

Breathing, maintaining ‘vita’ signs

Arousal – sleep, wakefulness, alertness

Muscle tone

Coordinating sensorimotor functions (perception and action)

Myelencephalon

1 major structure – medulla

Most caudal (or ventral) in brain

Serves vital functions (breathing, blood pressure, vomiting, muscle tone)

Origin of reticular formation

Reticular formation

Cell group that runs through core of hindbrain/midbrain

Output to forebrain – key for alertness, sleep

Output to spinal cord – key for movement, muscle tone

Metencephalon

2 major structures – pons, cerebellum

Pons has some of reticular formation and works with medulla to regulate sleep, alertness, some vital functions (breathing)

Cerebellum also called ‘little brain’ – key for balance, coordination, fine control of movement

RAPID sensorimotor integration

Damage can affect ability to know when to stop, judge distance, coordinate movements together

Mesencephalon (midbrain)

2 major areas

Tectum

Superior colliculi – visual function (guide eye movements, fixate gaze)

Inferior colliculi – auditory function (locate direction of sounds in space)

Tegmentum – 4 major structures

Reticular formation

Periaqueductal gray – mediates pain reducing effects of opiate drugs

Substantia nigra (“black substance”) – role in motor system

Red nucleus – role in motor system

Forebrain – 2 major divisions

Diencephalon – Includes thalamus and hypothalamus

Thalamus - Sensory input to cortex

Consists of 2 lobes and many pairs of nuclei

Hypothalamus – Motivational behavior

Conveys messages to pituitary gland to alter release of hormones for motivated behaviors – aggression, eating, drinking, sex

Telencephalon – Largest division of human brain

Most complex functions – voluntary movement, sensory integration, learning, memory, language, problem solving, etc.

Principal structures: cerebral cortex, basal ganglia, limbic system

Telencephalon – cerebral cortex

Outer tissue layer of telencephalon is the cerebral cortex

Convolutions of cortex increase its surface area, especially in humans

Convolutions create major fissures, sulci (grooves), and gyri (bumps)

Sulcus – small groove (furrow) on cortical surface of cerebral hemisphere

Fissure – large groove on cortical surface

Gyrus – convolution (bump) on cortical surface, separated by sulci or fissures

Telencephalon – hemispheres and lobes

Divided in 2 halves or hemispheres

Each side gets sensory info and controls movement from opposite (contralateral) side of body

Hemispheres joined by major fiber tracts – most prominent are corpus callosum and anterior commissure

4 lobes named for bones of skull over them

Boundaries roughly created by major fissures

Occipital – analysis of visual input

Parietal – analysis of touch, pain, spatial information, head and body positions

Temporal – hearing, complex visual processing, emotional behaviors, language

Frontal – planning of movements, impulse control, recent memory

Telencephalon – occipital lobe

Posterior end of cortex

Processes visual input

Location of primary visual cortex

Damage results in blindness in some portion of the visual field

Telencephalon – parietal lobe

Superior to lateral fissure, between occipital lobe & central sulcus

Processes skin senses, body position, movement – involved in spatial attention/coordination & integrating sensory input

Parietal lobe has somatosensory cortex – located along extent of post-central gyrus (gyrus just posterior to central fissure)

Sensory systems are spatially organized forming a body map (homunculus) in somatosensory cortex so that CNS knows where something is felt

Damage to parietal lobe has diverse effects:

Neglecting a side of body or space (contralateral neglect)

Confusing left-right

Difficulty writing and doing math

Telencephalon – temporal lobe

Inferior to lateral fissure

Functions:

Hearing, language (superior temporal gyrus)

Identifying complex visual patterns (inferior temporal gyrus)

Remembering (medial portion)

Association areas – Carry out further processing and integration of multiple senses together

Telencephalon – frontal lobe

Anterior to central sulcus, superior to lateral fissure

Complex functions – executive functions, inhibiting yourself, planning, perspective taking, volitional control of movement

Telencephalon – primary motor cortex

Frontal lobe has primary motor cortex located along extent of pre-central gyrus (gyrus just anterior to central fissure)

Telencephalon – hemispheres and lobes

Motor paths also spatially organized with parts of motor cortex sending output to specific parts (muscle groups) of body

Prefrontal cortex – integration of all sensory input (most anterior part of frontal lobe)

Key for higher functions

Damage has diverse effects, including major changes in personality

Most (not all) cortical areas have 6 layers

Molecular layer, external granular layer, pyramidal cell layer, inner granular layer, inner pyramidal cell layer, fusiform layer

Unique cell composition

Different inputs, outputs (p. 52)

Telencephalon – ‘subcortical’ systems

Limbic system – evolved early; serves emotional functions, learning, memory, aggression, motivation (cingulate cortex, hippocampus, amygdala)

Basal ganglia – cell groups serving motor and reward functions (caudate, putamen, globus pallidus, amygdala\*)

Involved in Parkinson’s disease

Peripheral nervous system

Nerves of PNS enable brain and spinal cord to communicate with body and external environment

Somatic nervous system – Part of PNS that interacts with external environment; gets sensory input and sense output to muscles to control movement

Autonomic nervous system – Controls internal environment (organs, blood vessels, glands, etc.);

Sympathetic nervous system – prepares us for action

Parasympathetic nervous system – nonemergency behaviors

Two divisions control vital functions without conscious effort or awareness

What comprises the PNS?

Cranial nerves – sensory, motor functions primarily for head, neck, shoulders (some exceptions)

Spinal nerves – sensory, motor functions throughout body

31 pairs, connecting to sides of spinal cord at each vertebra

Key terms

Bundle of axons – cranial/spinal nerves in PNS, tract in CNS

Group of cell bodies – ganglion in PNS, nucleus in CNS

Protection of the CNS

Chemical protection

Blood-brain barrier – tightly-packed cells of blood vessel walls that prevent entry of toxic substances

Physical protection (barriers, buoyancy)

Skull

Meninges

Cerebrospinal fluid

Chemical protection

BBB is formed by difference in walls of blood vessels in CNS

Outside: cells of capillaries have gaps allowing substances to pass freely

Inside: cells of capillaries have tight junctions limiting flow of substances

Physical protection

CNS encased in bone & covered by 3 protective meninges

Dura mater – tough outer membrane

Arachnoid mater – web-like middle membrane

Pia mater – think inner membrane, adheres to CNS surface

Cerebrospinal fluid (CSF) serves as cushion

Cerebral spinal fluid

Supports, cushions CNS

Circulates in subarachnoid space, through ventricles of brain, down central canal of spinal cord

CSF made continuously by cells in ventricles

CSF give buoyancy

CSF flow can be blocked

Tumor can push against cerebral aqueduct

Results in massive pressure build up

Ventricle cells continue to make CSF

Ventricle – hollow space – filled with CSF

Lateral ventricles – in telencephalon

3rd ventricle – in diencephalon

Cerebral aqueduct – connects 3rd and 4th ventricles – in mesencephalon

4th ventricle – between cerebellum, pons – in metencephalon

Basics of development

Embryo surface 🡪 neural plate (Day 18)

Neural plate 🡪 neural groove (Day 20-21)

Edges curl, meet 🡪 neural tube (Day 21-23)

Cell birth (proliferation)

Cells divide, multiple in ventricular zone

Enabled by ventricular lining of pluripotent stem cells 🡪 progenitor cells

These 🡪 neuroblasts and glioblasts that become neurons and glia

At peak: 250,000 new cells are born every minute

Largely done by five months

Cell migration

Begins ~8 weeks after conception, nearly over by ~29 weeks

Damage has more serious consequences

Astrocytes guide many immature neurons from ventricular zone to destination

During migration, ~ billion future neurons move along glia in a day

Assembled inside-out (stacked)

Many infections, insults, and toxins can result in microcephaly, lissencephaly, ventriculomegaly

Cell differentiation (& aggregation)

Starts after cells begin to migrate and aggregate to form “communities”

Includes forming of specialized cells, axons, dendrites

Cell maturation

Accelerates ~week 20, continues after birth

2 ways: dendritic growth (more branching, new spines), and axonal growth

Synapse development

5th month: simple synaptic contacts

7th month: synaptic contacts of cortical neurons

After birth: synaptic contacts rise rapidly during first year

Errors in synapse formation can have profound consequences

Also called circuit formation

Axons grow toward targets to make “functional connections”

Cell death and synapse pruning

Proliferation yields excess of neurons – still unclear why

Cells die because of genetic program, apoptosis

Synapses not part of functional network are pruned

Active synapses strengthened

Inactive ones removed

Glial development (myelination)

Astrocytes, oligodendrocytes will be generated after neurogenesis is nearly done

Continues throughout life

Myelination of cortex begins after birth, continues until late teens, even 20’s

Some areas myelinate earlier (those for simpler functions)

Adolescence and beyond

Human brains mature slowly

Limbic regions mature faster than prefrontal areas

Possible reason for increased emotional/reward behaviors (regulatory prefrontal areas not fully online)

Possible basis of high risk-taking

Brain tumors

Tumor (neoplasm) – mass of cells, grows independently of body and serves no use

30% of brain tumors are meningiomas – in meninges

Usually benign – encapsulated within own membrane

Often surgically removable

Meningiomas

Compete for space

Pressure causes headache, vomiting, double vision, slow heart rate, seizures, & other symptoms depending on location

Malignant tumors

Most brain tumors are malignant

Grow diffusely – invade and infiltrate nearby tissue

No clear membrane/boundary that encapsulates mass

Difficult to remove/destroy

About 10% of malignant tumors are metastatic – originated elsewhere

Origin of tumors

In adulthood, benign & malignant tumors do not arise from neurons, which are not capable of dividing

Many arise in glia

Gliomas among most serious – highly malignant & fast growing

Strokes

Cerebrovascular events where brain’s blood supply is disturbed by bleeding or blockage – causing cell death

3rd leading cause of death and most common cause of adult disability

2 kinds of strokes

Hemorrhagic strokes – cerebral hemorrhage = bleeding in brain

Ischemic strokes – cerebral ischemia = blockage of blood supply

Closed-head injuries

Also called traumatic brain injuries (TBIs)

Due to blows that don’t penetrate skull – brain collides with skull

Sites of injury are coup & countercoup

Coup & countercoup injuries can directly damage neurons and glia, as well as cause contusions – damage to cerebral circulatory system that results in hematomas (bruises) and edema (swelling)

Circulatory damage – excess glutamate release results in excitotoxicity as in stroke

Astrocytes can help clear glutamate

Coup/countercoup injuries also cause concussions – involve a change in consciousness or mental state with no immediate evidence of structural damage

Features are cognitive, psychological: lack of concentration, slowed processing speed, headaches, deficits in higher-order functions, mood changes

Plasticity and recovery

Regeneration – regrowth of severed axons

Myelin provides a guide tube for neuron to grow through, and axon is guided to destination much as in development

More prominent in PNS  
 Neurogenesis – birth of new neurons

Occurs in several areas in adult brain – most extensive in hippocampus and near lateral ventricles

Compensation – nearby, local, intact areas form new synapses to perform functions of lost, damaged areas

Reorganization – more dramatic, other hemisphere or distributed areas take on new functions

Possibilities for repair on horizon – neuron growth enhancers, providing guide tubes or scaffolding, counteracting regrowth inhibitors

Stem cells are an ideal means of neural repair

**Methods & Ethics**

Ethical positions

“Minimalists” favor strict regulation and place ethical consideration on type of animal, level of harm, necessity

“Abolitionists” hold that all animals have same rights as humans – any animal use is unethical

Justification considers all likely benefits compared to level of harm – no clear dividing line

Experiments vs non-experiments

Experiments manipulate independent variables

In non-experiments, there is no such control

Quasi-experimental studies, cast studies, series field research

Experiments enable cause-effect conclusions; non-experiments do not because there is no control

Case studies, series

Focus on 1 person or small group

Usually compared to ‘controls’

More in-depth than other approaches

Results may not be generalizable

Usually involves people with rare brain damage

Field research

Observe animals in natural habitats

Staining techniques

Golgi stains – highlight individual neurons

Myelin stain – emphasize white matter and, therefore, neural pathways

Nisal stain – emphasize cell bodies of neurons

Autoradiography

Inject radioactive material and see where it gets taken up in brain

Microscopy

Light microscopes – cell bodies, dendrites, axons, and large organelles in neurons

Limited capability due to the nature of light

Electron microscopes – pass beams of electrons through a thin slice of tissue onto detector

High resolution, magnifying objects up to 250,000 times

Can reveal objects in 3-D

Electrophysiology

Recording of electrical or electromagnetic activity

Electroencephalography (EEG)

Records electrical activity from scalp

High temporal resolution (ms), but poor spatial resolution

Gross EEG recordings – indicate level of consciousness

Magnetoencephalography (MEG)

Records electromagnetic fields generated by activity of neurons

Very high temporal resolution, and better spatial resolution than EEG

Invasive electrophysiology

Single unit recording: electrical activity from 1 cell

Multiple unit recording: populations of cells

Brain imaging – enables us to quantify, visualize brain structure and activity

Computed tomography (CT)

Also called X-ray computed tomography

Structural (not functional) images

Head put in ring with X-ray tube (emitter) & detector + dye injected

X-rays pass through head 🡪 detector measures radioactivity that gets through

Magnetic resonance imaging (MRI)

Involves interaction between radio waves and magnetic fields

No X-rays (radiation)

Passes strong magnetic fields through head/body

Structural MRIs have a very high spatial resolution

CT vs MRI

Both provide structural images

MRI has better resolution than CT and doesn’t involve radiation exposure

Functional magnetic resonance imaging (fMRI)

Measures changes in neural activity by recording blood flow changes in active brain areas

Very widely used in human studies, also with animals

Interpretations difficult

Cannot make causal conclusions

Positron emission tomography (PET)

Measures activity by injecting radioactive chemicals, mostly radioactive glucose

Provides images of brain activity because active areas need glucose

Scan is image of levels of radioactivity in parts of brain

Diffusion tensor imaging (DTI)

Measures white matter fibers that are communication paths of brain

Allows us to understand structure of brain networks

Brain stimulation

Electrical, electromagnetic, or other stimulation of cells or gross areas

Transcranial magnetic stimulation (TMS)

Provides a way to manipulate neural activity

Brief magnetic pulses

Can “activate” or “deactivate” regions

Observe changes in behavior

Often used to circumvent problems brain imaging studies have in determining causation

Invasive electrical stimulation

Used to “activate” area of NS

Effects often opposite to lesions

Lesion methods

Destroy part of CNS to evaluate effects on behavior

Rationale is that function can be inferred from behaviors that animals can no longer do after area is damaged

Interpretations complicated – all brain regions are interconnected

Aspiration – tissue removed by suction

Radio-frequency – electrolytic, strong head-inducing current

Chemical – damage by toxin

Knife cuts – eliminates nerve or connecting fibers

Cryogenic – coolant pumped in cryoprobe, neurons stop firing, effects are reversible

Genetic approaches

Gene editing, ‘knock out’ models – render a gene inoperative

Development of strains – breeding to develop animals that exhibit particular behaviors, characteristics

Investigating heredity

Family studies determine how strongly a characteristic is shared among family members

Difficulty separating heredity and environment

Adoption studies allow measurement of children’s similarity to adoptive parents vs biological parents

In vitro fertilization can provider greater control of early environmental effects

Twin studies assess how similar twins are in some characteristic

A useful measure for identifying genetic influence in disorders is the concordance rate

Frequency that relatives share a characteristic