Neuroanatomy

Neurones

Classification by Morphology
1. Unipolar – perikaryon has one neurite
2. Bipolar – perikaryon has two neurites
3. Multipolar – each neurone has one axon and more than one dendrite

Classification by size
1. Golgi Type I – long axon
2. Golgi Type II – short axon terminating near the parent cell
3. Amacrine – no axon

Neuroglial cells
• all probably of ectodermal origin
• ten times more common than neurones

Astrocytes
• most numerous class of neuroglia
• two types:
  1. fibrous astrocytes
  2. protoplasmic astrocytes
• cell processes often closely applied to capillary blood vessels (perivascular end feet)
• other end feet are applied to the pia mater, forming the external glial limiting membrane
• when the brain or spinal cord is injured:
  • the astrocytes near the lesion undergo hypertrophy
  • the cytoplasmic processes become more numerous
  • there may be some increase in cell numbers due to mitosis
  • this is known as gliosis:
    • Alzheimer’s disease
    • frontal lobe dementia
    • Pick’s disease
    • general paresis
    • CJD
• roles:
  • providing physical support
  • exchange of metabolites between neurons and blood

Oligodendrocytes
• responsible for producing and maintaining the myelin sheaths in the central nervous system, in an analogous way to Schwann cells in the peripheral nervous system
• also involved in phagocytosis
Microglia

- the function of *resting microglial cells* is unknown
- *reactive microglial cells* arise from monocytes that enter the nervous system and have a phagocytic role - they are found in large numbers at sites of inflammation

Ependymocytes and tanycytes

- form the **ependyma** which lines the ventricular system
- tanycytes may be involved in the control of the endocrine system by the pituitary gland by responding to hormones in the CSF

Organization of the cerebral cortex

Cell types

- the cells in the cerebral cortex can be divided into five basic neuronal types:
  1. pyramidal cells
  2. stellate cells (granule cells)
  3. multiform (polyform) cells
  4. cells of Martinotti
  5. horizontal cells of Cajal
- intracortical cells (all connections within the cortex) include:
  - stellate cells
  - cells of Martinotti
  - horizontal cells
- pyramidal cells and multiform cells form the outputs from the cerebral cortex

Morphology of the neocortex

- six cellular layers:

<table>
<thead>
<tr>
<th>Layer</th>
<th>Cell types</th>
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</thead>
<tbody>
<tr>
<td>1. plexiform layer</td>
<td>horizontal cells and dendrites of pyramidal cells</td>
</tr>
<tr>
<td>2. external granular layer</td>
<td>small pyramidal cells and a few granule cells</td>
</tr>
<tr>
<td>3. external pyramidal layer</td>
<td>pyramidal cells</td>
</tr>
<tr>
<td>4. internal granular layer</td>
<td>stellate cells, few small pyramidal cells</td>
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<tr>
<td>5. internal pyramidal layer</td>
<td>large pyramidal cells</td>
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<tr>
<td>6. multiform layer</td>
<td>multiform cells</td>
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</tbody>
</table>

- Brodmann constructed his map of the brain depending on cytoarchitectural appearance
Outputs from the cortex

1. to cortical areas
   • to other areas in the same hemisphere
   • to homologous areas of the contralateral cortex, via:
     • corpus callosum
     • anterior commissure
     • habenular commissure

2. to subcortical areas:
   • basal ganglia
   • diencephalon
   • brain stem
   • spinal cord

The Blood brain barrier

• Consists of:
  • Arachnoid mater
  • Endothelial lining of the brain capillaries
  • Gliovascular membrane (perivascular end feet of astrocytic processes)
  • Capillary basement membrane

• is lacking in a few places:
  • area postrema in the medulla
  • subfornical organ
  • neurohypophysis

• allows the pH of CSF to be regulated independently of plasma pH – un-ionized CO\textsubscript{2} crosses the barrier much more easily than bicarbonate ions
• CSF pH is 0.1 less than the plasma pH
  • weak bases tend to accumulate in the CSF whereas weak acids tend to be excluded
• large amino acids cross the barrier freely – phenylalanine, leucine, valine, and isoleucine compete with tryptophan for the same transport system
### Developmental organization of the brain

- at 18 days, the *neural plate* develops
- the neural plate gives rise to three *placods* (optic, auditory, and nasal), from which the sense organs develop, and to the formation of the *neural tube*
- a bilateral column of cells is separated from the neural ectoderm at its junction with the skin ectoderm to form the *neural crest*
- the CNS develops from the neural tube
- the neural crest gives rise to all peripheral ganglia, the pia and the arachnoid, adrenal medulla, and the receptor cells of the carotid body

- phylogenetically older parts of the brain (e.g. hippocampus, spinal cord) develop mainly by cell proliferation from a small number of progenitor cells near the ventricular surface
- newer structures (e.g. neocortex) develop mainly by cellular migration

### Organization of the mature brain

<table>
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<th>Primary brain vesicle</th>
<th>Secondary brain vesicle</th>
<th>Contents in mature brain</th>
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<td>Rhombencephalon (hindbrain)</td>
<td>Myelencephalon</td>
<td>Caudal part of the Medulla</td>
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<td></td>
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<td>Oblongata</td>
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<tr>
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<td>Metencephalon</td>
<td>Pons</td>
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<td></td>
<td>Oral part of the Medulla</td>
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<td>Cerebellum</td>
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<tr>
<td>Mesencephalon (midbrain)</td>
<td>Mesencephalon</td>
<td>Tectum (superior and inferior colliculi)</td>
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<td>Basis Pedunculi</td>
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<td></td>
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<td>Tegmentum (red nucleus, fibre tracts)</td>
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<tr>
<td>Prosencephalon (forebrain)</td>
<td>Diencephalon</td>
<td>Thalamus</td>
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<td>Epithalamus (inc. pineal gland, and habenular gland)</td>
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<td></td>
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<td>Hypothalamus (inc. pituitary gland)</td>
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<td>Subthalamus</td>
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<td>Telencephalon</td>
<td>Cerebral Hemispheres and cortex</td>
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<td>Olfactory system (rhinencephalon)</td>
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<td></td>
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<td>Corpus striatum</td>
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<td>Medullary centre</td>
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<td></td>
<td>Pallium</td>
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</table>

**Paleocortex:** olfactory areas  
**Archicortex:** hippocampus, limbic system  
**Neocortex:** makes up 90% of the cerebral cortex
Brainstem

- consists of:
  1. medulla oblongata
  2. pons
  3. midbrain
- fourth ventricle is partly in the medulla and partly in the pons

Medulla Oblongata

- rests on the basilar portion of the occipital bone and concealed from above by the cerebellum
- consists of a closed portion containing a continuation of the central canal of the spinal cord, and an open portion in which the fourth ventricle is located
- contents:
  1. pyramid - consists of corticospinal fibres (a.k.a. pyramidal tract)
  2. the olive - marks the position of the inferior olivary nucleus
  3. fasciculi gracilis and cuneatus
  4. cranial nerves:
     a) abducens (VI)
     b) facial (VII)
     c) vestibulocochlear (VIII)
     d) glossopharyngeal (IX)
     e) vagus (X)
     f) accessory (XI)
     g) hypoglossal (XII)

The Pons

- consists of a basal portion (a relay station between the cortex of a cerebral hemisphere and the opposite cerebellar hemisphere - involved in voluntary movement) and a dorsal portion (contains ascending and descending tracts)
- contents:
  1. trigeminal (V) nerve nucleus
  2. motor nucleus of facial (VII) nerve
  3. vestibular (VIII) nuclei
  4. abducens (VI) nerve nucleus
  5. isthmus of brain stem - contains the lateral lemniscus which is the main auditory tract of the brain stem
  6. reticular formation
  7. locus coerules - lies at the rostral end of the fourth ventricle
  8. trapezoid body - contains acoustic fibres
  9. medial longitudinal fasciculus

Midbrain

- extends from the pons to the mammillary bodies of the diencephalon
- contents:
  1. inferior and superior colliculi:
a) the inferior colliculus is a relay nucleus on the auditory pathway to the thalamus and thence to the cerebral cortex  
b) the superior colliculus is involved in the voluntary control of ocular movements, and in movements of the eyes and head in response to visual and other stimuli  

2. oculomotor (III) nerve  
3. trochlear (IV) nerve  
4. raphe nuclei  
5. red nucleus  
a) motor nucleus; has afferents from cerebellum and cerebral cortex  
6. substantia nigra  
7. ventral tegmental area  
8. crus cerebri  

The Substantia Nigra  
• large nucleus situated between the tegmentum and the basis pedunculi throughout the midbrain, and extending into the subthalamic region of the diencephalon  
• the dopaminergic cells composing the pars compacta contain granules of melanin  

Afferent pathways:  
• corpus striatum  
• subthalamic nucleus  
• raphe nuclei of midbrain  
• pontine reticular formation  

Efferent pathways:
- neostriatum (caudate nucleus)
- amygdaloid body in the temporal lobe

**Function**
- probably has a regulatory effect on the neostriatum through the action of dopamine as a neurotransmitter

**The mesolimbic dopaminergic system**
- the *ventral tegmental area*, between the substantia nigra and the red nucleus, is a population of dopaminergic neurones
- originates in area A10
- innervates:
  - olfactory tubercle
  - septal nuclei
  - stria terminalis
  - cingulate cortex
  - parahippocampal gyrus

**Clinical correlations**

**Medial medullary syndrome**
- results from occlusion of the medullary branch of the vertebral artery
- results in:
  - contralateral hemiparesis
  - contralateral disturbance of the sensations of position and movement
  - paralysis of the tongue is ipsilateral, and deviation is towards the affected side

**Lateral medullary (Wallenberg’s) syndrome**
- due to occlusion of a vessel supplying the lateral area of the medulla
- results in:
  - ipsilateral loss of pain and temperature in the area of distribution of the trigeminal nerve
  - contralateral sensory loss - touch sensation is diminished rather than abolished (since the medial lemniscus is intact)
**Reticular formation**
- consists of a portion of the brain stem where the fibres present a ‘netlike’ appearance
- receives data from most of the sensory systems and has efferent connections with all levels of the CNS
- contributes to sleep, the motor system of the brain and spinal cord, and the regulation of visceral activity

**Raphe nuclei**
- the neurones of the raphe produce serotonin and use this as a neurotransmitter
- Afferents:
  - spinal cord
  - primary motor cortex of the frontal lobe
  - parietal lobe
  - vestibular nuclei
  - cerebellar nuclei
  - periaqueductal grey matter
- Efferents:
  - thalamus
  - spinal cord
activity of the raphe nuclei induces sleep, due to release of serotonin in more rostral parts of the brain

- electrical stimulation of the periaqueductal grey matter or the nucleus raphe magnus results in loss of pain sensation
- encephalins are released at synapses in the periaqueductal grey matter, the raphe nuclei, and the substantia gelatinosa in the spinal cord - the analgesic effects of these chemicals requires integrity of the raphe spinal tract

The Reticular Activating System (RAS)

- sensory data conveyed by the lemniscal system (medial, spinal, and trigeminal lemnisci) when projected from the thalamus to the somaesthetic cortical area, is interpreted in a specific manner with respect to the nature of the stimulus
- much of the cortex is stimulated, with an effect on levels of consciousness and on alerting reactions to sensory stimuli
- impulses from the trigeminal area of distribution have a significant effect on consciousness
- some general anaesthetics are thought to suppress transmission through the RAS, although conduction continues along lemniscal routes
- prolonged coma results from damage to the pontine or mesencephalic reticular formation

The Locus coeruleus

- cells contain large quantities of noradrenaline

  - Afferents:
    - some raphe nuclei
    - hypothalamus
    - amygdala and cingulate gyrus

  - Efferents:
    - cerebral cortex
    - diencephalon
    - brain stem
    - cerebellum
    - spinal cord
The Diencephalon

Structure
- consists of 4 components on each side:
  1. thalamus:
     a) subdivided into nuclei which have different afferent and efferent connections
  2. subthalamus:
     a) consists of the subthalamic nucleus, and also parts of the reticular formation and substantia nigra
  3. epithalamus:
     a) includes the pineal gland, and structures concerned with autonomic responses to emotional changes
  4. hypothalamus:
     a) the main cerebral centre for integrative control of the autonomic nervous system and of several endocrine glands
     b) the neurohypophysis which includes part of the pituitary gland is an outgrowth of the hypothalamus

Thalamus
- there are a number of thalamic nuclei, all of which except the reticular nucleus sends axons to the cerebral cortex
- there are few if any connections between the nuclei of the thalamus

Intralaminar Nuclei
1. centromedian nucleus
2. parafascicular nucleus

Ventral Group of Nuclei
1. Medial geniculate body
   a) involved in discriminative aspects of hearing
2. Lateral geniculate body/ nucleus (LGN)
   a) contains a detailed point-to-point projection of the retina
   b) involved in awareness of visual stimuli and the discriminative and mnemonic aspects of vision
3. Ventral Posterior Nucleus
   a) part of the pathway for conscious appreciation of sensations arising from skin, muscles, and internal parts of the body
   b) contains a topographical projection of the contralateral half of the body
4. Ventral Lateral Nucleus
5. Ventral Anterior Nucleus
6. Ventral Medial Nuclei
Posterior group of nuclei
1. part of the pulvinar
2. part of the medial geniculate body
3. suprageniculate nucleus
4. nucleus limitans

Lateral group of nuclei
1. Lateral Dorsal Nucleus
   a) part of the limbic system
2. Lateral Posterior Nucleus
   a) projects to the somatosensory association cortex of the parietal lobe
3. Pulvinar

Medial group of nuclei
1. Mediodorsal Nucleus
   a) part of the limbic system and contributes to those aspects of emotions considered as ‘moods’
   b) lesions around the third ventricle involving the mediodorsal nucleus are seen in Korsakoff’s syndrome and this area probably has a role in memory
   c) memory deficits have been reported following surgical destruction of the mediodorsal thalamic nuclei
2. Medioventral Nucleus
   a) part of the limbic system

Anterior group of nuclei
1. consists of three nuclei which are considered to be part of the limbic system

Subthalamus
1. sensory fasciculi
2. rostral extensions of midbrain nuclei
3. fibre bundles from the cerebellum and globus pallidus
4. subthalamic nucleus
   a) a motor nucleus
   b) a lesion in this nucleus results in hemiballismus

Epithalamus
1. habenacral nuclei
2. connections with the pineal gland
Hypothalamus

- surrounds the third ventricle
- functions:
  - autonomic control of basic body functions, e.g., heart, bowel, blood pressure
  - regulation of body temperature
  - regulation of food and water intake
  - experience of pleasure
  - rage and aversion
- the amygdala and hypothalamus have sex-specific patterns of neuronal and dendritic development
- the anterior hypothalamus is involved in the relaxation response
- the posterior hypothalamus is involved in the fight-or-fright response

Hypothalamic damage

- uncontrolled laughter (sham mirth) occurs in hypophyseal and hypothalamic tumours
- hypothalamic rage (sham rage) due to stimulation of hypothalamic nucleus

Hypothalamic nuclei

1. Supraoptic nucleus
2. Paraventricular nucleus
   a) involved in the eating of certain types of food
3. Suprachiasmatic nucleus
   a) forms the brain’s timepiece; keeps an approximate 24 hr clock
4. Ventromedial nucleus
   a) satiety centre which inhibits food intake
   b) controls parasympathetic activities
5. Dorsomedial nucleus
6. Infundibular nucleus
7. Premammillary nucleus
8. Mammillary body and posterior nucleus
9. Lateral nucleus
   a) involved in the stimulation of eating and control of drinking
   b) controls sympathetic activities, and is involved in the somatic correlates of heightened emotionality

Efferent pathways

1. periventricular fibres
2. dorsal longitudinal fasciculus
3. mamillothalamic fasciculus
**Amygdala**

- ‘the seat of social and emotional intelligence’
- consists of two main nuclei - **medial** and **lateral**

**Medial amygdala**

- has afferents from olfactory tract
- rich in encephalin-containing cells

**Lateral amygdala**

- able to modify output from hypothalamus and initiate appropriate higher functions, i.e. hypothalamus signals hunger and the amygdala signals the correct response from the body

**Afferents**

- the contralateral amygdala
- dopaminergic brain stem nuclei
- frontal association area
- lateral olfactory stria
- noradrenergic brain stem nuclei
- serotonergic brain stem nuclei
- septal nucleus
- temporal association area

**Efferents**

- hypothalamus
- septal nucleus
- corpus striatum
- frontal association area
- lateral olfactory stria
- temporal association area
- thalamus

**The Hippocampus**

**Structure**

- made up of 3 layers:
  i) molecular layer (outer)
  ii) pyramidal layer
  iii) polymorphic layer (inner)

**Afferents**

- olfactory projections
- amygdala
- frontal lobe
• temporal lobes:
  • dendate gyrus
  • hippocampus
  • parahippocampal gyrus

Efferents
• thalamus
• septal nuclei
• medial hypothalamus

Functions
• main role is that of attention, information processing, memory, new learning, cognitive mapping of the environment
• prevents extremes of arousal by maintaining a state of quiet alertness
• most complex organically-produced hallucinations are caused by tumours of the most anterior part of the temporal lobe (including the amygdala and hippocampus)
• left sided lesions affect verbal memory
• right sided lesions affect visual memory

Septal nuclei
• consist of two nuclei:
  1. Nucleus of the diagonal band of Broca
  2. Nucleus of the medial septum
• involved with memory and arousal

Anterior cingulate gyrus
• associated with processing and modulating the expression of emotional nuances, emotional learning and vocalization, formation of long term attachments, and maternal behaviour
The Limbic System

- described by Broca in 1878

**Primary nuclei**
1. hypothalamic nuclei
2. amygdaloid nucleus
3. hippocampus
4. septal nuclei
5. thalamic nuclei:
   a) *anterior, lateral dorsal, and medioventral nuclei*
6. mamillary bodies
7. superior central nucleus
8. ventral tegmental area
9. raphe nucleus

**Cortical areas**
1. cingulate gyrus
2. hippocampal formation:
   a) dentate nucleus
   b) hippocampus
c) parahippocampal gyrus
3. olfactory tubercle
4. secondary olfactory area
5. subcallosal gyrus
6. indusium griseum
7. paraterminal gyrus

Connecting tracts
1. cingulum
   a) hippocampus to cingulate gyrus
2. anterior commissure
3. dorsal longitudinal fasciculus
4. stria terminalis
   a) hypothalamus to amygdala
5. stria medullaris thalami
6. amygdalofugal bundle
   a) hypothalamus to amygdala
7. fornix
   a) hypothalamus to hippocampus
8. medial forebrain bundle
   a) hypothalamus to septal nuclei
   b) involved in the positive reinforcement of behaviours
9. mamillothalamic tract
   a) mamillary bodies (hypothalamus) to anterior thalamic nucleus

Circuits of the limbic system
- the largest components contain a ring of interconnected neurons called the circuit of Papez, which links the neocortex to the limbic system via the cingulate gyrus
  - hippocampus
  - mamillary body
  - thalamus
  - cingulate gyrus
- input:
  - neocortex
  - thalamus
  - septal area
  - raphe nuclei
  - ventral tegmental area
  - catecholamine nuclei of the reticular formation
- output:
  - neocortex
  - regions of the reticular formation that influence the autonomic system indirectly
Functional considerations

- bilateral removal of the temporal lobes (including the hippocampal formations and amygdaloid bodies) is followed by docility and lack of emotional responses such as fear or anger
  - there is increased sexual activity, often perverted
- lesions to the amygdala produce similar changes, although the sexual behaviour is less affected
- electrical stimulation of the amygdala in humans induces feelings of fear or anger
- summary of functions:
  - strong affective responses such as fear, anger, and sexual behaviour
  - changes in visceral function:
    - changes in gastrointestinal movements and secretion
    - piloerection
    - pupillary dilatation
    - changes in respiratory movements
  - role in memory (especially the hippocampus)
  - the hippocampus may also have a role in the sleep-wake cycle

- memory disturbance occurs in damage to:
  - mammillary bodies
  - hippocampus
  - fornix
  - substantia innominata
The Corpus Striatum
- a substantial region of grey matter near the base of each cerebral hemisphere
- the term ‘basal ganglia’ refers to the corpus striatum, subthalamic nucleus, and substantia nigra
- consists of:
  1. caudate nucleus
  2. lentiform nucleus
     a) putamen
     b) globus pallidus

- the paleostriatum (a.k.a. pallidum) refers to the globus pallidus in mammals
- the neostriatum (a.k.a. striatum) refers to the putamen and the caudate nucleus

Connections
1. Neostriatum
   a) Afferent:
      i) cerebral cortex, especially the frontal and parietal lobes
      ii) thalamus, especially the centromedian nucleus
      iii) substantia nigra - from the pars compacta; provides significant dopaminergic input to the neostriatum
   b) Efferent:
      i) globus pallidus
2. **Paleostriatum**
   a) Afferent:
      i) globus pallidus
   b) Efferent:
      i) hypothalamus
      ii) reticular formation
      iii) substantia nigra
      iv) subthalamic nucleus
      v) ventral lateral nucleus of the thalamus > projects to the premotor cortex in the frontal lobe
      vi) ventral anterior nucleus of the thalamus

**Functions**
- the striatum inhibits the pallidum
- the pallidum inhibits the thalamocortical neurons
- GABA is the inhibitory transmitter
- when no movements are being made, the cells of the striatum are quiet and the cells of the pallidum are active
- shortly before a movement, the above situation is reversed
- removal of pallidal inhibition allows the ventral thalamic nuclei to be stimulated by other afferent fibres, most of which come from the premotor area of cortex
- the nigrostriatal dopaminergic neurons are active all the time

**Dyskinesias**
- **Huntington’s chorea:**
  - neuronal degeneration in the corpus striatum, most marked in the neostriatum
- **Athetoid movements** are most associated with pathological changes in the neostriatum and cerebral cortex
- In **Wilson’s disease**, the degenerative changes are most pronounced in the putamen
The Cerebellum

Central nuclei
1. fastigial nucleus
2. globose nucleus } in apes and humans, represents the nucleus
3. emboliform nucleus } interpositus
4. dentate nucleus
   a) most prominent of the nuclei

The medullary centre
• contains fibres from the cerebellar hemispheres which are decussating

Functional anatomy
1. vestibulocerebellum
   a) consists of the flocculonodular node and a region of the vermis known as the uvula
   b) receives input from the vestibular nerve and nuclei
   c) influences motor neurons through the vestibulospinal tract, the medial longitudinal fasciculus, and reticulospinal fibres
   d) involved in adjustment of muscle tone and maintenance of equilibrium
2. spinocerebellum
a) consists of parts of the vermis and adjacent parts of the hemispheres
b) site of termination of the spinocerebellar tracts, which convey proprioceptive and other sensory information
c) receives information from all three sensory nuclei of the trigeminal nerve, and also the red nucleus
d) involved in the control of muscle tonus and synergy of collaborating muscles

3. **pontocerebellum**
   a) the lateral parts of the hemispheres and the superior vermis in the posterior lobe; also the dentate nucleus
   b) fibres pass through the red nucleus
   c) ensures a smooth and orderly sequence of muscular contractions and the intended precision in the force, direction, and extent of volitional movements
   d) connections are ipsilateral

**Cells of the cerebellum**
- **glomerulus:**
  - mossy fibre
  - dendrites of granule cells
  - axon of Golgi cell
- **Purkinje cells:**
  - use GABA as neurotransmitter
  - axons are the only cells leaving the cortex
  - terminate in central nuclei of cerebellum
  - also send efferents to:
    - thalamus
    - Golgi cells
    - reticular neurones
- intracortical circuits are inhibitory
- most input to the cortex is excitatory

**The Extrapyramidal System**
- includes:
  - basal ganglia (caudate and lentiform nucleus)
  - cerebellum:
    - dentate nucleus
  - brain stem nuclei:
    - substantia nigra
    - midbrain nuclei
    - tectal nuclei
    - lateral vestibular nucleus (Reiter’s nucleus)
The Pyramidal System

- originates in the motor cortex
- descends through:
  - corona radiata
  - internal capsule
  - ventral midbrain
  - medulla oblongata (forms the pyramids)
- 85% of the fibres decussate in the medulla to form the lateral corticospinal tract
- 15% of the fibres form the ventral corticospinal tract
- sends fibres to:
  - red nucleus
  - reticular formation
  - pontine nuclei
- terminates in:
  - interneurones of dorsal horn (laminae IV, V, and VI)
  - ventral horn (lamina VII) – contains Renshaw cells (interneurones)

Clinical considerations

- degeneration leads to:
  1. ataxia
  2. wide-based gait
  3. loss of vibration sense
  4. loss of deep pain sensation
  5. positive Romberg’s sign
The Cerebral Cortex

The Frontal Lobes

Frontal Operculum

- consists of areas 44, 45, and 47
- **Broca’s area** – on the dominant side, and consists of areas 44 and 45
  - a lesion in this area can lead to Broca’s/Expressive nonfluent aphasia
  - lesions in the non-dominant frontal operculum can lead to dysprosody

Superior mesial region

1. **supplementary motor area (SMA)**
2. **anterior cingulate cortex**

- lesions of the left or right superior mesial region can lead to akinetic mutism

Inferior mesial region

1. **orbital cortex**
   a) functions include:
      i) social behaviour
      ii) personality
   b) lesions of the orbital cortex (either side) can lead to a form of acquired sociopathy
2. **basal forebrain:**
   a) contains the following nuclei:
      i) diagonal band of Broca
      ii) nucleus accumbens
      iii) septal nuclei
      iv) substantia innominata
   b) lesions of the basal forebrain (either side) can lead to amnesia (retrograde and anterograde) and confabulation

Dorsolateral prefrontal cortex (DLPFC)

- functions include:
  - problem-solving
  - perceptual judgement
  - memory
  - programming and planning sequences of behaviour
  - verbal regulation
  - level of response emission
  - adaptability of response pattern
  - tertiary level of motor control
- lesions in this region can cause:
  - abnormal cognitive executive functions
  - impairment of verbal (left) or non-verbal (right) intellectual functions
  - memory impairment affecting recency and frequency judgements
  - poor organization
• poor planning
• poor abstraction
• disturbances in motor programming
• impaired verbal fluency (left-sided lesions)
• impaired design fluency (right-sided lesions)

Frontal lobe syndrome
• personality change:
  • disinhibition
  • reduced social and ethical control
  • sexual indiscretions
  • poor judgement
  • elevated mood (fatuous euphoria)
• perseveration
• contralateral spastic paresis
• ‘Utilization syndrome’
• palilalia
• impairment of attention, concentration, and initiative
• motor Jacksonian fits
• Witzelsucht (inappropriate jocularity)
• aphasia
• primary motor aphasia
• motor agraphia
• ipsilateral optic atrophy
• anosmia
• magnetism (ask pt. to draw a clock face)
• grasp reflex, and other primitive reflexes
• urinary incontinence if the lesion is lateral
The Parietal lobes

Temporoparietal junction
- left-sided lesions:
  - receptive aphasia
- right-sided lesions:
  - phonagnosia (inability to recognise familiar voices)
  - amusia (inability to recognise and process music)

Inferior parietal lobule
1. **angular gyrus**
2. **supramarginal gyrus**
   - left-sided lesions (affecting the arcuate fasciculus):
     - conduction aphasia – patient cannot repeat what is said to them
     - tactile agnosia
     - dysphasia
     - right-left disorientation
     - finger agnosia (can be elicited by the ‘In-Between Test’)
     - agraphia
     - body image disorders
     - sensory extinction
     - astereognosia (inability to recognise objects by palpation)
     - alexia
     - dysgraphesthesia (inability to recognise letters or numbers written on the hand)
   - right-sided lesions:
     - anosognosia (lack of awareness of disease, particularly of hemiplegia)
     - neglect
     - tactile agnosia
     - asomatognosia (inability to recognize parts of the body)
     - constructional dyspraxia
   - Angular gyrus:
     - inability to read
     - inability to write

Gerstmann’s syndrome
- lesion of dominant parietal lobe:
  1. right-left disorientation
  2. finger agnosia
  3. dysgraphia
  4. dyscalculia
The Temporal lobes

Superior temporal gyrus
• area 22, forms, on the left, Wernicke’s area
  • lesions here can cause a receptive aphasia

Posterior Inferolateral region
1. post. portion of the middle temporal gyrus
2. post. portion of the inferior temporal gyrus
3. post. portion of the fourth temporal gyrus

• lesions in this region can lead to:
  • prosopagnosia
  • impaired object recognition

Anterior Inferolateral region
1. ant. portion of the middle temporal gyrus
2. ant. portion of the inferior temporal gyrus
3. ant. portion of the fourth temporal gyrus
4. temporal pole

• left-sided lesions can lead to:
  • anomia
  • defects in accessing the reference lexicon
• right-sided lesions may lead to:
  • inability to name facial expressions
• bilateral lesions lead to:
  • retrograde amnesia

The Mesial Temporal Region
1. parahippocampal gyrus (areas 27 and 28)
2. amygdala
3. entorhinal cortex
4. hippocampus

• left-sided lesions:
  • anterograde amnesia affecting verbal information
• right-sided lesions:
  • anterograde amnesia affecting non-verbal information
• bilateral lesions:
  • verbal and non-verbal anterograde amnesia

• Kluver-Bucy (due to bilateral damage of amygdala, uncus, and hippocampus)
  • social and emotional agnosia (unable to discern the meaning or significance of common objects)
• hypermetamorphosis/ hyperorality (perseverative oral exploration)
• sexual indiscretion
• loss of fear, leading to aggression
• affective blunting
• visual agnosia
The Occipital lobes
1. primary visual cortex
2. visual association cortices

- lesions of the dorsal region and adjoining parietal region can lead to partial (unilateral) or full-blown (bilateral) Balint’s syndrome:
  1. simultanagnosia (the ability to understand individual details of a scene, but is unable to recognize the full meaning)
  2. ocular apraxia or psychic gaze paralysis
  3. optic ataxia

- bilateral dorsal lesions:
  - astereopsis
  - impaired visual motion perception

- depending on site of lesion, the following can occur:
  - achromatopsia (loss of colour perception) – due to damage to the lingual gyri
  - hemiachromatopsia
  - acquired dyslexia
  - apperceptive visual agnosia
  - visual agnosia
  - prosopagnosia (unable to recognize familiar faces) - can occur with bilateral inferior occipital lesions
  - disturbances of visual recognition
  - complex visual hallucinations
  - visual field defects
  - visual disorientation
  - Anton’s syndrome - denial of visual disability and confabulation of visual detail
The Basal Ganglia

Components
1. corpus striatum
   a) caudate nucleus
   b) lentiform nucleus
      i) globus pallidus
      ii) putamen
2. amygdaloid nucleus
3. claustrum

Connections
1. Afferents:
   a) caudate nucleus
   b) cerebral cortex
   c) putamen
   d) substantia nigra
2. Efferents:
   a) globus pallidus
   b) hypothalamus
   c) reticular formation
   d) substantia nigra
   e) subthalamus
   f) thalamic nuclei

Fronto-subcortical circuits
- Alexander et al. (1986)
- connect the frontal cortex with the basal ganglia and the thalamus
- involved in:
  - motor activity
  - eye movements
  - behaviour
- the overall structure is:
  - frontal lobe cortex ➔ caudate nucleus ➔ globus pallidus/ substantia nigra ➔ thalamus ➔ frontal lobe cortex

<table>
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<th>Circuit</th>
<th>Origin</th>
<th>Function</th>
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<td>SMA</td>
<td>motor function</td>
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<td>2. Oculomotor circuit</td>
<td>frontal eye fields</td>
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<td>DLPFC</td>
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<td>anterior cingulate cortex</td>
<td>motivation</td>
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</table>
Somatosensory systems

Spinothalamic system

- carries information from:
  1. mechanoreceptors (crude touch, pressure, tickle and itch, sexual sensation)
  2. thermoreceptors (warm and cold sensation)
  3. pain receptors

Dorsal column system

- carries information only from mechanoreceptors:
  1. fine, precisely localised touch
  2. vibration
  3. kinaesthetic sensation
  4. fine pressure sensation
- contains thick myelinated fibres
The Cranial Nerves

I  Olfactory nerve

II  Optic nerve
- most optic tract fibres synapse in the thalamic lateral geniculate body
- those concerned with pupillary and ocular reflexes pass directly to the pretectal nucleus and superior colliculi
- from the lateral geniculate body the optic radiation passes, via the retrolenticular part of the internal capsule, to the visual cortex

III  Oculomotor nerve
- two main nuclei:
  1. main oculomotor nucleus – supplies all the extrinsic ocular muscles with the exception of the lateral rectus and superior oblique
  2. accessory parasympathetic nucleus (a.k.a. Edinger-Westphal nucleus) – sends preganglionic parasympathetic fibres to the constrictor pupillae and ciliary muscles

IV  Trochlear nerve
- supplies the superior oblique

V  Trigeminal nerve

Nuclei
1. main sensory nucleus
2. spinal nucleus
3. mesencephalic nucleus
4. motor nucleus

Sensory components
1. Ophthalmic Nerve
   a) frontal nerve
      i) upper eyelid
      ii) scalp (anterior to the lambdoid suture)
   b) lacrimal nerve
      i) lacrimal gland
      ii) lateral conjunctiva
      iii) upper eyelid
   c) nasociliary nerve
      i) eyeball
      ii) medial lower eyelid
iii) nasal skin
iv) nasal mucosa

2. **Maxillary Nerve**
   a) infraorbital nerve
      i) skin of the cheek
   b) superior alveolar nerve
      i) upper teeth
   c) zygomatic nerve
      i) skin of the temple
      ii) skin of the cheek

3. **Mandibular nerve**
   a) auriculotemporal nerve
      i) skin of the temple
   b) buccal nerve
      i) skin of the cheek
      ii) mucous membrane of the cheek
   c) inferior alveolar nerve
      i) lower teeth
      ii) lower lip
      iii) skin of the chin
   d) lingual nerve
      i) anterior 2/3 of the tongue
      ii) mucous membrane of the mouth

**Motor component**
- supplies:
  - muscles of mastication
  - anterior belly of the digastric
  - mylohyoid
  - tensor tympani
  - tensor veli palatini

**VI  Abducent nerve**
- supplies the lateral rectus muscle

**VII  Facial nerve**

Main motor nucleus
- supplies:
  - muscles of facial expression
  - auricular muscles
  - posterior belly of the digastric
  - stapedius
  - stylohyoid
- upper facial muscles receive bilateral innervation
Parasympathetic nuclei

1. **Lacrimal nucleus**
   a) lacrimal gland

2. **Superior salivary nucleus**
   a) nasal gland
   b) palatine gland
   c) sublingual gland
   d) submandibular gland

Sensory nucleus

- receives taste fibres, via the geniculate ganglion, from:
  - anterior 2/3 of the tongue
  - floor of the mouth
  - hard palate
  - soft palate

**Chorda tympani**

- this is a branch of the facial nerve given off before it passes through the stylomastoid foramen
- it joins the lingual branch of the mandibular division of the trigeminal nerve

**VIII Vestibulocochlear nerve**

**Cochlear nerve**

- fibres are the central processes of the cochlear spinal ganglion cells, terminating in the anterior and posterior cochlear nuclei

**Vestibular nerve**

- terminate in the lateral, medial, superior, and inferior vestibular nuclei

**IX Glossopharyngeal nerve**

**Main motor nucleus**

- supplies the glossopharyngeus

**Parasympathetic nucleus**

- receives input from:
  - hypothalamus
  - olfactory system
  - tractus solitarius nucleus
  - trigeminal sensory nucleus

**Sensory nucleus**

- receives taste from the posterior 1/3 of the tongue
X  **Vagus nerve**

Main motor nucleus
- supplies:
  - intrinsic muscles of the larynx
  - constrictor muscles of the pharynx

Parasympathetic nucleus
- receives input from:
  - hypothalamus
  - glossopharyngeal nerve
  - heart
  - lower respiratory tract
  - gastrointestinal tract, as far as the transverse colon
- supplies:
  - the heart
  - lower respiratory tract
  - GIT, as far as the distal 1/3 of the transverse colon

Sensory nucleus
- receives taste information from the interior ganglion of the vagus nerve
- sensation from the posterior 1/3 of the tongue

XI  **Accessory nerve**

Cranial root
- supplies, via the vagus nerve, muscles of the:
  - larynx
  - pharynx
  - soft palate

Spinal root
- supplies:
  - sternocleidomastoid
  - trapezius

XII  **Hypoglossal nerve**
- supplies:
  - intrinsic muscles of the tongue
  - styloglossus
  - hyoglossus
  - genioglossus
Major Neurochemical Pathways

<table>
<thead>
<tr>
<th>Neurotransmitter</th>
<th>Areas</th>
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<tr>
<td>Noradrenaline</td>
<td>A1-A7</td>
</tr>
<tr>
<td>Dopamine</td>
<td>A8-A15</td>
</tr>
<tr>
<td>5-HT</td>
<td>B1-B9</td>
</tr>
<tr>
<td>Acetylcholine</td>
<td>Ch1-Ch6</td>
</tr>
</tbody>
</table>

**Ascending Noradrenergic pathways**

**Origin**
- all the NA-containing neurones are situated in the lower brain stem:
  - locus coeruleus in the dorsal pons

**Termination**
- 3 ascending pathways terminate in:
  - ipsilateral cerebral cortex
  - thalamus
  - hypothalamus
  - limbic system
  - olfactory bulb
- the 4\(^{th}\) (descending) terminates in the cerebellar cortex
- the 5\(^{th}\) (descending) sends collaterals to the lower brain stem and then descends to the spinal cord

**Nigrostriatal dopaminergic pathway**

**Origin**
- A8 neurones in the reticular formation of the mesencephalon
- A9 neurones in the pars compacta of the substantia nigra

**Termination**
- caudate nucleus
- putamen
- amygdala

**Functions**
- sensorimotor coordination – part of the extrapyramidal motor system
Mesolimbic-mesocortical dopaminergic pathway

Origin
• A10 neurones in the ventral tegmental area of the mesencephalon

Termination
• nucleus accumbens
• olfactory tubercle
• stria terminalis
• lateral septum
• cingulate cortex
• medial prefrontal cortex

Function
• play a role in the regulation of behaviour by positive reinforcers

Basal forebrain cholinergic pathway

Origin
• Ch4 neurones in the nucleus basalis of Meynert
• Ch2 and Ch3 neurones in the diagonal band of Broca
• Ch1 neurones in the medial septal nucleus

Termination
• Ch4: cerebral cortex, amygdala, and corpus striatum
• Ch1 and Ch2: hippocampal formation
• Ch3: olfactory bulb

Brainstem cholinergic pathway

Origin
• Ch5 neurones in pedunculopontine nucleus
• Ch6 neurones in the laterodorsal tegmental nucleus

Termination
• thalamus
• cerebral cortex
• basal forebrain
• corpus striatum
• globus pallidus
• subthalamic nucleus
• substantia nigra
Functions
- Ch5 neurones are connected with extrapyramidal structures
- Ch6 neurones send more projections to the limbic system and the medial prefrontal cortex

Glutamate system

Origin
- cerebral cortical pyramidal cells
- hippocampal pyramidal cells
- primary sensory afferents
- cerebellar granule cells
- cerebellar climbing fibres

Ascending 5-HT system

Origin
- superior raphe nuclei:
  - caudal linear nucleus
  - dorsal raphe nucleus
  - median raphe nucleus
  - suprarenalicular nucleus

Termination
- forebrain structures:
  - suprachiasmatic nucleus
  - substantia nigra
  - limbic system
  - primary sensory areas of the cerebral cortex
  - association areas of the cerebral cortex

Functions
- implicated in sleep, temperature regulation, appetite, feeding, aggression, anxiety, sexual activity
- suggested that they may play a role in selective attention

GABA systems
- GABA is the principle inhibitory neurotransmitter
- formed from the transamination of alpha-ketoglutarate
- GABA reduces the likelihood that postsynaptic neurons will fire
- GABA systems’ normal inhibition of dopamine systems is lost in Huntington’s disease
- found in a number of major sites:
1. **spinal cord**
   a) mainly in the *substantia gelatinosa* of the grey matter of the dorsal horn

2. **cerebellum**
   a) *Purkinje cell layer* contains high concentrations of GABA
   b) it is believed that the Purkinje cells provide a GABA-ergic inhibitory outflow to Deiter’s nucleus (*lateral vestibular nucleus*)

3. **basal ganglia**
   a) particularly in the *substantia nigra, globus pallidus, and nucleus accumbens*
   b) believed to exert an inhibitory feedback controlling influence on the ascending dopaminergic nigro-striatal projection

4. **retina**
   a) found in the horizontal cell layer
   b) possible mediator of lateral inhibition

5. **thalamus**
   a) may be involved in the control of sensory traffic through the thalamus

---

**Other neurotransmitters**

**Glycine**
- an amino acid which has a powerful inhibitory neurotransmitter effect in the spinal cord – brain concentrations are 25% of spinal cord concentrations
- affects post-synaptic membranes
- it hyperpolarises motor neurones
- strychnine competes for the same receptor

**Substance P**
- is a peptide
- concentrated in the intestine and nervous tissue
- found in the spinal cord
- may be involved in neurotransmission
- most likely to be an excitatory neurotransmitter

**Endorphins**
- found in the substantia gelatinosa in the spinal cord and plays an important role in the modulation of pain
- include: DYNORPHIN A, MET-ENKEPHALIN

**CCK 8**
- found in cerebral cortex, hypothalamus, and limbic system

**Galanin**
- mainly inhibitory neuropeptide

**Nitric Oxide (NO)**
- also acts as a second messenger
Arterial Supply to the Brain

1. **Internal Carotid a.**
   a) hypophysial arteries
      i) comprise the pituitary portal system
   b) ophthalmic artery
      i) supplies the eye and other orbital contents
   c) posterior communicating artery
      i) forms part of the circle of Willis
   d) anterior choroidal artery
      i) supplies the choroid plexus, amygdala, hippocampus, globus pallidus, LGN, and internal capsule
      ii) said to be especially prone to thrombosis

2. **Middle Cerebral a.**
   a) frontal branch
   b) parietal branch
   c) temporal branch
d) a unilateral lesion of the auditory cortex causes no impairment of hearing because of the bilateral cortical projection from the organ of Corti

3. **Anterior Cerebral a.**
   a) anterior communicating a.
   b) pericallosal a.
   c) callosomarginal a.
   d) recurrent artery of Heubner
      i) contributes to the blood supply of the corpus striatum

4. **Vertebral a.**
   a) anterior spinal a.
   b) posterior spinal a.
   c) posterior inferior cerebellar a.
   d) basilar a.
      i) anterior inferior cerebellar a.
      ii) labyrinthine a.
      iii) pontine a.
      iv) superior cerebellar a.

5. **Posterior Cerebral a.**
   a) temporal branches
   b) calcarine branch
   c) parieto-occipital branch
   d) posterior choroidal a.

The Circle of Willis

- made up of:
  1. anterior cerebral a.
  2. anteromedial central a.
  3. posterior communicating a.
  4. posteromedial central a.
  5. posterior cerebral a.

Blood supply to the internal capsule

1. Anterior cerebral artery – supplies the inferior half of the anterior limb
2. Middle cerebral artery – supplies the superior halves of the anterior and posterior limbs
3. Anterior choroidal artery – supplies the posterior 2/3 of the posterior limb
4. Internal carotid artery – supplies the anterior 1/3 of the posterior limb

Blood supply to the optic radiation

1. Posterolateral branches of the posterior cerebral artery
2. Anterior choroidal artery
3. Posterior cerebral artery
Lower motor neuron lesions
• features include:
  1. flaccid paresis or paralysis
  2. weak or absent tendon reflexes
  3. muscle atrophy
  4. fibrillation potentials, detected on electromyography
  5. sprouting at nodes of Ranvier and at motor end plates (on biopsy)

Upper motor neuron lesions
• features include:
  1. weak or absent voluntary movements
  2. atrophy does not occur
  3. spasticity, due to the continuous operation of the stretch reflex
  4. exaggerated tendon reflexes
  5. upgoing plantar reflex
  6. superficial reflexes are suppressed or absent (e.g. abdominal & cremasteric reflexes)

The Light and Accommodation reflexes
• involves:
  1. Short ciliary nerves
  2. Ciliary ganglion
  3. Oculomotor nerve
  4. Pre-tectal area
  5. Edinger-Westphal nucleus
  6. Posterior commissure
  7. Optic tract
  8. Lateral Geniculate nucleus

The corneal reflex
• involves:
  1. afferent fibres are in the ophthalmic nerve
  2. efferent fibres are in the facial nerve
  3. spinal nucleus of the trigeminal nerve

Nystagmus
• a rhythmic oscillation of the eyes
• it is a sign of disease of either the ocular or the vestibular systems and its connections
• it is defined as pendular or jerk
Pendular nystagmus
- movements to and fro which are similar in velocity and amplitude
- it is binocular, and occurs in all directions of gaze
- it is due to a congenital lesion, or where there is poor fixation of gaze (e.g. severe visual impairment)

Jerk nystagmus
1. **Vestibular**
   a) only occurs in one direction of gaze (away from the side of the lesion) and is made worse by gaze in that direction
2. **Brainstem**
   a) up-beat nystagmus is associated with lesions of the floor of the fourth ventricle
   b) down-beat nystagmus (rare) is associated with compressive lesions of the foramen magnum
3. **Cerebellar nystagmus**
   a) is towards the side of the lesion

Horizontal
- results from disease of the CNS e.g.
  - MS
  - vertebrobasilar ischaemia
  - Wernicke’s encephalopathy
  - phenytoin toxicity

Vertical
- is due only to central lesions

Papilloedema
1. Raised ICP
   - SOL
   - abscess
   - hydrocephalus
   - haemorrhage
   - haematoma
   - benign intracranial hypertension
2. Obstruction of ocular venous drainage
   - central retinal vein occlusion
   - cavernous sinus thrombosis (e.g. in polycythaemia)
3. Systemic disorders
   - hypertension
   - vasculitis, e.g. temporal arteritis
   - hypercapnia
   - hypopituitarism
4. Optic nerve damage
• demyelination (optic neuritis)
• ischaemia – anterior ischaemic optic neuropathy
• toxins (e.g. methanol)

5. Infiltration of the optic disc
• sarcoidosis
• glioma
• lymphoma
• leukaemia

6. Other
• posterior uveitis
• posterior scleritis

**Reflexes**

- **Biceps:** C5,6
- **Triceps:** C6,7
- **Supinator:** C5,6
- **Finger:** C8
- **Cremasteric:** L1,2

- **Knee jerk:** L3,4
- **Ankle jerk:** S1,2
- **Plantar:** S1,2

**Cranial nerve lesions**

**Oculomotor nerve**

- lateral strabismus (due to unopposed action of the lateral rectus)
- inability to direct eye medially or vertically
- ptosis
- dilation of pupil (if parasympathetic fibres interrupted)
- loss of light and accommodation reflexes

**Abducens nerve**

- medial strabismus
- inability to direct eye laterally
- diplopia