

The Reticular Formation Consciousness & Disorders

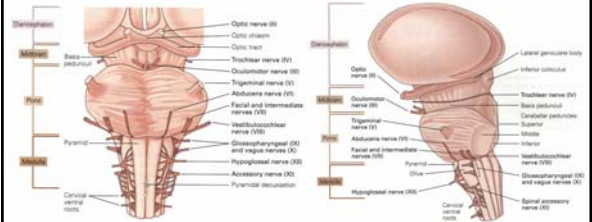
Martin Paré

Assistant Professor
Physiology & Psychology

<http://brain.phgy.queensu.ca/pare>

Organization of the Brain Stem

The Brain Stem contains three subdivisions: the Midbrain, the Pons, and the Medulla Oblongata, from which originate the cranial nerves.



Organization of the Brain Stem

The brain stem contains three types of structures:

- The nuclear groups associated with the cranial nerves
- The long tracts (motor and sensory)
- The Reticular Formation

The Reticular Formation

The reticular formation represents a rostral extension of the interneuronal network in the intermediate gray matter of the spinal cord.

Although it appears as a loosely organized collection of cells, the reticular formation is highly organized and differentiated, consisting of distinct neuronal populations with specific functions.

Anatomy of the Reticular Formation

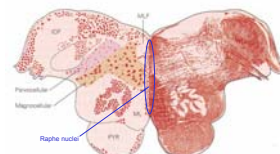
The reticular formation can be divided into three longitudinal zones arranged in a lateral-to-medial sequence:

- The lateral (Parvocellular) zone
- The medial (Magnocellular) zone
- The Raphe nuclei



Anatomy of the Reticular Formation

The lateral reticular formation contains relatively small neurons that are positioned close to the motor nuclei of the cranial nerves. These interneurons help coordinate autonomic reflexes and simple behavior mediated by the cranial nerves.



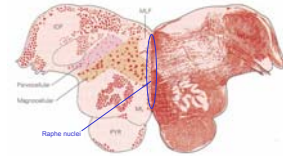
Anatomy of the Reticular Formation

The medial reticular formation contains relatively large neurons that are the source of most of the long ascending and descending projections of the reticular formation. These projection neurons modulate motor responses and posture, pain sensation, autonomic functions, and arousal.



Anatomy of the Reticular Formation

The Raphe nuclei are thin plates of neurons in and adjacent to the sagittal plane. These cells are also involved in modulating the action of neurons involved in motor responses, pain, autonomic functions, and arousal.



Reticular Formation Interneurons

Neurons in the ventrolateral medullary reticular formation are important for coordinating a variety of stereotyped behaviors related to the visceral functions of the vagus nerve:

- Gastrointestinal responses (swallowing, vomiting)
- Respiratory activities (respiratory rhythm, coughing, hiccuping, sneezing)
- Cardiovascular responses (baroreceptor reflexes and responses to cerebral ischemia and hypoxia)

Reticular Formation Interneurons

The coordination of orofacial motor responses involves the lateral medullary and pontine reticular formation:

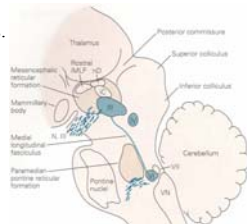
- Chewing is coordinated by neurons near the trigeminal motor nucleus.
- Lip movements are coordinated by neurons near the facial motor nucleus.
- Movements of the tongue are coordinated by neurons near the hypoglossal nucleus.

These neurons coordinate these movements with each other as well as with respiratory movements, and that they are highly responsive to sensory feedback from the nucleus of the solitary tract and the trigeminal sensory nuclei.

Reticular Formation Interneurons

The paramedian reticular formation of the pons adjacent to the abducens nucleus and in the midbrain adjacent to the oculomotor nucleus coordinate eye movements:

- The pontine reticular formation controls horizontal eye movements.
- The midbrain reticular formation controls vertical eye movements.



Reticular Formation Interneurons

Neurons in the lateral zone of the reticular formation surrounding the facial motor nucleus are also important in organizing emotional facial expressions (smiling and crying).

Reticular Formation Interneurons

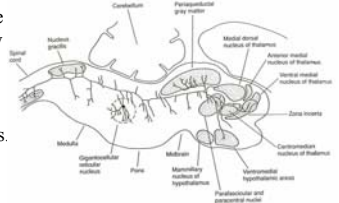
In summary, just like the intermediate gray matter of the spinal cord coordinate the sensory and motor functions of the spinal nerves related to their segmental level, the reticular formation of the brain stem contains ensemble of neurons that coordinate reflexes and simple stereotyped motor patterns mediated by the adjacent cranial nerves.

Note that these simple motor responses may be assembled into more complex behaviors under voluntary control by the forebrain, but the precise patterns of motor responses are organized locally in the brain stem.

Reticular Formation Projection Neurons

Many reticular neurons have extensive and complex axonal projections. They may innervate multiple levels of the spinal cord, send collaterals to the brainstem and diencephalon, have bifurcating axons that give rise to both ascending and descending connections.

They may also have large dendritic fields that allow them to receive synaptic inputs from ascending sensory pathways and descending cortical axons.



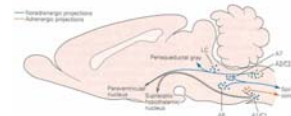
Reticular Formation Modulatory Systems

The reticular formation is composed of morphologically and biochemically defined groups of projection neurons that form 5 different modulatory systems:

- Noradrenergic
- Adrenergic
- Dopaminergic
- Serotonergic
- Cholinergic

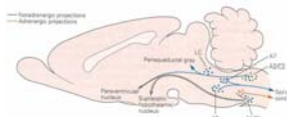
Noradrenergic System

Noradrenergic neurons are located into two columns, one dorsal and one ventral. In the medulla, the nucleus ambiguus (A1 group) and the nucleus of the solitary tract (A2 group) project to the hypothalamus and control cardiovascular and endocrine functions.



Noradrenergic System

Neurons in the ventrolateral reticular formation of the pons (A5 & A7 groups) provide mainly projections to the spinal cord that modulate autonomic reflexes and pain sensation.



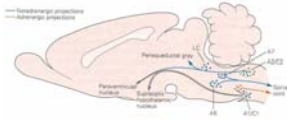
Noradrenergic System

The largest collection of noradrenergic neurons is within the pons in the locus ceruleus. The locus ceruleus projects to every major regions of the brain and spinal cord. Its activity helps maintaining vigilance and it enhances responsiveness to novel stimuli. It influences both arousal in the forebrain and pain perception in the brain stem and spinal cord.



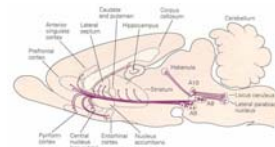
Adrenergic System

Some neurons in the medulla identified as catecholaminergic were later found to synthesize epinephrine. Adrenergic cells in the nucleus ambiguus (C1) project to the spinal cord and provide tonic excitatory input to vasomotor neurons. Those in the nucleus of the solitary tract (C2) project to parabrachial nucleus, which is involved in gastrointestinal functions.



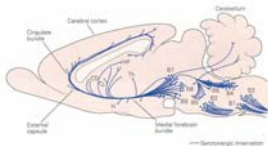
Dopaminergic System

The largest group of dopaminergic neurons is in the midbrain, including the substantia nigra (*pars compacta*) and the adjacent ventral tegmental area (A8-A10). The mesostriatal pathways is important in the initiation of motor responses, whereas the mesocortical and mesolimbic pathways are thought to be implicated in emotion and cognition.



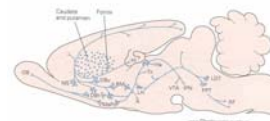
Serotonergic System

Serotonergic neurons are found mainly in the raphe nuclei. Ascending projections to the forebrain from the rostral groups of raphe neurons help regulating the wake-sleep cycles, whereas descending projections from the caudal groups of raphe neurons regulate muscle tone and pain perception.



Cholinergic System

Some large cholinergic neurons are found in the mesopontine tegmentum in both the pedunculopontine nucleus (PPT) and laterodorsal tegmental nucleus (LDT). They send descending axons to the pontine and medullary reticular formation and provide extensive ascending innervations of the thalamus. They play a major role in regulating the wake-sleep cycles.



Functions of the Reticular Formation

The ascending and descending projections of the reticular formation are involved in 4 different types of function:

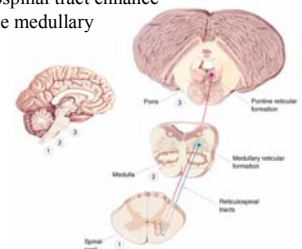
- The regulation of motor responses
- The modulation of pain sensation
- The coordination of autonomic functions
- The control of consciousness

Motor Control

The reticulospinal tracts are two long descending pathways associated with the control of movements and posture.

The pontine (medial) reticulospinal tract enhance the extensor tone, whereas the medullary (lateral) reticulospinal tract inhibit extensors.

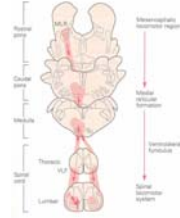
In the spinal cord, both of these motor tracts terminate in the intermediate zone of the ventral horn.



Motor Control

The medial reticulospinal tract originates from large neurons in the pontine reticular formation. It facilitates spinal motor neurons that innervate axial muscles and extensor responses in the legs to maintain posture.

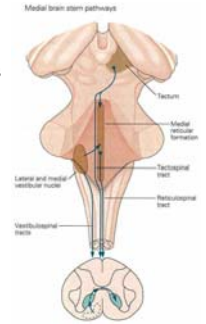
This tract also carries descending motor commands generated with the reticular formation itself, e.g., the Midbrain Locomotor Region (MLR) is capable of producing locomotion patterns.



Motor Control

The medial brain stem motor pathways also includes three other tracts:

- The medial *vestibulospinal* tract projects to the cervical spinal cord and mediates the vestibulocollic reflex, which helps stabilizing the head in space.
- The lateral *vestibulospinal* tract projects to the lumbar spinal cord and influences limb extensors involved in balance.
- The *tectospinal* tract projects to the cervical spinal cord and is involved in orienting movements of the head.



Motor Control

The lateral reticulospinal tract originates from neurons in the medullary reticular formation. Activity in this tract inhibits the firing of spinal and cranial motor neurons and produces a loss of tone – atonia –, as during REM sleep.

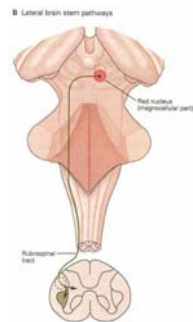


Motor Control

The lateral brain stem motor pathways also include:

- The *rubrospinal* tract, which projects to cervical spinal cord and facilitates contralateral arm flexors.

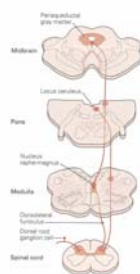
In summary, the ensemble of these brain stem tracts is a major alternate route to the corticospinal tract.



Pain Sensation

The sensation of pain is modulated by monoaminergic projections that originate from neurons in the periaqueductal gray region and serotonergic raphe magnus nucleus, and from noradrenergic cell groups in the pons, including the locus ceruleus.

In the spinal cord, these projections inhibit nociceptive neurons through direct & indirect connections in the superficial layers of the dorsal horn.



Autonomic Functions

Centers controlling inspiration, expiration, and the normal rhythm of breathing have been identified in the medulla and pontine reticular formation.

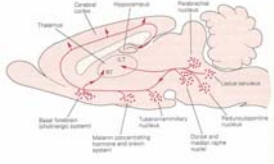
Other centers controlling heart rate and blood pressure have been identified in the medullary reticular formation.

Gastrointestinal responses can also be coordinated by neurons in the medullary reticular formation.

Ocular (pupillary) reflexes are regulated by midbrain nuclei (Edinger Westphal).

Consciousness

Ascending monoaminergic (NE, 5-HT) projections from the rostral reticular formation to the cerebral cortex and thalamus increase wakefulness and vigilance as well as the responsiveness to sensory stimuli, a state known as arousal. These pathways are joined by histaminergic and cholinergic inputs to form an ascending **reticular activating system (RAS)**.

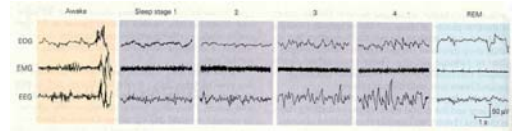


Electroencephalogram (EEG)

EEGs assess the electrical activity of the cerebral cortex.

During alert wakefulness, the EEG consists of low-voltage, fast (>12Hz) wave: **desynchronized EEG**.

During deep sleep, the EEG is dominated by high-voltage, slow (<3Hz) wave: **synchronized EEG**.



Electroencephalogram (EEG)

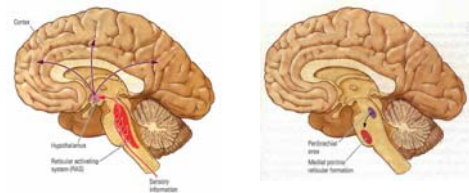
There are four stages of slow-wave sleep, in which the voltage of the electrical activity gradually augments.

The last stage of desynchronized EEG sleep is followed by rapid eye movement (**REM**) sleep, in which a low-voltage, desynchronized EEG pattern prevails. The fast cortical activity in this **paradoxical** sleep resembles that expressed during wakefulness, but it is accompanied by atonia.



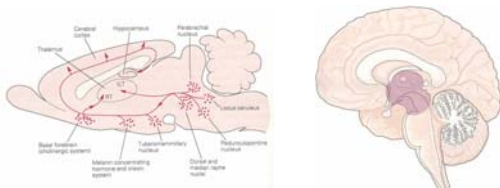
Wake-Sleep Cycle

Activation of the ascending **reticular activating system** induces wakefulness and its inactivation leads to slow-wave sleep. In contrast, REM sleep is mediated by activation of the peribrachial area and the medial pontine reticular formation.



Loss of Consciousness

The ascending reticular activating system divides into two branches at the junction of the midbrain and diencephalon. Lesions that impact the RAS or disrupt either of its two branches impair consciousness, i.e., lead to structural coma.



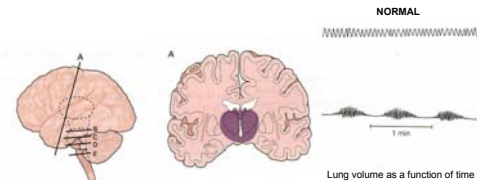
Defective Functional Systems in Coma

The testing of four functional systems gives important clues to the cause of structural coma:

- Respiratory patterns
- Skeletomotor responses
- Pupillary light response
- Oculomotor reflex

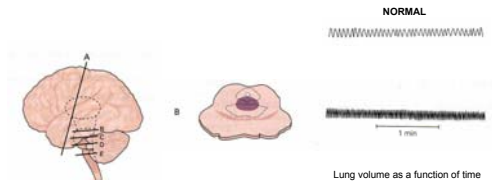
Respiratory System

When there is diffuse forebrain depression, as in a metabolic coma, the respiration may take a *waxing-and-waning* pattern with periods of *apnea*, called Cheyne-Stokes respiration.



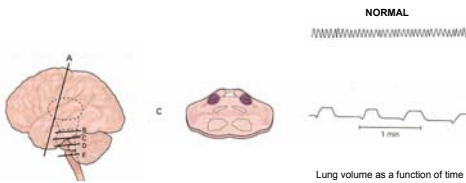
Respiratory System

Injury to the midbrain (B) can cause *hyperventilation*.



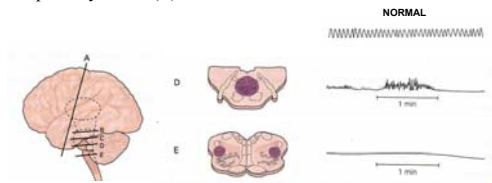
Respiratory System

Injury to the rostral pons (C) may produce a peculiar pattern of respiration known as *apneusis*, in which the breathing halts briefly at full inspiration (inspiration cramps).



Respiratory System

Injury to the lower pons (D) or upper medulla (E) may cause respirations to become irregular and of uneven depth, known as *ataxic* breathing (D). This pattern often heralds a respiratory arrest (E).



Skeletomotor System

Damage to the upper midbrain (above red nucleus) may cause *decorticate rigidity*: flexion of upper limbs and extension of lower limbs in response of painful stimulation.



Rubrospinal tract (which projects only to the cervical cord) counteracts the facilitation of arm extensors provided by the vestibulospinal tract, but the facilitation of leg extensors by vestibulospinal and pontine reticulospinal tracts is unaffected.

Skeletomotor System

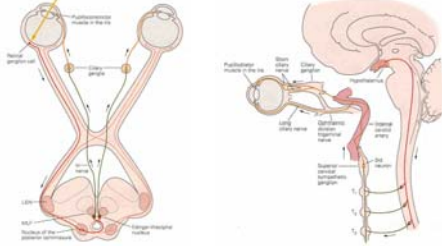
Damage to the lower midbrain or upper pons (below the red nucleus and above the vestibular nuclei complex) may cause *decerebrate rigidity*: extension of both upper and lower limbs.



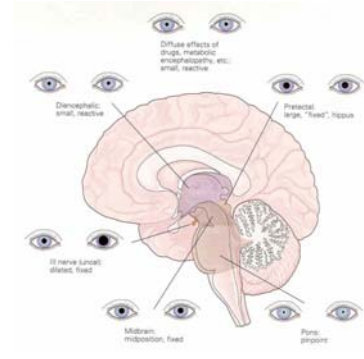
Limbs are tonically extended because the facilitation of the vestibulospinal and pontine reticulospinal tract on both upper and lower extensor motoneurons is unimpeded.

Pupillary System

The state of the pupil represents a balance between the tone in the parasympathetic pupilloconstrictor system (*left*) and the tone in the sympathetic pupillodilator pathway (*right*).

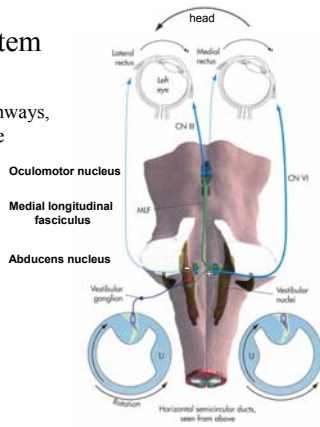


Pupillary System



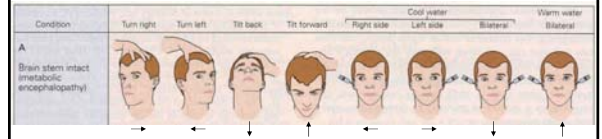
Oculomotor System

More than any other pathways, those concerned with eye movements run in parallel with the ascending arousal system.



Oculomotor System

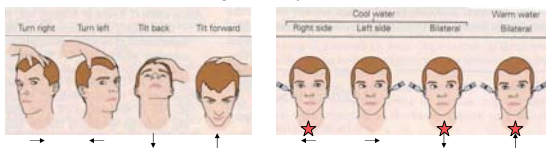
Within an intact brain stem, conjugate eye movements are produced in response to vestibular stimulation, i.e., by turning the head or irrigating the ear canal with cool or warm water. Head turn induces eye movements in the opposite direction. Cool water in the ear canal sets up a convection current in the semicircular canals, resulting in conjugate deviation of the eyes toward that side. Warm water has the opposite effect.



Oculomotor System

A focal injury to the pons involving the abducens nerve would cause loss only of abduction of the ipsilateral eye. Damage to the lateral pons may remove the vestibular input on that one side and block caloric responses in that ear, but the eyes will still respond to the head turns because of input from the other ear.

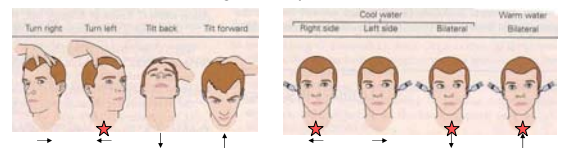
Punctuate right lateral pontine lesion



Oculomotor System

More extensive injury to the pons on one side will cause loss of movements of both eyes toward that side. This symptom is called *gaze paralysis*.

Extensive right lateral pontine lesion



Oculomotor System

A lateral injury to the medial longitudinal fasciculus (MLF) would only prevent adduction of the ipsilateral eye. This symptom is called *internuclear ophthalmoplegia*. A bilateral MLF lesion thus prevents adduction of both eyes.

Bilateral MLF lesion



Oculomotor System

A bilateral lesion involving the midbrain oculomotor nuclei – which control vertical eye movements and the medial recti – would allow only abduction of the eyes. Adduction, elevation and depression of the eyes would all be impaired.

Midbrain lesion



Other Functional Systems

Corneal blink reflex (pons)

Afferent route – Trigeminal (V) nerve

Efferent route – Facial (VII) nerve

Gag reflex (medulla)

Afferent input – Glossopharyngeal (IX) nerve
(palate, pharynx, tonsil)

Efferent input – Vagus (X) nerve
(symmetrical palatal contraction)