Embryology of the Central Nervous System (1)

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After gastrulation the **notochord** (a flexible, rod-shaped body that runs along the back of the embryo) has been formed from the mesoderm. During the third week of gestation the notochord sends signals to the overlying ectoderm, inducing it to become **neuroectoderm**. This results in a strip of neuronal stem cells that runs along the back of the embryo. This strip is called the **neural plate**, and is the origin of the entire nervous system. **The neural plate folds outwards to form the neural groove.** Beginning in the future neck region, the neural folds of this groove close to create the **neural tube** (this form of neurulation is called primary neurulation). The ventral (front) part of the neural tube is called the **basal plate; the dorsal (rear) part is called the alar plate**. The hollow interior is called the **neural canal**. By the end of the **fourth week of gestation**, the open ends of the neural tube (the neuropores) close off.
Central Nervous System

The central nervous system (CNS) appears at the beginning of the third week as a slipper-shaped plate of thickened ectoderm, the neural plate, in the mid dorsal region in front of the primitive node. Its lateral edges soon elevate to form the neural folds.
With further development, the neural plate (thickened ectoderm) forms the neural tube.

Fusion between neural folds begins in the cervical region and proceeds in cephalic and caudal directions. Once fusion is settled, the open ends of the neural tube form the cranial and caudal neuropores that communicate with the overlaying amniotic cavity.

The cranial neuropore is closed first (in the region of the anterior portion of the developing prosencephalon), this is followed by the closure of the caudal neuropore.

Final closure of the cranial neuropore occurs at the 18 - 20- somite stage (25th day). Closure of the caudal neuropore occurs approximately 2 days later. Closure of the cranial neuropores giving rise to the lamina terminalis of the brain.
A-C. Transverse sections through successively older embryos showing formation of the neural groove, neural tube, and neural crest. Cells the neural crest, migrate from the edges of the neural folds and develop into spinal and cranial sensory ganglia.
Dorsal view of a human embryo

A. Dorsal view of human embryo at approximately day 22. Seven distinct somites are visible on each side of the neural tube.

B. Dorsal view of human embryo at approximately day 23. The nervous system is in connection with the amniotic cavity through the cranial and caudal neuropores.
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<th>week 4</th>
<th>week 5</th>
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<td><strong>Prosencephalon</strong> (Forebrain) vesicle</td>
<td><strong>Telencephalon</strong></td>
<td><strong>Rhinencephalon</strong>, Amygda, Hippocampus, Cerebrum (Cortex), Basal Ganglia, lateral ventricles</td>
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<td>Brain</td>
<td><strong>Diencephalon</strong></td>
<td>Epithalamus, Thalamus, Subthalamus, Pineal, Hypothalamus, Pituitary, 3rd ventricle</td>
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<td><strong>Mesencephalon</strong> (Midbrain) vesicle</td>
<td><strong>Mesencephalon</strong></td>
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<td><strong>Rhombencephalon</strong> (Hind Brain) vesicle</td>
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<td><strong>Myelencephalon</strong></td>
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Development of the brain
During the 3rd and 4th week of embryonic life

The cephalic end of the neural tube shows three dilations, the primary brain vesicles:
1. The prosencephalon, or forebrain;
2. The mesencephalon, or midbrain;
3. The rhombencephalon, or hindbrain.

Simultaneously it forms two flexures:
A. The **cervical flexure** at the junction of the hindbrain and the spinal cord.
B. The **cephalic flexure** in the midbrain region.
In the fifth week, the alar plates (sensory area) of the prosencephalon expand and give rise to two lateral outpocketing secondary vesicles, the cerebral hemispheres (Telencephalon).

The basal plates (motor area) of the prosencephalon become the Diencephalon. The latter is characterized by the outgrowth of optic vesicles which eventually become the optic nerve, retina and iris.)
During the 3\textsuperscript{rd} and 4\textsuperscript{th} week of embryonic life
Vesicles of the cranial part of the neural tube. The 3 primary vesicles develop into 5 secondary vesicles (week 5).
The ventral (front) part of the neural tube is called the **basal plate**; the dorsal (rear) part is called the **alar plate**. The central cavity is called the **neural canal**.
Formation of the spinal cord

The spinal cord forms from the lower part of the neural tube. The wall of the neural tube consists of neuroepithelial cells, which differentiate into neuroblasts, forming the mantle layer (the gray matter). Nerve fibers emerge from these neuroblasts, form the marginal layer (the white matter of the spinal cord). The ventral part of the mantle layer (the basal plates) forms the motor areas of the spinal cord, whilst the dorsal part (the alar plates) forms the sensory areas. Between the basal and alar plates is an intermediate layer that contains neurons of the autonomic nervous system.
Transverse section in the neural tube showing the neuroepithelial cells, differentiate into neuroblasts, forming the mantle layer (the gray matter).
A longitudinal groove, the sulcus limitans, marks the boundary between the basal and alar plates.

The dorsal and ventral midline portions of the neural tube, known as the roof and floor plates, respectively, do not contain neuroblast; they serve primarily as pathways for nerve fibers crossing from one side to the other.

In addition to the ventral motor horn and the dorsal sensory horn, a group of neurons accumulates between the two areas and forms a small intermediate horn. This horn, containing neurons of the sympathetic portion of the autonomic nervous system, is present only at thoracic (T1-T12) and upper lumbar levels (L2 or L3) of the spinal cord.
Formation of the spinal cord
Neuroblasts, or primitive nerve cells, arise exclusively by division of the neuroepithelial cells. Initially they have a central process extending to the lumen (transient dendrite), but when they migrate into the mantle layer, this process disappears, and neuroblasts are temporarily round and apolar.

With further differentiation, a bipolar neuroblast.

The process at one end of the cell elongates rapidly to form the primitive axon, and the process at the other end shows a number of cytoplasmic arborization, the primitive dendrites. The cell is then known as a multipolar neuroblast and with further development becomes the adult nerve cell or neuron.

Once neuroblast form, they lose their ability to divide.
Histological differentiation of nerve cells in the spinal cord. Axons of neurons in the basal plate break through the marginal zone and become visible on the ventral aspect of the cord. Known collectively as the ventral motor root of the spinal nerve, they conduct motor impulses from the spinal cord to the muscles.

Axons of neurons in the dorsal sensory horn (alar plate) behave differently from those in the ventral horn. They penetrate into the marginal layer of the cord, where they ascend to either higher or lower levels to form association neurons.
Development of neural crest and dorsal root ganglion

During folding of the neural plate, a group of cells appears along each edge (the crest) of the neural folds. These neural crest cells are ectodermal in origin and extend throughout the length of the neural tube. Crest cells migrate laterally and give rise to sensory ganglia (dorsal root ganglia) of the spinal nerves and other cell types. During further development, neuroblasts of the sensory ganglia form two processes.

1- The centrally growing processes penetrate the dorsal portion of the neural tube. In the spinal cord, they either end in the dorsal horn or ascend through the marginal layer to one of the higher brain centers.
These processes are known collectively as the **dorsal sensory root of the spinal nerve**.

2- **The peripherally growing processes** join fibers of the **ventral** motor roots and thus participate in **formation of the trunk of the spinal nerve**. Eventually these processes terminate in the sensory receptor organs. Hence, neuroblasts of the sensory ganglia derived from neural crest cells give rise to the **dorsal root neurons**.

In addition to forming sensory ganglia, **cells of the neural crest differentiate** into sympathetic neuroblasts, Schwann cells, pigment cells, odontoblasts, meninges, and mesenchyme of the pharyngeal arches.
Development of the neural crest and dorsal nerve root ganglion
Development of the Glial cells

The majority of primitive supporting cells, the gliablasts, are formed by neuroepithelial cells after production of neuroblasts ceases. Gliablasts migrate from the neuroepithelial layer to the mantle and marginal layers.

1- In the mantle layer, they differentiate into protoplasmic astrocytes and fibrillary astrocytes.

2- Another type of supporting cell possibly derived from gliablasts is the oligodendroglial cell. This cell, which is found primarily in the marginal layer, forms myelin sheaths around the ascending and descending axons in the marginal layer.

3- In the second half of development, a third type of supporting cell, the microglial cell, appears in the CNS. This highly phagocytic cell type is derived from mesenchyme.

4- When neuroepithelial cells cease to produce neuroblasts and gliablasts, they differentiate into ependymal cells lining the central canal of the spinal cord.
Origin of the nerve cell and glial cells

- Neuroepithelial cells
- Ependymal cell
- Bipolar neuroblast
- Gliablast
- Multipolar neuroblast
- Protoplasmic astrocyte
- Fibrillar astrocyte
- Oligodendroglia
- Mesenchymal cell
- Microglia
Myelination

Schwann cells myelinate the peripheral nerves. These cells originate from neural crest, migrate peripherally, and wrap themselves around axons, forming the neurilemma sheath.

Beginning at the fourth month of fetal life, many nerve fibers take on a whitish appearance as a result of deposition of myelin, which is formed by repeated coiling of the Schwann cell membrane around the axon.

The myelin sheath surrounding nerve fibers in the spinal cord originates from the oligodendroglial cells. Some of the motor fibers descending from higher brain centers to the spinal cord do not become myelinated until the first year of postnatal life. Tracts in the nervous system become myelinated at about the time they start to function.
Myelination of spinal nerve

In the spinal cord, the myelin sheath is formed by 
oligodendroglia cells; outside the spinal cord, the sheath is formed by 
Schwann cells.
In the third month of development, the spinal cord extends the entire length of the embryo, and spinal nerves pass through the intervertebral foramina at their level of origin. With increasing age, the vertebral column and dura lengthen more rapidly than the neural tube, and the terminal end of the spinal cord gradually shifts to a higher level. At birth, this end is at the level of the third lumbar vertebra. As a result of this disproportionate growth, spinal nerves run obliquely from their segment of origin in the spinal cord to the corresponding level of the vertebral column. The dura remains attached to the vertebral column at the coccygeal level. In the adult, the spinal cord terminates at the level of L2 - L3. The dural sac and subarachnoid space extend to S2. Below L2 to L3, a threadlike extension of the pia mater forms the filum terminale, which is attached to the periosteum of the first coccygeal vertebra and which marks the tract of regression of the spinal cord. Nerve fibers below the terminal end of the cord is, the cauda equina.
Terminal end of the spinal cord in relation to that of the vertebral column At various stages of development.
A. Approximately the third month. B. End of the fifth month. C. Newborn