

# NEURAL TUBE

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October 31, 2025

## RECOMMENDED CITATION

mohammad looti (2025). *NEURAL TUBE*. PSYCHOLOGICAL SCALES. Retrieved from <https://scales.arabpsychology.com/?p=63507>

## NEURAL TUBE

**Primary Disciplinary Field(s):** Developmental Biology, Neuroscience, Embryology

### 1. Core Definition

The **Neural Tube** is the definitive embryonic precursor structure from which the entire central nervous system (CNS)--comprising the brain and the spinal cord--is derived. Its formation is one of the earliest and most critical events in vertebrate embryogenesis, occurring through a tightly regulated process known as neurulation. This structure is fundamentally a transient, cylindrical organ that establishes the primary longitudinal axis of the developing nervous system. The tube forms when the neural plate, a thickened region of the embryonic ectoderm, undergoes extensive morphogenetic changes involving folding, elevation, and subsequent fusion of its lateral edges along the dorsal midline.

The morphological transformation from a flat plate to a closed tube is mediated by complex cellular movements, including changes in cell shape (apical constriction) and directed tissue migration (convergent extension). In human development, this crucial process typically begins around the third week of gestation and must be completed by the fourth week. The successful closure of the neural tube is paramount, as failure at any stage results in severe congenital malformations known collectively as neural tube defects (NTDs), which have significant clinical consequences.

A defining characteristic of the neural tube is its internal space, or lumen, often referred to as the **neurocoel**. This central cavity represents the future ventricular system of the brain and the central canal of the spinal cord. As the embryo matures, the rostral (head) portion of the tube expands rapidly and differentiates into the highly convoluted structures of the brain (forebrain, midbrain, hindbrain), while the caudal (tail) portion elongates and forms the functional segments of the spinal cord. The neurocoel within these developing structures fills with cerebrospinal fluid and becomes essential for CNS homeostasis throughout life.

### 2. Etymology and Historical Development

The understanding of the neural tube's formation evolved significantly with advances in experimental embryology during the late 19th and early 20th centuries. Scientists began to systematically observe and manipulate amphibian and chick embryos, mapping the fate of early tissues. The recognition that the nervous system arose from the dorsal ectoderm, rather than mesoderm, was a pivotal discovery. This led to the identification of the neural plate and the subsequent folding process characteristic of neurulation.

A key conceptual breakthrough came from the work on embryonic induction, particularly the studies by Hans Spemann and Hilde Mangold in the 1920s, concerning the 'organizer' region

(specifically, the dorsal lip of the blastopore in amphibians, corresponding to the notochord in mammals). They demonstrated that signals emanating from this underlying mesodermal tissue were necessary and sufficient to induce the overlying ectoderm to differentiate into the neural plate and initiate the complex movements required for neural tube formation. This organizer concept placed the induction of the neural tube at the center of early developmental patterning.

Modern developmental biology has transitioned from purely descriptive and manipulative embryology to detailed molecular analysis. Research now focuses heavily on the signaling cascades that regulate closure, including the roles of bone morphogenetic proteins (BMPs), Wnt signaling pathways, and, critically, the involvement of the cytoskeleton components (actin and myosin) that drive the necessary cell shape changes. This molecular understanding has been instrumental in identifying genetic predispositions and environmental factors contributing to defects in tube closure.

### 3. The Process of Neurulation

Neurulation is broadly divided into two processes: **Primary Neurulation** and Secondary Neurulation. Primary neurulation is responsible for forming the brain and the majority of the spinal cord (up to the caudal lumbar region). This process begins with the transformation of the neural plate. The lateral edges of the plate elevate, forming the **neural folds**, while the center dips slightly, creating the neural groove. Critical to this stage is the establishment of pivot points: the Medial Hinge Point (MHP) along the midline, anchored to the notochord, and the Lateral Hinge Points (LHPs), which facilitate the inward rolling motion of the folds.

The mechanism driving the elevation and folding is primarily intrinsic to the neuroectoderm cells themselves. Cells at the MHP and LHPs undergo **apical constriction**, a process where actin and myosin bundles contract at the apical (dorsal) surface of the cells, causing them to become wedge-shaped. This change in morphology pushes the tissue to curve inward, propelling the neural folds towards the dorsal midline. Once the opposing folds meet, the outer layers of ectoderm fuse above the neuroectoderm, and the underlying neuroectoderm cells fuse internally, separating the newly formed neural tube from the superficial epidermis.

As a direct consequence of the fusion of the neural folds, a population of highly migratory cells, known as the **Neural Crest Cells**, delaminates from the lateral edges of the now-closed tube. These cells are often referred to as the 'fourth germ layer' due to their astonishing pluripotency and contribution to numerous non-neural tissues, including the peripheral nervous system (PNS), melanocytes, cartilage, and bone of the face and skull. The success of neural tube closure is therefore intrinsically linked to the proper dispersal and differentiation of the neural crest lineage.

**Secondary Neurulation** accounts for the formation of the caudal-most segments of the spinal cord (sacral and coccygeal regions). Unlike the primary process, this involves the condensation of

caudal mesenchymal cells into a solid structure known as the medullary cord. This cord subsequently undergoes cavitation, meaning internal spaces form and coalesce to create a hollow central lumen that connects with the central canal formed during primary neurulation. Failure in this secondary process can lead to specific, lower spinal NTDs.

#### 4. Derivatives and Spatial Organization

The neural tube rapidly undergoes regional specialization along both its rostral-caudal and dorsal-ventral axes. Rostrally, the tube develops three primary swellings or vesicles: the **Prosencephalon** (forebrain), the **Mesencephalon** (midbrain), and the **Rhombencephalon** (hindbrain). These vesicles further subdivide, eventually forming the major structures of the brain, including the cerebrum, cerebellum, and brainstem. This segmentation is crucial for establishing the specialized functional areas of the mature CNS.

Differentiation along the dorsal-ventral plane determines the functional identity of neurons within the spinal cord and brainstem. Signaling molecules released by surrounding tissues establish key morphogen gradients. The underlying notochord and floor plate (the ventral midline of the neural tube) secrete **Sonic Hedgehog (Shh)**, which establishes a ventral identity, promoting the formation of motor neurons. Conversely, the roof plate (the dorsal midline) and the overlying ectoderm secrete BMPs and Wnt signals, establishing a dorsal identity, which leads to the formation of sensory and association neurons.

This functional segregation results in the division of the spinal cord wall into two distinct regions separated by the sulcus limitans: the **Basal Plate** (ventral), which houses general somatic and visceral motor nuclei, and the **Alar Plate** (dorsal), which contains general somatic and visceral sensory nuclei. This fundamental organizational blueprint is maintained from the developing neural tube into the adult spinal cord and brainstem, dictating how sensory information enters and motor commands exit the CNS.

The lumen of the neural tube, the neurocoel, is transformed into the interconnected fluid-filled spaces of the adult brain and spinal cord. In the brain, the neurocoel expands dramatically to form the lateral, third, and fourth ventricles, which are continuous with the aqueduct of Sylvius. The ventricular system, derived from this early cavity, is lined by ependymal cells and functions to produce and circulate the cerebrospinal fluid (CSF). Caudally, the lumen narrows significantly to become the minute **central canal** that runs the length of the spinal cord.

#### 5. Clinical Significance: Neural Tube Defects (NTDs)

The most critical clinical significance of the neural tube lies in the severe developmental anomalies that arise from its failure to close completely--the **Neural Tube Defects (NTDs)**. Because neurulation occurs so early in gestation (weeks 3 and 4), these defects are often present before

the mother is aware of the pregnancy, making prevention paramount. NTDs are among the most serious congenital birth defects compatible with survival, often resulting in profound neurological disability or death shortly after birth.

The two most common and devastating forms of NTDs are **Anencephaly** and **Spina Bifida**. Anencephaly results from the failure of the anterior (rostral) neural pore to close. This leads to the absence of the major portion of the brain, skull, and scalp, as the exposed neural tissue degenerates *in utero*. Infants with anencephaly are either stillborn or die shortly after birth. Spina Bifida, resulting from the failure of the posterior (caudal) neural pore to close, is characterized by incomplete closure of the vertebral arches and varying degrees of protrusion of the meninges and/or spinal cord tissue.

While NTDs are complex and multifactorial, involving both genetic susceptibility and environmental factors, a breakthrough in prevention occurred with the realization that maternal nutritional status plays a critical role. Studies conclusively demonstrated that periconceptional supplementation with **folic acid** (a B vitamin) dramatically reduces the incidence of both anencephaly and spina bifida. Consequently, public health initiatives worldwide now advocate for mandatory folic acid fortification of staple foods and recommended supplementation for all women of childbearing age, highlighting the profound impact of molecular nutritional requirements on early embryogenesis.

## 6. Significance and Impact

The formation of the neural tube is perhaps the singular most defining event in the development of the vertebrate body plan. Its creation establishes the fundamental axis of the body and partitions the ectoderm into three distinct and functionally critical components: the neural tube (CNS), the neural crest (PNS and associated structures), and the epidermis (surface covering). This intricate separation and organization dictate the structural complexity required for higher life forms.

The study of neurulation remains a cornerstone of developmental biology research. Understanding the precise molecular and mechanical forces that govern cell shape change and tissue movement provides vital insights into other processes dependent on epithelial remodeling, such as tissue repair and cancer metastasis. Moreover, the inherent vulnerability of the neural tube to genetic and environmental insults during the critical closure period underscores the fragility of early development and drives continuous research into preventative medicine, pharmacogenetics, and prenatal screening.

## 7. Further Reading

[Neural Tube \(Wikipedia\)](#)

[Neurulation \(Developmental Biology Textbook Chapter\)](#)

[Facts About Spina Bifida and Folic Acid \(CDC\)](#)

[Anencephaly \(Wikipedia\)](#)

[Cerebrospinal Fluid \(Wikipedia\)](#)

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