

## Rat Spinal Cord Development

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### Abstract

The study of the central nervous system is one of the promising scientific areas. A lot of dissertations are devoted to this topic. The rat is an important object in the study of the spinal cord in the normal state and in pathology. It is important to clearly understand the stages of development and morphology of the spinal cord of the rat in order to extrapolate information in the experiment.

Below will be presented information about the development of the spinal cord of rats.

**Keywords:** Spinal Cord; Rat; Development

The study of the central nervous system is one of the promising scientific areas. A lot of dissertations are devoted to this topic. The rat is an important object in the study of the spinal cord in the normal state and in pathology. It is important to clearly understand the stages of development and morphology of the spinal cord of the rat in order to extrapolate information in the experiment.

Below will be presented information about the development of the spinal cord of rats.

### Development of the matrix layer

The formation of the central nervous system at the gastrula stage of the rat embryo is associated with the interaction of ectodermal cells and mesodermal cells (chordomesoderm). This process is known as primary neural induction [1,3,4,17]. Under undisturbed conditions, the induced tissue transforms into a neural tube as a result of neurulation [9,11,17].

During neurulation, cells move due to their shape change and regional differences [4,11,17]. Cell shape is determined by

microtubule elongation and apical constriction of microfilaments [4,6,8,14,17]. In the matrix layer of the neural tube, four parts can be identified: two thick lateral plates and two thin "caps".

The multi-layered appearance of the side plates is associated with the migration of mitotic neuroblast nuclei [4,8,15,16]. The lateral laminae are usually divided into the ventral basal lamina and the dorsal alar lamina. The first is the spinal motor neuron generation area, and the second is the spinal cord interneuron generation area. Altman and Bayer proposed the division of the lateral laminae into three zones; hence the third zone is located dorsally from the basal lamina and is occupied by projecting neurons, originally designated as commissural and funicular cells [4,6,8,14,16].

Neuroblasts and glioblasts develop in the matrix layer (subventricular zone), where the main population of CNS stem cells is contained. In general, neuroblasts differentiate into three types of neuronal cells in the spinal cord: motor neurons, switch neurons, and interneurons. In the past, neuroblasts and glioblasts

were thought to share a common ancestor, but glioblasts actually originate from the so-called O2A progenitor cell [14,15,21,26], which develops under the influence of a type 1 astrocyte into a type 2 astrocyte (oligodendrocyte) [4,6,8,14,15]. In addition to these types of glial cells, microglial cells also arise from the progenitor cell [26].

Future motor neurons of the spinal cord are formed in the ventral basal plate on the 10-14th day of embryonic development. The ventral spinal cord is formed as follows: future neurocytes go in the direction along an orthogonal line to the ventral part of the developing nervous system (neural tube) [4,8,6,14,26]. Nucleus intermediolateralis is formed by motor neurons. These neurons are derived from the pars ventralis matrix layer [4,15].

The formation of future interneurons occurs on the 13-16th day of embryonic development. The cells enter the peripheral part of the dorsal neural tube and form the posterior horns of the spinal cord [8,16].

#### Development of the mantle layer

Pars ventralis of the mantle layer is formed by the motor neurons of the spinal cord and is called the ventral horn, which can be distinguished on the 12th day of embryogenesis. Further neuroblasts pass into motor neurons of the spinal cord [4,10,20]. The development of the mantle of the spinal cord is multistage - it includes 5 stages. In the first 3 stages, axonogenesis occurs (during the course, immature neurons form processes-axons). This happens as follows: neuron progenitor cells move to the lateral part of the space, their shape changes to a more spherical one, and an outgrowth is formed in the cytoplasm, from which the axon grows. Dendrogenesis occurs in phases 4 and 5. During this period, first develop bipolar, and then multipolar motor neurons, then grow dendrites [8,10,20].

There are three types of motor neurons: larger  $\alpha$ -motor cells and smaller  $\beta$ - and  $\gamma$ -motor cells. Motor neurons at the level of the cervical and lumbar extensions gather into lateral (innervation of the skeletal muscles of the body and limbs) and medial (innervation of the axial muscles) motor columns [1,2,6,10,26].

The assembly of motor neurons into columns begins on the 13th day of embryogenesis and ends approximately by the 17th

day. In the adult rat, the motor columns in the spinal cord are commonly referred to as plate IX of Rexed. The thoracic region of the spinal cord contains a single motor column. The lateral horn of the spinal cord consists of preganglionic motor neurons in the nucleus intermediolateralis [4,6,8,10,26]. The most lateral part of the seventh plate of Rexed in the spinal cord is represented by the lateral horn. At the level of the lumbar region, the lateral horn can't be seen, despite the fact that preganglionic motor neurons are located in the nucleus intermediolateralis [1,4,8,26].

The intermediate part of the mantle layer is occupied by contralateral or ipsilateral projecting neurons [4]. These relay cells are produced within 3 days, from days 11 to 13 of embryogenesis, with peak production on day 12. Relay neurons have a wide range of sizes (8-40  $\mu$ m) and shapes (fusiform, stellate and triangular). Cells that are control-laterally projecting are formed much earlier than those that are homolaterally projecting. Neurons of the intermediate gray matter are located in the plates of Rexed I and IV-VIII of the spinal cord. Their axons innervate the higher centers of the brain [3,4] or propriospinal axons [4,8,26].

Intermediate gray matter can be seen around day 13 of embryogenesis [26]. Subsequently, laterally located relay neurons are presumably pushed mechanically towards the dorsal layer of the dorsal horn. This is the Waldeyer layer or marginal layer. It forms the plate of Rexed I in the spinal cord of the rat [14,15,21,26,28].

The dorsal part of the mantle layer of the spinal cord is known as the dorsal horn and is mostly occupied by interneurons. Rexed's plate I contains marginal cells of the layer of Waldeyer. The dorsal horn contains a heterogeneous group of cells: the small ones are located in substantia gelatinosa (Rexed II plate), the larger ones are located in the Rexed III plate. The formation of the dorsal horn, plate I-III in the rat spinal cord occurs on the 13-14<sup>th</sup> day of embryogenesis [4,6,8,10,26].

In the formation of the spinal cord, there are two features that have a certain pattern. First, the ventral and dorsal gradient in the formation of different cell classes (motor and relay neurons and interneurons) in the matrix layer. The migration of these cells to the periphery of the matrix layer occurs along the ventral-dorsal gradient. The second pattern of development is the rostral-to-caudal gradient, which is most clearly seen in the cervical region of the spinal cord [4,14,18,20,26].

### Development of the marginal layer

The development of the marginal layer of the rat spinal cord depends on the growth of axons of spinal cord neurons and the arrival of axons of neurons in the higher parts of the brain and on the periphery [1,18,26].

The first anterior motor roots come out approximately on the 12<sup>th</sup> day of embryogenesis. Further, the central processes of the dorsal ganglion cells enter the spinal cord in the zone of entry of the radix dorsalis and form an elliptical bifurcation zone of the radix dorsalis [1,13,16,19]. On the 13<sup>th</sup> day, the initial contralateral fibers can be recognized in the ventral commissure and the same-name funiculus. At this time, ipsilateral axons can also be found in the nascent lateral funiculus. However, they will be much less [18,22,23,24,26]. On days 14–17, the bifurcation zone of the dorsal root develops into the dorsal funiculus, which contains ascending, non-crossing, thick, myelinated branches of large cells of the dorsal ganglion [23,27], as well as descending fibers of the widely studied corticospinal tract [24,27]. Recently, it has been shown that the dorsal funiculus also contains unmyelinated fibers (a small amount of them) [13,19]. The corticospinal tract of the rat runs along the pars ventralis of the contralateral dorsal column. After birth, corticospinal fibers appear in the cervical spinal cord. In the second postnatal week, it reaches the level of the lumbar and sacral regions [26].

The ventral funiculus of the rat spinal cord is mainly occupied by descending fibrous tracts of the longitudinal bundle, which contains crossed tectospinal, crossed and non-crossed reticulospinal, non-crossed coeruleospinal [27], crossed and non-crossed vestibulospinal, and crossed and non-crossed intersticiospinal fiber systems [2,4,8,10,26]. Most of these tracts have been found to develop long before birth [14,26].

The lateral funiculus contains both ascending and descending fiber systems [3,14,26,28]. There are ascending uncrossed dorsal and crossed ventral spinocerebellar tracts [6,7,8,9,11,26] (the first fibers reach the cerebellum before birth) [14,15,26]. Another system is the descending crossed rubrospinal fiber tract. The first rubrospinal fibers reach the upper cervical levels of the spinal cord long before birth, the lower lumbar levels are reached around the day of birth [18,26,29].

After birth, oligodendrocytes begin the process of myelination. It takes place in the spinal cord. It will take approximately 3 weeks (the first 3 weeks) for myelination of all fiber optic tracts [21,22,26]. The myelin sheath around axons gives the marginal layer a white, opaque appearance and is collectively referred to as white matter.

Myelination of both descending and ascending fiber tracts follows a rostral to caudal gradient. In the central nervous system, myelin contains at least two inhibitors of neurite outgrowth [26]. Therefore, at the last stage of spinal cord development, an increase in myelin content may explain the inhibitory effect on the growth of the fiber system [9,11,17,26]. The inhibitory properties of myelin may also function as a directing factor for late-growing tracts of spinal fibers [7,15,19,22,24,26].

Thus, the materials of the article will create a fundamental basis for planning, conducting and interpreting the data obtained in the experimental study of the spinal cord, and can serve as a basis for further research.

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