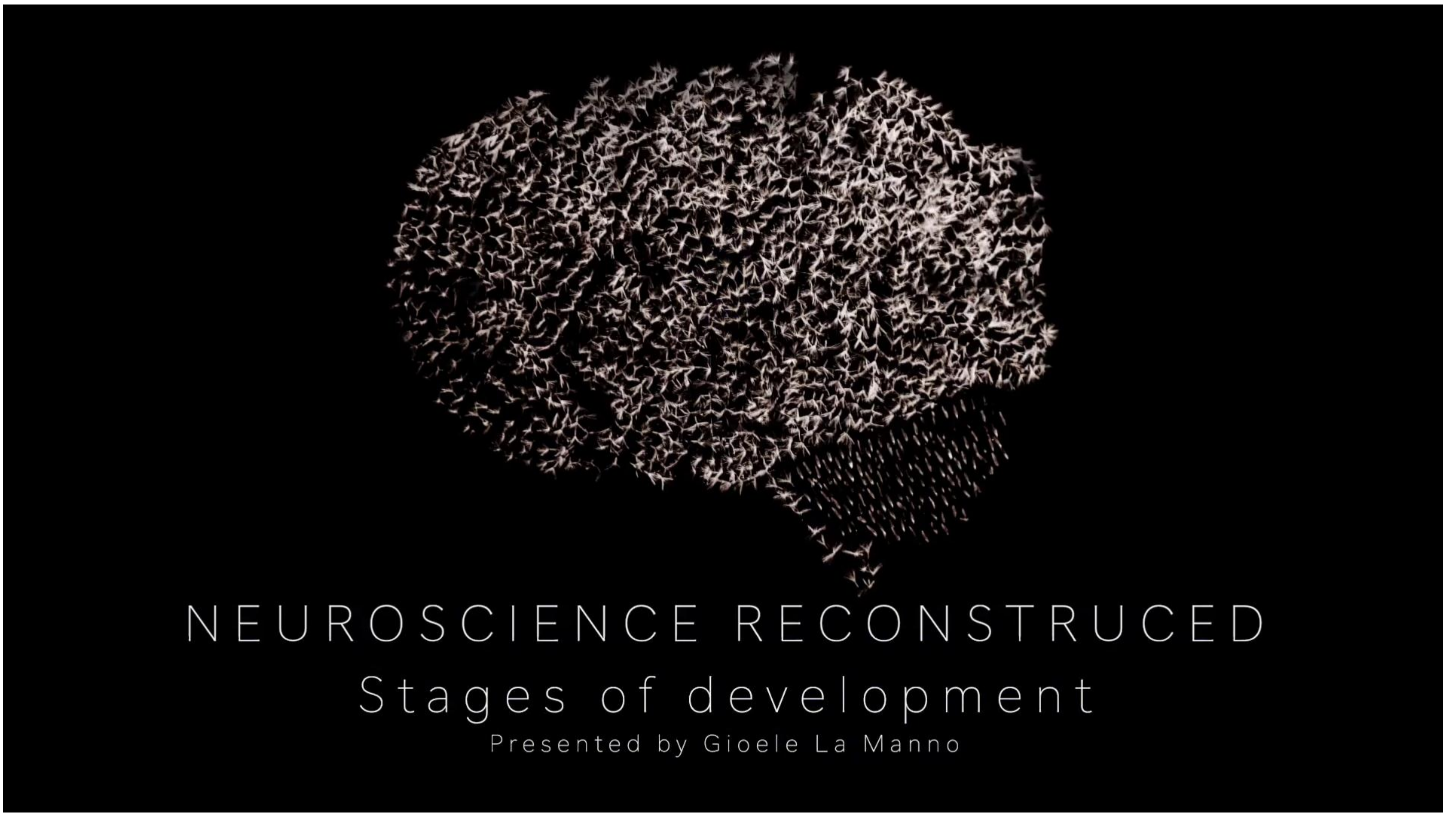

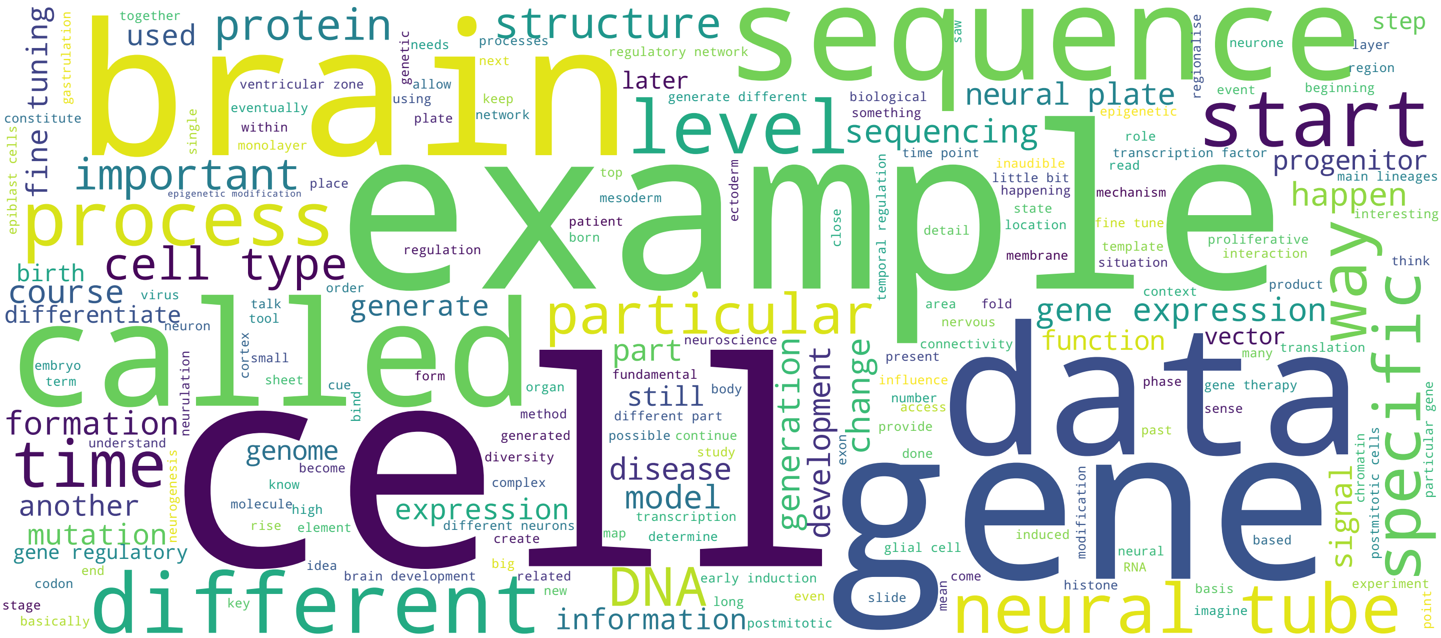

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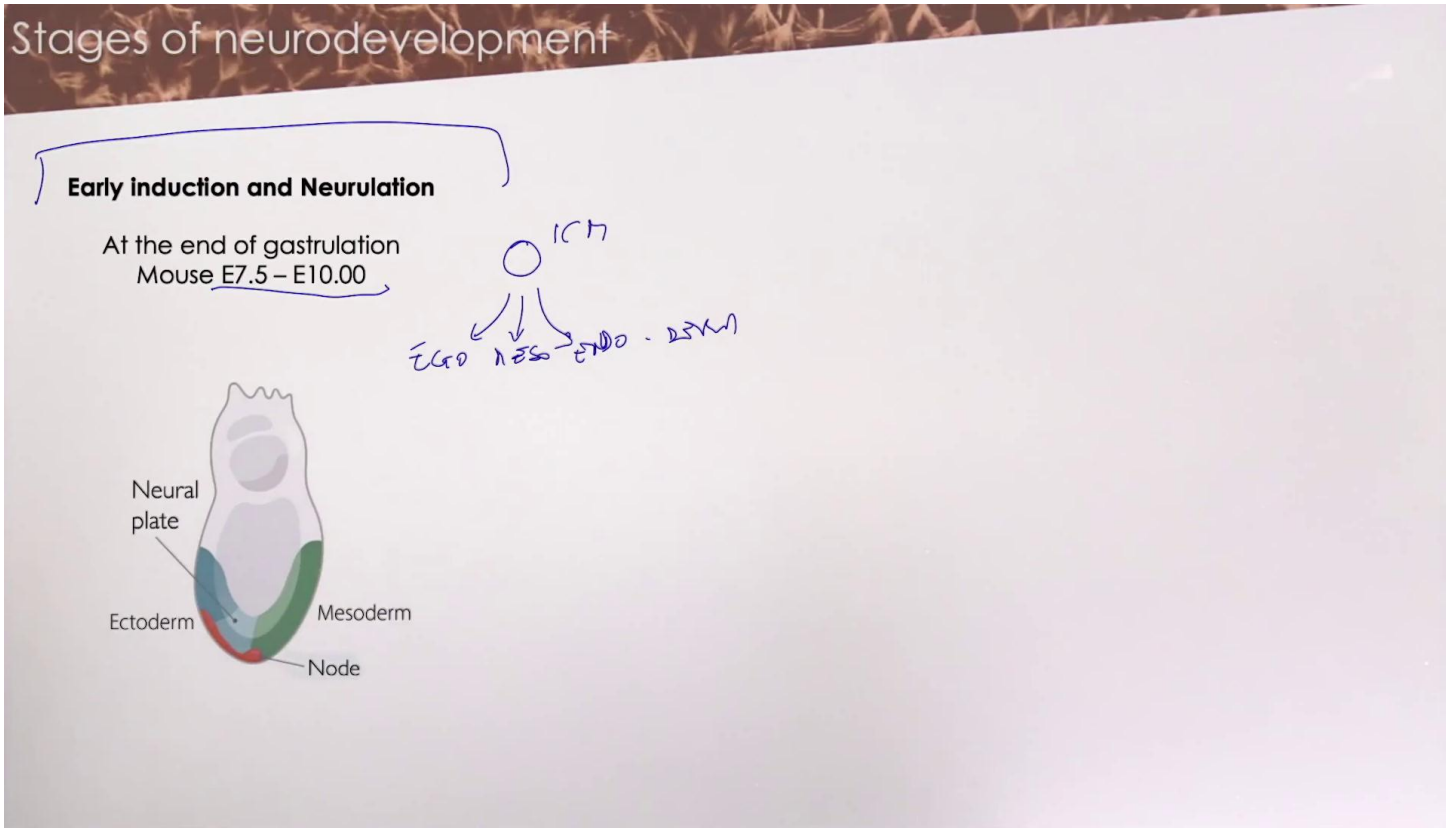
EPFL

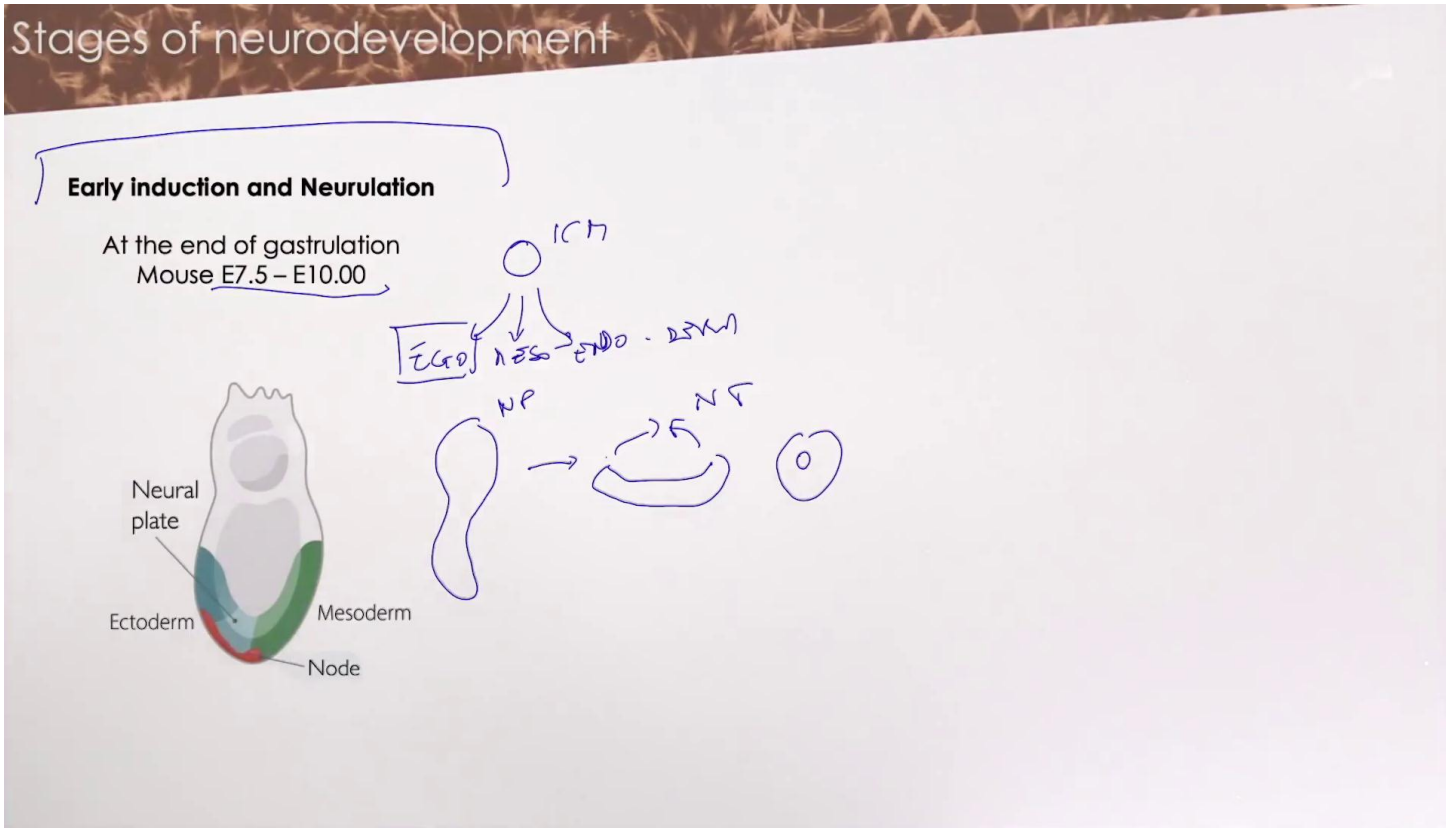


Let's now talk about different stages of neurodevelopment. We're going to start by identifying three main blocks that are conceptually different in the processes that are happening. For example, at the very beginning, fundamental induction and formation of segregated lineages, so cells with different fates that will generate different structures and organs, is one of the most important events. To keep in mind where we come from, we need to remember which stage we are. This first early induction of neurulations phase happens immediately after gastrulation. Gastrulation, just a quick review on basic developmental biology, we have generated for the inner cell mass and the epiblast cells, they're called epiblast cells, we generate three different main lineages, the ectoderm, the mesoderm, and the endoderm. These three main lineages will generate different cells in the body. For example, ectoderm generates, among others, skin, but in the entirety of the central nervous system, the mesoderm will give rise to different internal organs, and for example, cell types in the liver and the kidney. Endoderm will generate structures like the intestine and the oesophagus.

Notes

Summary

0m 10s

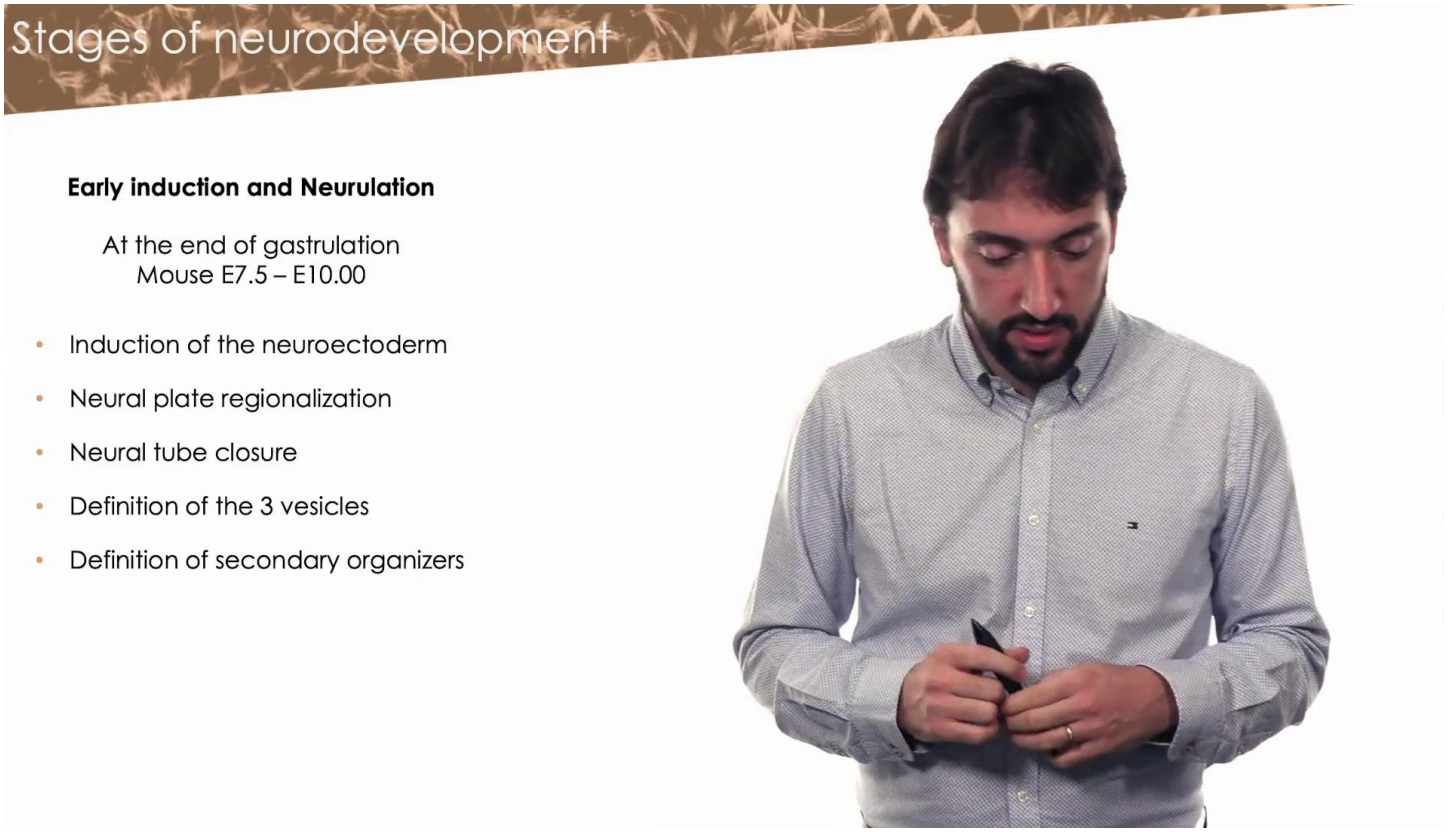


Very different cell types relate to different parts of the body. And from generation of the ectoderm is the key starting point when we think about early induction and neurulation. What needs to happen to the ectoderm, it needs to be first induced from the so-called neuroectoderm in the sheet of cells called the neural plate. This neural plate of cells constituted by epithelial-looking-cells, they form first a monolayer and then a multi-layered epithelium. These cells are, at the beginning, relatively similar to each other. They will be induced to regionalise. This regionalisation will give rise to the formation, the folding of the neural plate to the neural tube. We will see the plate of cells. The neural plate will fold, and then will close up and merge into a tube. Furthermore, this tube will then be regionalised anterior posteriorly, or [inaudible 00:02:51] to use another term, to form different vesicles that will generate different regions of the brain.

Notes

Summary

1m 41s

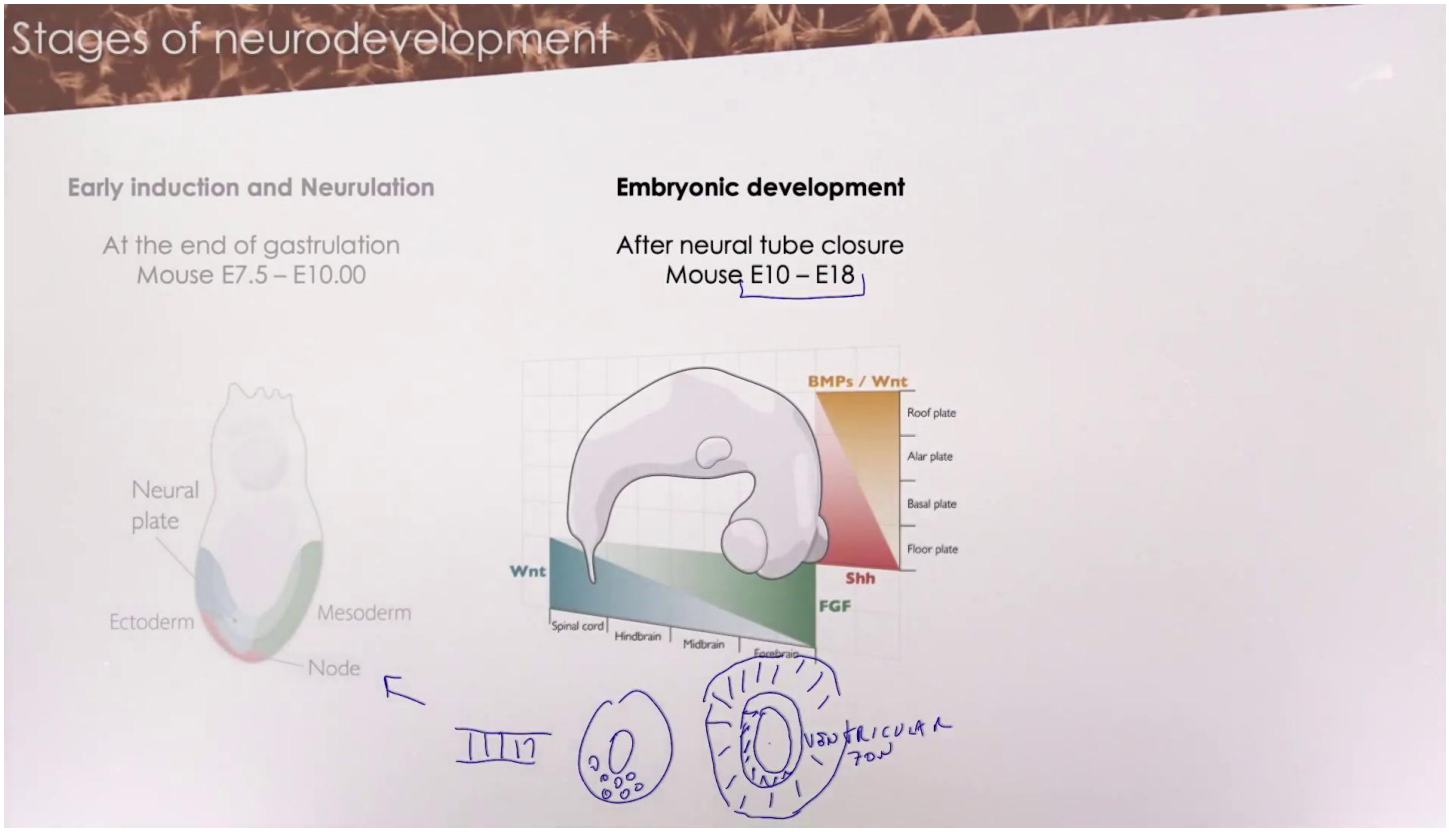


To sum up, after gastrulation, we need to first, induce the neuroectoderm, determine the formation of the sheet of epithelial cells, the neuroectoderm of cells, the neural plate. The neuro plate will be induced to fold, will generate a neural tube that will close and then regionalise in three particular vesicles, the forebrain, the midbrain and the hindbrain. This structure will then take over what is called, an organizer function. We're going to look at this later. Where we're going to have a shift first to another structure that we'll see the mesoderm and the node that we're inducing and telling the different parts of the embryonic brain to set the access to give special information, especially morphogenes and cues. The brain then itself, is going to constitute a particular set of cells called organisers, that then do this role intrinsically. The brain will then take over the role, particular cells in the brain will take the role to send mesessages to the neighbouring cells and fine-tune the generation morphology, and diversity in the brain.

Notes

Summary

3m 04s

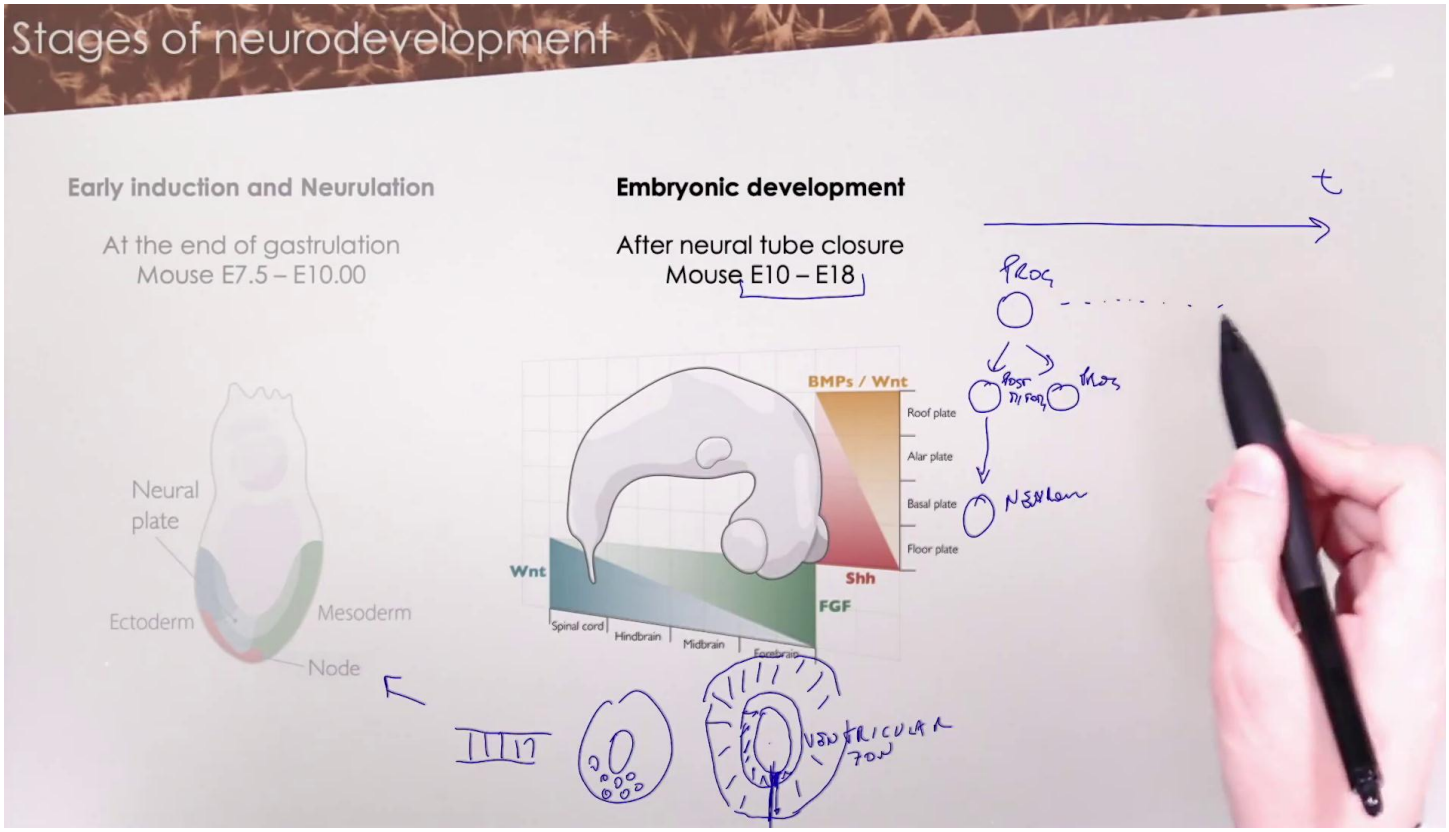


Then we can recognise a second phase of development after the initial early induction and neurulation, proper brain development to neural system. Now we have already defined the neural tube, the three main regions, the three main vesicles have been defined, and now such a specific process to nervous system development is going to take place. The first cells are going to start to differentiate and to become postmitotic. Before, we have just this tube of cells that are all quite proliferative. While we go forward in time, we are going to observe that these monolayers, what was first monolayer cells and then later a neural tube constituted by many proliferating cells, is going to stratify. Cells that are proliferative are going to accumulate immediately surrounding the lumen of the neural tube, what is called the ventricle, and what is going to transform into the lateral third and fourth ventricle. This layer is going to be called ventricular zone, and then we will have surrounding it, a mantle zone. [inaudible 00:05:55] the neural tube, where cells are going to be differentiating, and they're going to start to become, for example, neurons at the beginning, and then glial cells.

Notes

Summary

4m 22s

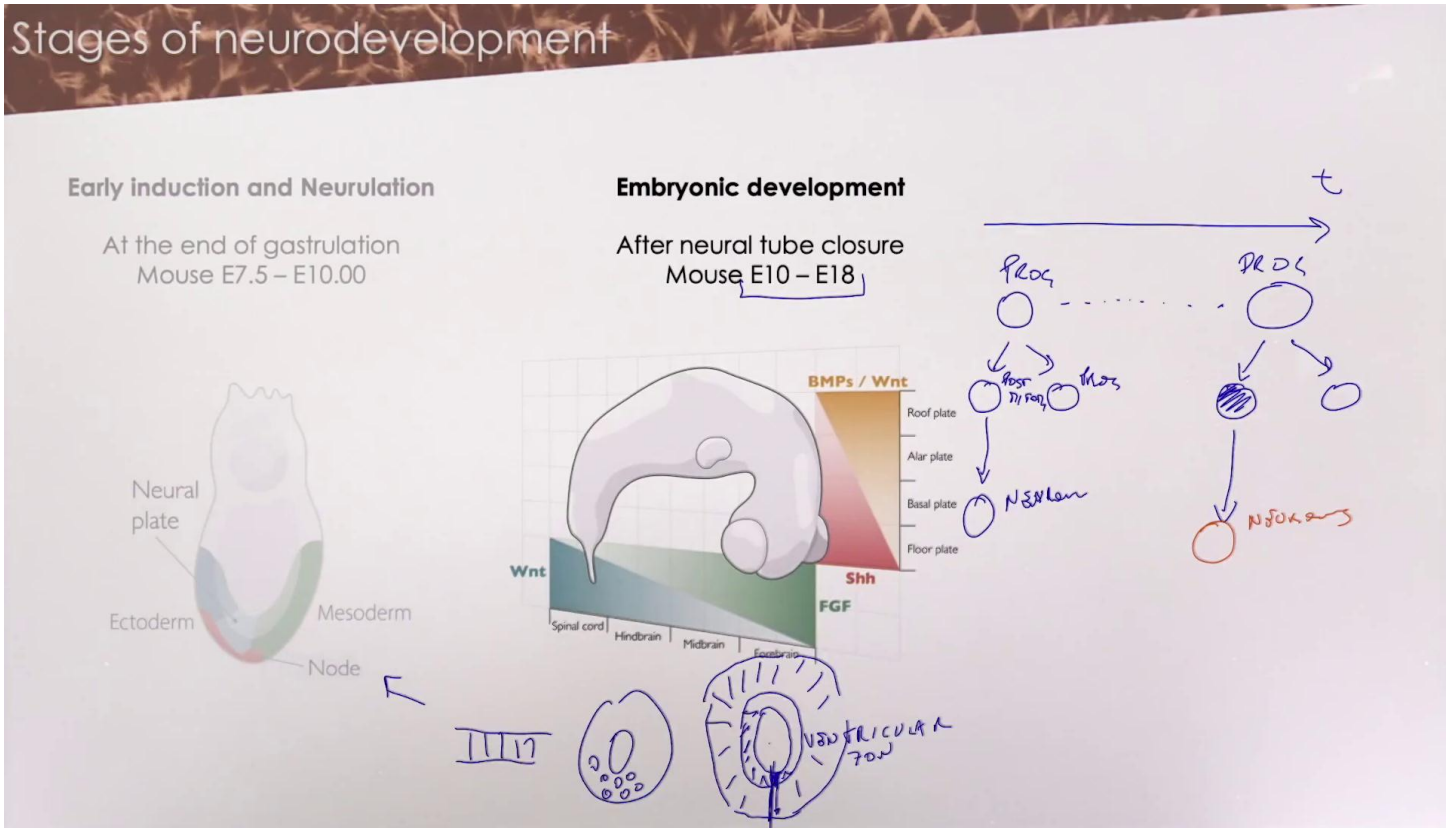


So there's going to be this segregation. If we take, for example, a section across this, the neural tube, we will see again this layer of cells that are proliferative, and then progressively towards the periphery, we're going to see cells that are postmitotic and differentiate. This process is happening differently, in different parts of the brain. Because of the cues that the cells has received in the past and the new cues that will be received thanks to secondary organisers, we're going to see them in the next few slides. The cells are going to commit to particular cellular type and fate, will have the generation of different neurons depending where the progenitor is positioned and also depending on the time of birth. So for example, if we consider the progenitor pool that is present in the ventricular zone, we will see a situation where in time, at very early time points, the division of the cells, the symmetric divisions from those progenitors, are going to generate other progenitor cells, but also cells that are postmitotic, and those cells are going to differentiate in particular neurons. However, the same process is going to happen later in time.

Notes

Summary

6m 05s

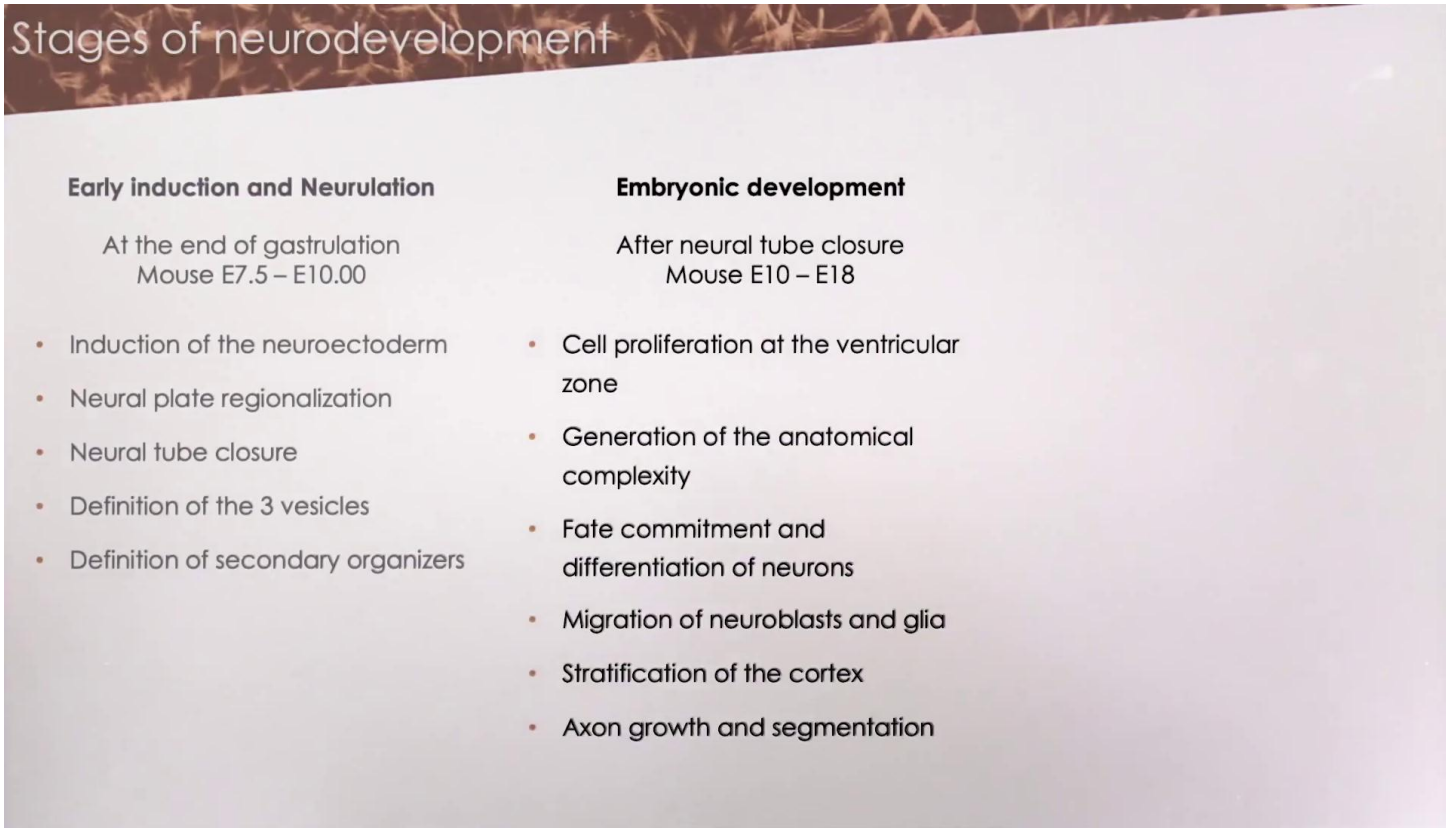


Both the progenitors are going to accumulate changes over time. They're going to change their gene expression. Again, a sequence, a cascade of events will determine them to change their gene expression. This will cause a change in the destiny, in the final fate of those postmitotic cells. The same asymmetric division will happen also later, but this will generate different kind of neurons and this is an example of temporal regulation of neurogenesis.

Notes

Summary

7m 29s

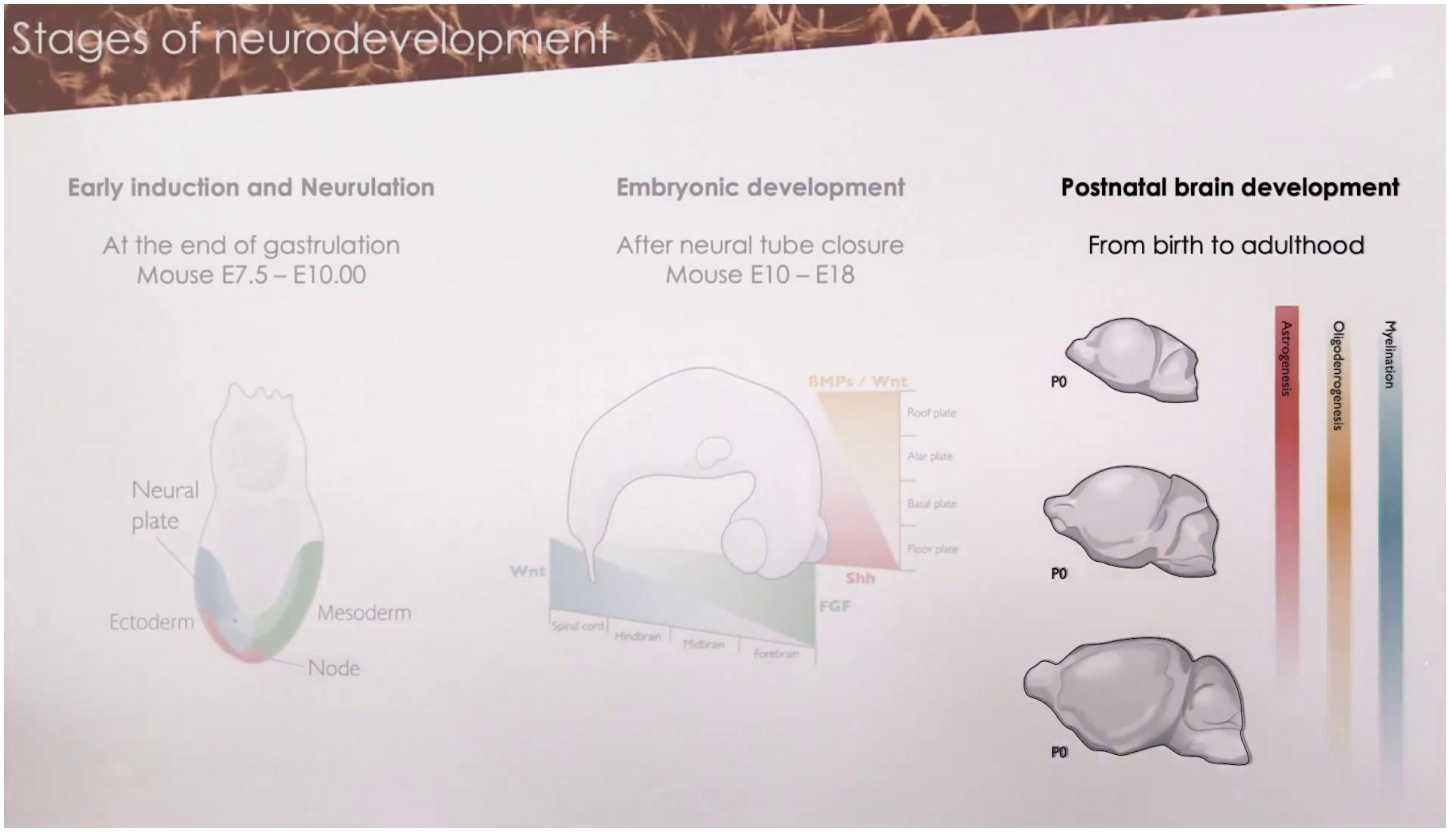


Okay, let's now sum up the events that happen in this time between E10 and E18. We will see continuation of cell proliferation, but also generation of postmitotic cells. There will be the formation of the ventricular zone. Anatomical complexity will be generated by an overlap of spatial cues and temporal driven changes. We will see fate commitments. Again, progenitors postmethologically decide, on the basis of the surrounding cues and on their past, to differentiate in different neurons. We're also going to see at the end of the lecture, migration of neurons. They're going to change their location to be attracted by other cues. In the cortex, for example, we very clearly characterise a process of stratification where a temporal regulation of neurogenesis like the one I described in the previous slide is going take an important role in the formation of the layered structure of the cortex. Then final events of fine-tuning of the connection, the connectivity of the brain, axon growth, and segmentation events are going to take place in this time point.

Notes

Summary

8m 08s

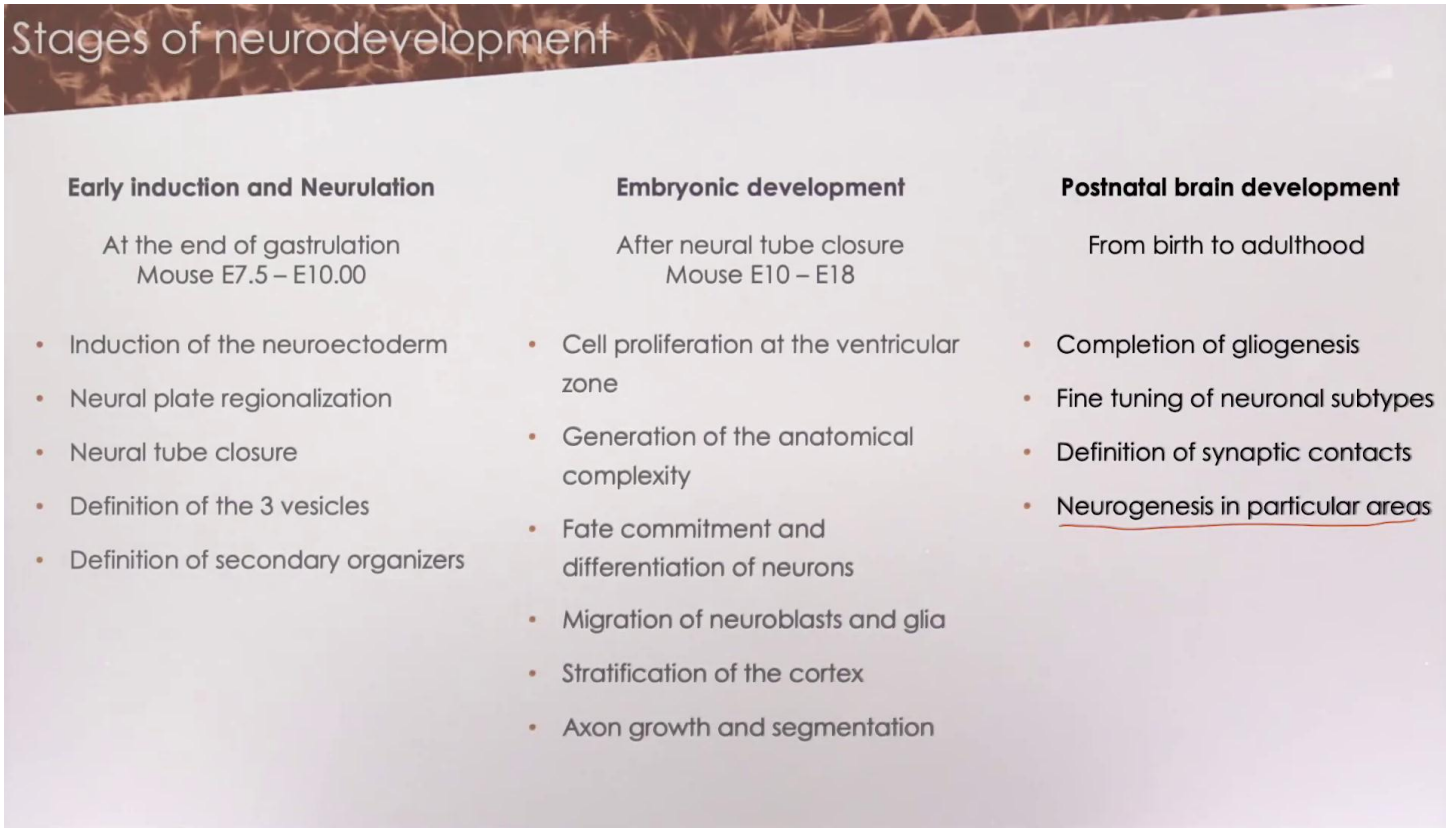


Then we have a final postnatal phase of brain development that it proceeds really from birth to adulthood. As opposed to humans, mice are born with a far from being fully developed brain. In comparison, humans are born with a much more mature brain. Some parts of the human embryonic development actually maps to postnatal mouse development. In those stages, astrogenesis will be completed. We have also important oligodendrogenesis part. These are process that constitute the maturation and the generation of two important glial cell type, the astrocytes and the oligodendrocytes. Oligodendrocytes is where we start the process of myelination, by which they will surround a neurons with a so-called myelin sheet made from their membranes. In this way, they will provide an improvement of neural transmission. Also in these stages, we will see a fine-tuning of neural cell types, fates, and functions. We're going to see a refinement of connectivity between different neurons, and the fine-tuning also starts to fine-tune the synaptic contacts, and an overall maturation of some cell types, that while were specified at birth, they can continue to acquire and activate later particular gene regulatory modules that were not yet expressed during brain development in the birth. Further fine-tuning and specification.

Notes

Summary

9m 17s



Just again, to sum up what we say, completion of giliogenesis, fine-tuning of neural subtypes, definition of synaptic context, and we also, important to say, in some areas we still have in specific areas like the hippocampus and the dentate gyrus in particular, we have still some neurogenisis cells that are proliferative. The rest of the brain at this point, non-proliferative and it's quite static in terms of cell generation.

Notes

Summary

11m 04s