



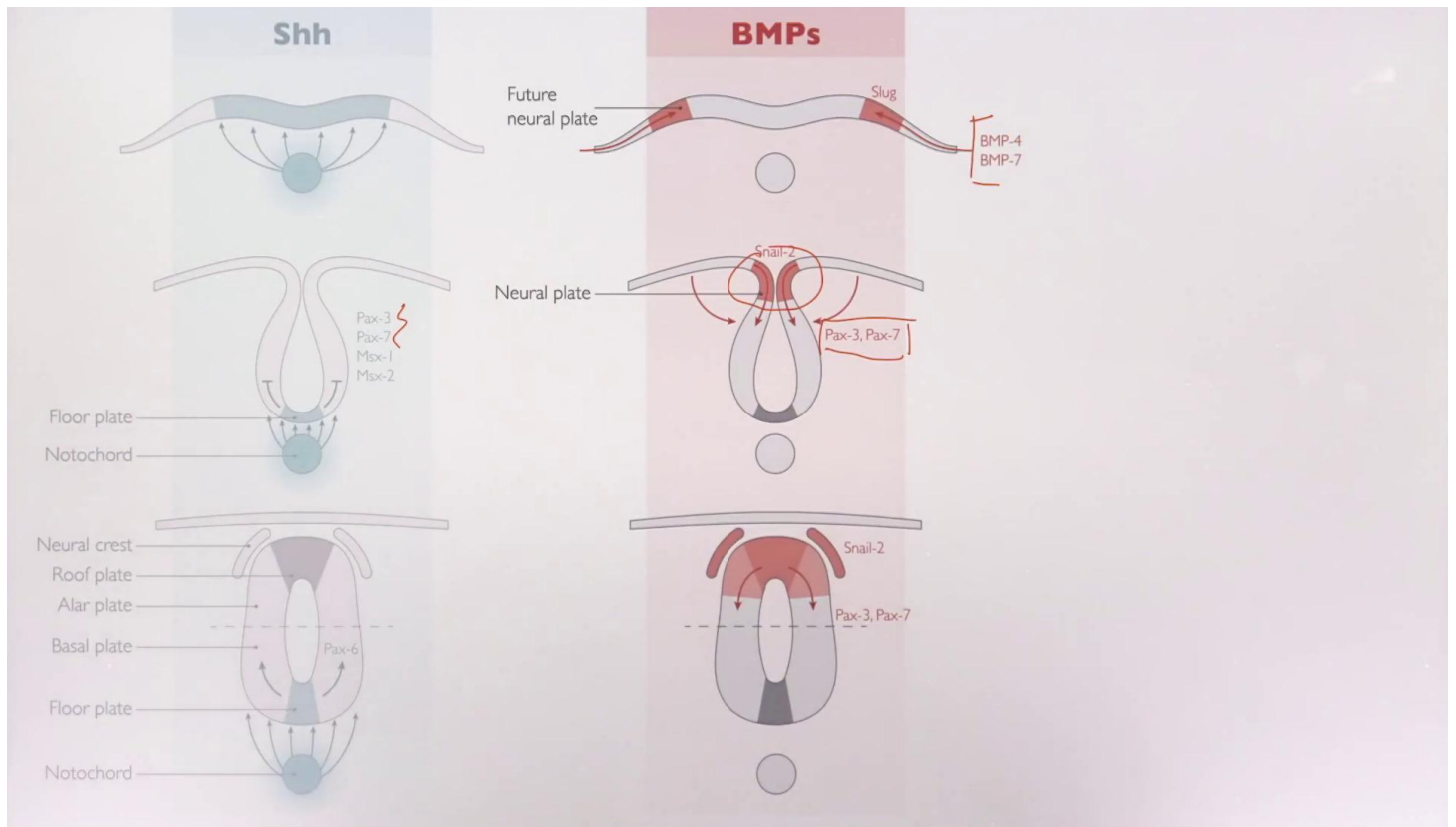
Let's now go a little bit more molecular and look at which particular cues and how they determine neurulation. First, important cue, Sonic Hedgehog, is a ventralising signal. At the beginning, Sonic Hedgehog gets completely provided by the pre-notocardal and notocardal tissue. We saw at the beginning, development is used to just determine the region that is going to become a proper neuroectoderm and will give rise to the neural lineage, as opposed to more lateral part, that we saw are going to give rise to the epidermis. Later on, the effect of Sonic will be inhibiting of a set of transcription factors that are going to be expressed then more laterally, like Pax3, Pax7, Msx1, Msx2. This will contribute to the polarisation of the neural tube in floor plate, basal plate, alar plate, and roof plate. Interestingly also, the more ventral part of the neural tube, gets such a high signal of Sonic, triggers gene regulatory networks that make the cell actually become themselves, cells that express Sonic and further signal it to the nearby cells. In this way, actually, the floor plate becomes what is called a secondary organiser.

Notes

Summary



0m 05s



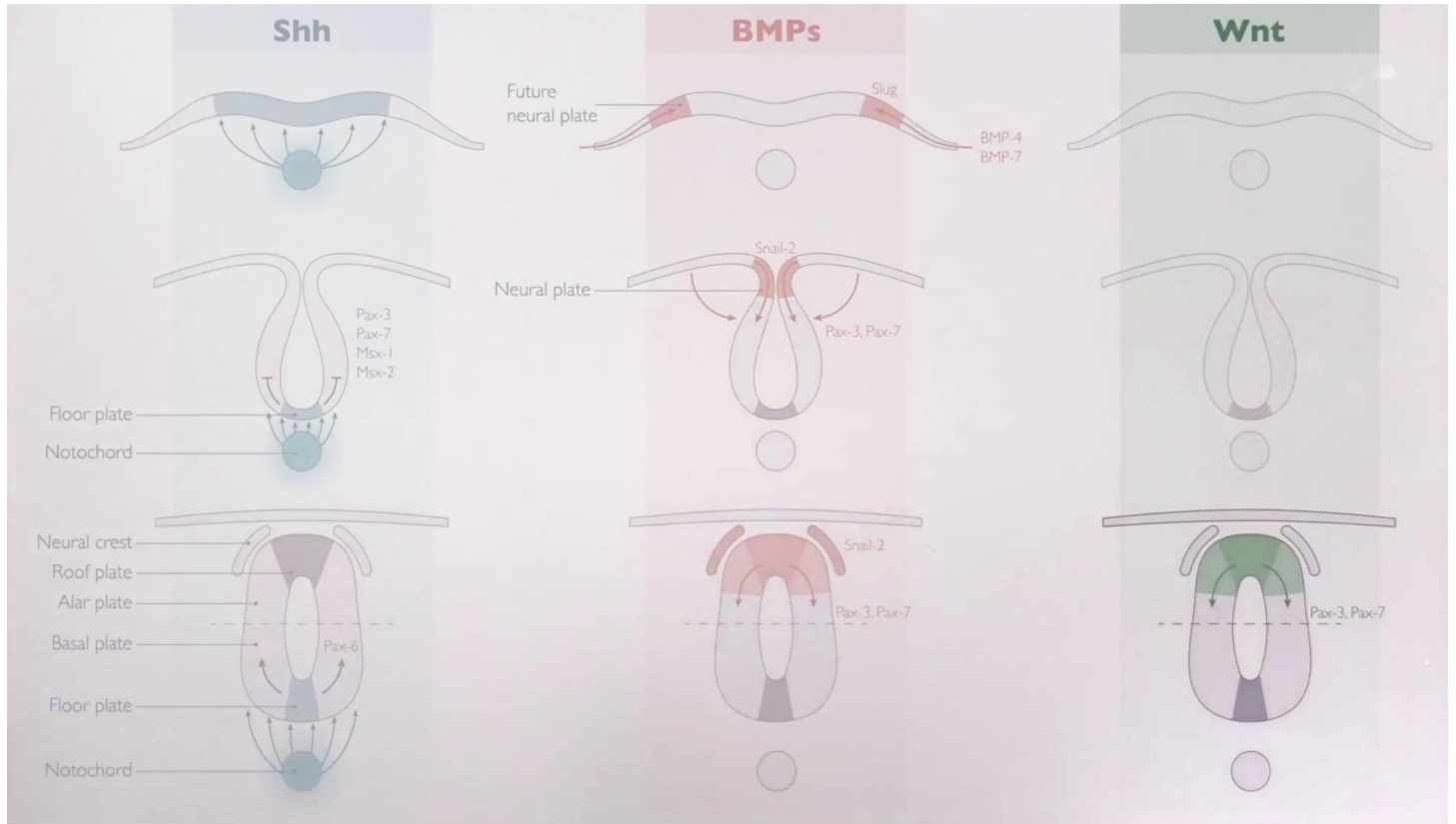
Cells of the neural tube, they organise first from the notochord, primary organiser, then they assume on themselves the role of keep going and signaling this ventral line signal to cells later on, while now the notochord becomes dispensable for this ventral signal. Overall, in this way, the symmetry of the neural tube gets maintained and the signal for the ventralisation kept being provided. Let's see what happened more laterally when the level of sonic are not high enough. Instead, more lateral signals from the BMP families like BMP4 and BMP7 are actually activating the... They're enough to activate the suppressional slug, and then later snail. This will determine actually a dorsal signaling that acts both in a sense directly from the lateral part, but also more specifically at the neural ridge, the region from which neural crest is going to be originated, that signal the activation of Pack 3 and Pack 7 that instead, you remember, were repressed by ventralising signals. Those ventralising and dorsalising signal play in concert and they oppose each other and they contribute to a stable and very precise definition of areas.

Notes

Summary



1m 43s



While, for example, one single ventralizing signal could provide that for ventralization, this opposition of these opposing signals generates an even more precise encoding for the position of the cells. Finally, in this case, for the roof plate, other signaling pathways like Wnt will kick in at particular later stages, and they will be involved in taking over part of the dorsal activation. This is also which exactly family of dorsalising genes with dorsal singular use depends also a little bit on which particular region of the brain we find ourselves. We're going now to talk a little bit about that also and about secondary organisers.

Notes

Summary

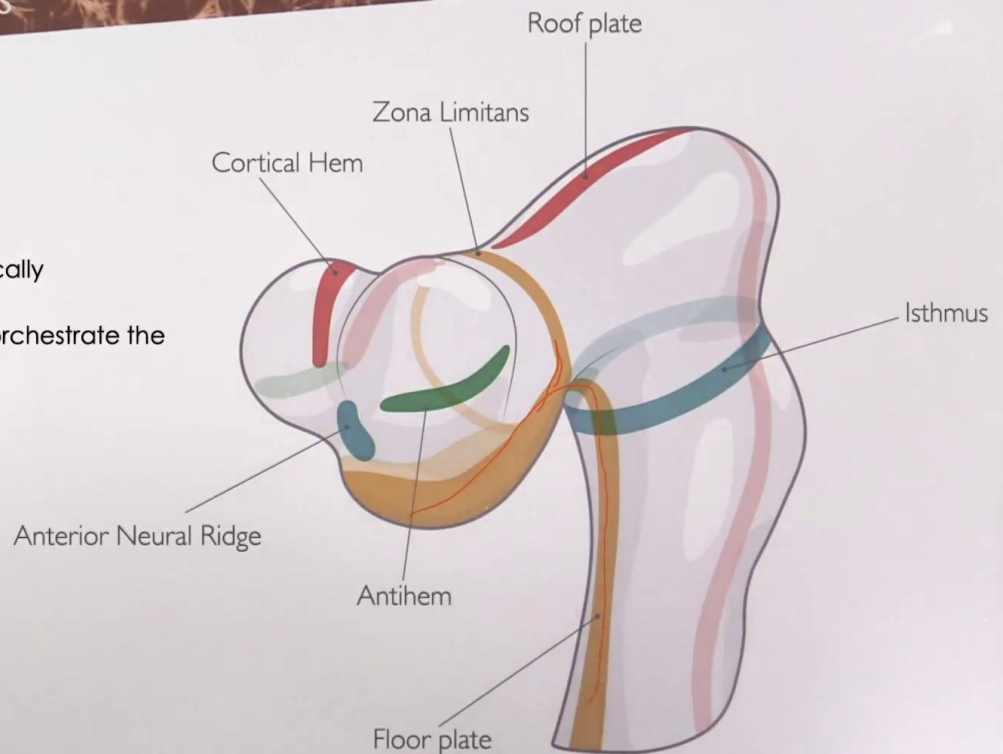


3m 17s

Secondary organizers

During gastrulation:

- Signals are provided extrinsically
- Specific neural progenitors orchestrate the morphogenesis of the brain



Ventralizing (Shh) organizers

Dorsalizing (Bmp, Wnt) organizers

Boundary (Fgf) organizers

As we have seen in the previous slide, from the example of Sonic Hedgehog, notochord, that is ventralising, generating cells in the fore plate of the neural tube then becomes what we call the secondary organisers, a set of neuroepithelial cells that is able itself to signal, to take over the role of secreting particular morphogenes for the continuation of development so that the neural tube can become autonomous for providing the signal. This is not only something that happens in the floor plate, but it's a more general pattern, it's more general idea in how the neural tube develops. This specific neural progenitors that orchestrate the morphogenes of the brain called signal organizer, they acquire specific set of signals that makes them unique and provide unique cues to the surrounding tissue. Let's have a little bit of a look in actual depiction of the neural tube of a stage of development that you might recognise being approximately 9 and 10. The ventralising organizer that we talked about before, the floor plate lines up all the ventral part of the neural tube. It actually even extends in particular region, the zonal limitans intrathalamica, at the boundary between the metencephalon, the midbrain, and the forebrain.

Notes

Summary

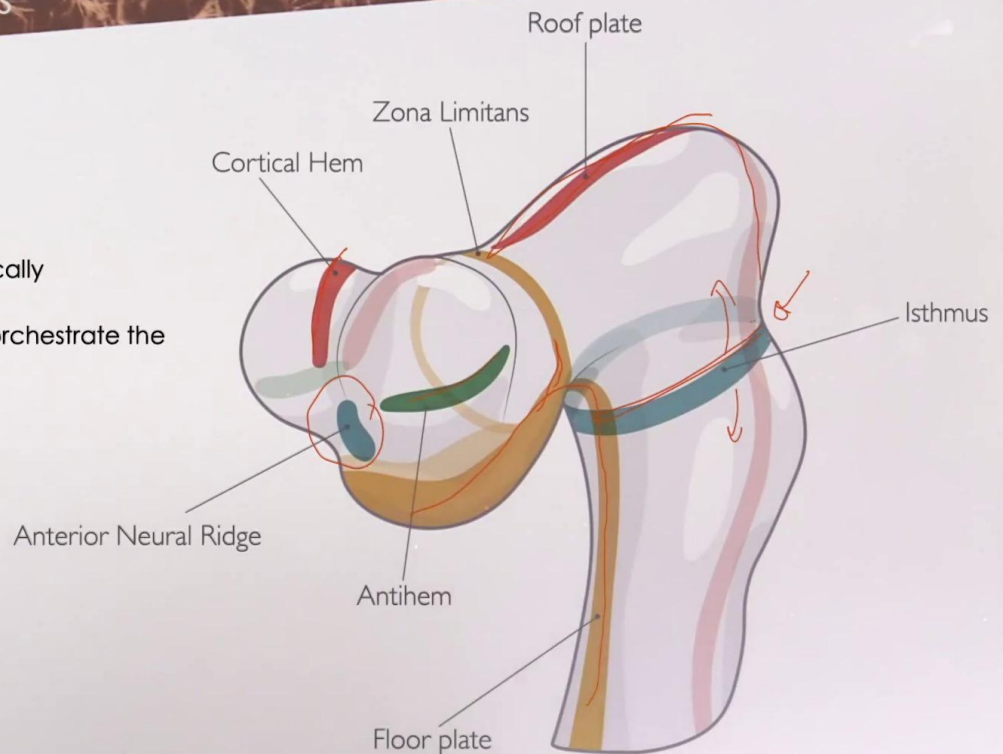


4m 06s

Secondary organizers

During gastrulation:

- Signals are provided extrinsically
- Specific neural progenitors orchestrate the morphogenesis of the brain



Ventralizing (Shh) organizers

Dorsalizing (Bmp, Wnt) organizers

Boundary (Fgf) organizers

We've been talking about dorsalisation. Line up of cells that are present dorsally all along the neural tube, they express BMPs and Wnts. But now we see also other important organiser, for example, the anterior neural ridge is the remnant of the anterior signaling. We saw the KK1, we saw earlier in gastrulation. We saw, for example, anterior transcription factor, Sox1. This is like the remnant of those signal and takes over the role of signaling to other cells, what is the anterior posterior axis. We have other structures and other organiser that also appear later, like the so-called hem and the antihem that's organised within the telencephalon within the forebrain, mediolateral axis that's going to be important for the determination of the cell types at the level of the cortex. We have a very important organiser, it's called the isthmus or the midbrain-hind brain boundary that really provides a fine and very precise lineup of cells that distinguish the region of the midbrain from the hindbrain and induces both upwards and downward, different sites to the corresponding cell. It's a particular organizer that express different FGFs and has also an asymmetric role. It's signalling differently.

Notes

Summary

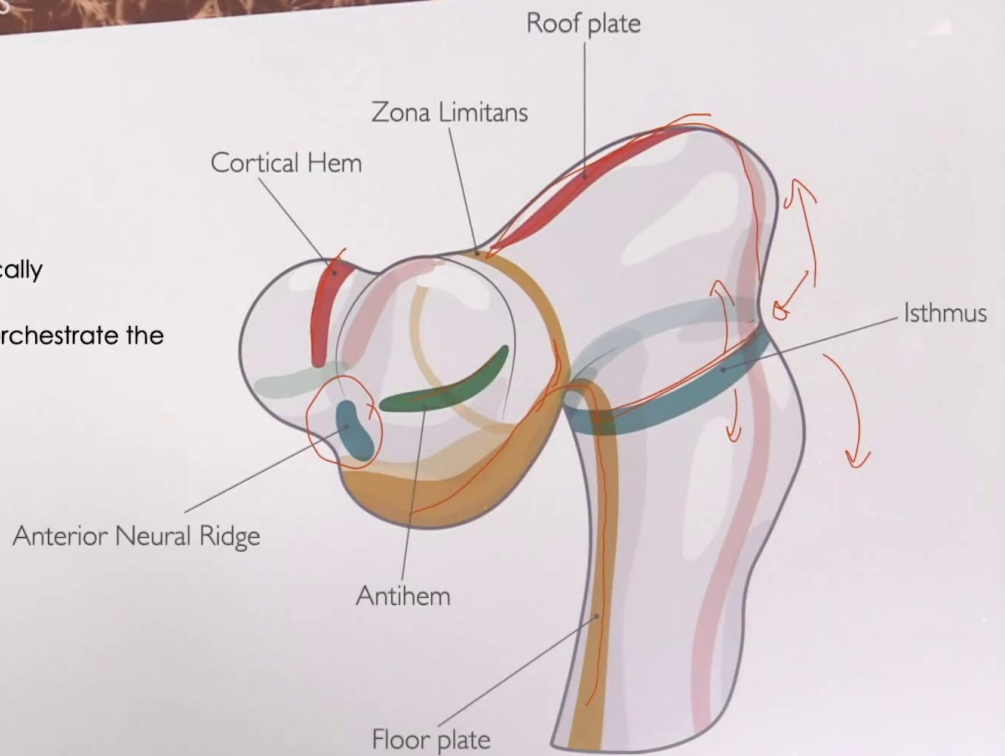


5m 45s

Secondary organizers

During gastrulation:

- Signals are provided extrinsically
- Specific neural progenitors orchestrate the morphogenesis of the brain



Ventralizing (Shh) organizers

Dorsalizing (Bmp, Wnt) organizers

Boundary (Fgf) organizers

It's polarising, signals differently to the more rostral and the counterpart. To conclude, the establishment of secondary organisers is important for brain development. It constitutes the step where the role of providing special cues is relayed from other structures that were originated during gastrulation, to cells of the neural tube themselves. This will allow a more fine regulation and formation of specific regions in the complex anatomy of the brain.

Notes

Summary

