Development of the caudal part of the human embryo

Chapter 7
Impact

Our studies have enhanced the understanding of the development of the caudal part of the body, in particular the gut. We have analysed 3D reconstructions of serial sections of human embryos and foetuses between 4 - 10 weeks of development. Visually, we emphasized the development of the gut, the vertebrae, the arteries, autonomic nervous structures, and some mesenchymal tissues in these 3D reconstructions. Informative pictures of relevant caudal structures of embryos and foetuses have, therefore, been visualised. The 3D modelling also allowed us to quantify growth of these structures relative to neighbouring structures and to growth of the embryo as a whole. The products of our reconstructions, therefore, confer a realistic "biography" on each of the structures mentioned above.

Educational impact

Several output tools can be used to enhance a clear understanding of 3D models and their developmental features. Firstly, such 3D-models can be used to compare or to confront definitive adult structures with their developmental ancestors or precursors. 3D modelling is a powerful tool to visualize the developmental path from an embryonic to an adult structure, which can be exported in a variety of formats. The key problem of teaching or learning developmental anatomy is that no realistic images are available for interrogation. In this sense, developmental anatomy differs from gross (adult) anatomy, which can be demonstrated on cadavers. Developmental morphology is commonly described with the help of drawings in which other processes cannot or have not been included and, hence, require imagination. In our approach, the first format that supports our descriptions digitally is the 3D PDF format which allows readers to inspect our models or their constituting parts from all sides. This format is as easily available for classrooms as lecture handouts. With this tool, students can interrogate the reconstruction database on their own computers in a similar way as they would use the lecture handouts. Although the 3D PDF format allows inspection of 3D embryonic structures, it does not allow students to directly compare different stages of development. We have investigated, therefore, whether printing our models physically would benefit students' understanding. Since we introduced physical 3D models of embryos in our classes, students gave feedback that such models allow them to understand changes in embryonic structures mentioned during lectures more easily than the 3D-PDF models alone. Our motto is "Better visualisation results in better understanding of (developmental) anatomy". In addition to digital and physical models,

therefore, we are presently testing other visualisation methods that may further enhance the transfer of knowledge.

Medical impact

Congenital malformations are among the more popular applications of developmental anatomy. We posit that comprehensive descriptions of developmental phenomena may lead to more accurate pathogenic models of congenital malformations. More accurate descriptions of normal development often entail better and potentially testable pathogenic mechanisms, and a better understanding of the associated dysfunction will probably result in a better repair procedure. Our study focused on the development in caudal body region where anorectal malformations are a common congenital anomaly. Most manifestations of this congenital malformation involve the cloacal subdivision. It has been described for years as being caused by the improper downgrowth of the urorectal septum or lateral folds. Our study described in chapter 2 suggests that the malformation is caused by the dysregulation of growth in the ventral and dorsal compartments of the cloaca. That study showed that the ventral cloaca is a growth area, whereas development of the dorsal cloaca is regressive and fails to show growth. In fact, our series of reconstructions strongly suggests that the formation of the urorectal septum results from the different growth modes in the dorsal and ventral parts of the cloaca. The changing shape of the vertebral column suggests that the early growth differences are also seen in the adjacent tissues. In persisting cloaca (no separation between dorsal and ventral components of the cloaca), dorso-ventral differences in growth are absent or less pronounced and only the ectodermal anal canal, if present, appears to represent the exit of the gut. The rectal fistulae, when present, do not develop randomly, but typically provide access to derivatives of the urogenital sinus, and suggest persisting continuity between the dorsal and ventral parts of the cloaca. Our data, therefore, suggest that the cause of cloacal malformations has to be sought in differential growth between the dorsal and ventral sides of the caudal end of the body (see Chapter 2, Figure 8). We would suggest that the focus of research should be a more detailed analysis of differential growth in the (human) embryo and a far more detailed description of the manifestations of anorectal malformations. We hypothesize that such data will further our understanding of anorectal malformations and, by knowing better what structures remain functionally intact, improve the outcome of surgical repair.