Embryo morphogenetic changes at the end of gastrulation

Starting from the three-layered embryo at the end of gastrulation, describe the morphogenetic changes that lead to the formation of the neural tube, divided into separate brain vesicles, and organisation of tissues and the body plan in the tailbud stage embryo (equivalent to 4-5 weeks of gestation in humans).

Between weeks three and four of development the human embryo undergoes a series of morphogenetic changes that transform it from a flat three-layered disc into a tube via a process called neurulation (Price, Jarman, Mason, & Kind, 2011). Examination of the growth steps involved in neural tube formation informs our understanding of the establishment of brain vesicles and further organisation of tissues and body plan into the embryonic tailbud stage at 4-5 weeks gestation.

The following definitions provide a frame for this discussion. Morphogenesis means the generation of form, shape and tissue organisation (Bard, 2008). Neurulation is development specific to the nervous system (Filas, Xu, & Taber, 2013). It occurs in two phases – primary neurulation which establishes the brain and spinal cord down to S4-5 whilst the rest of the cord is formed in a secondary later phase (Sadler, 2005). This discussion will focus on primary neurulation. The concept of body plan refers to broad anatomical features shared by animals of the same phylum at a mid-embryonic (phylotopic) stage of development. (Irie & Kuratani, 2014).

At around 20 days, the embryo consists of three germ layers – the ectoderm (on top), with the mesoderm and endoderm layers below. Further development of the nervous system is now triggered by neural induction.

Medial ectoderm cells receive signals from the underlying mesoderm and decide on a “ neural fate” becoming neural tissue (rather than epidermal tissue) in the form of a thickening or neural plate (Stern, 2006). The notochord has a key mechanical and morphogenetic role in this process, assisting with folding and cell differentiation (Sadler, 2005).

By the end of week three the lateral edges of the neural plate are pushing up either side of a depressed mid-line (neural groove) to form two neural folds in a V shape. Somite blocks are forming from some of the mesoderm underneath the folds. Eventually the two neural folds meet in the middle and fuse to form the neural tube by the end of week 4. As the neural tube forms ectodermal cells from the tube migrate to form the neural crest. Neural crest cells contribute to many other important structures including the peripheral nervous system (Price et al., 2011).

Neurulation advances cranially and caudally. Rapid changes at the cranial end result in the development of the three primary brain vesicles – the forebrain (prosencephalon), midbrain (mesencephalon) and hindbrain (rhombencephalon) (Scott F. Gilbert, 2000). This gross anatomical organisation of the early brain is widely believed to give rise to the development of the five secondary brain vesicles in all vertebrates although some research suggests significant similarities rather than a universal rule (Ishikawa, Yamamoto, Yoshimoto, & Ito, 2012).

Further subdivisions at the anterior end produce changes as precursors to the eventual adult derivatives of the three primary vesicles; the prosencephalon divides into the anterior telencephalon – which will become the cerebral hemispheres – and the caudal diencephalon – which gives rise to nuclei such as the thalamus. The hindbrain flexes to form the myelencephalon – which becomes the medulla oblongata, separating from the pons at the cranial end – and the metencephalon which gives rise to the cerebellum (Scott F. Gilbert, 2000).

Looking at general organisation of tissue and body plan between 28-35 days – the cranial to caudal folding of the neural tube described above has occurred in parallel with an overall folding of the embryo into a “ comma” shape enclosing the forming internal organs in a layer of ectoderm. At this tailbud stage the essential template for the body plan is present and “ conserved” with strong human embryonic resemblance to other vertebrate embryos before further morphogenetic development into divergent adult structures (Irie & Kuratani, 2014). Common features as well as the neural tube and notochord are the somite blocks, the optic anlagen (developing eye) and pharyngeal pouches (S. F. Gilbert & Barresi, 2017).

Beyond the scope of this discussion, but worth noting in a pathological context neural tube defects (NTD’s) are one of the most common abnormalities caused by failure of the neural tube to close. Understanding of the epidemiology and aetiology of NTD’s is also informing schizophrenia research with the hypothesis of a shared risk factor around in-utero nutritional deficiencies (Zammit, Lewis, Gunnell, & Smith, 2007).

In summary, the morphogenetic changes that occur to transform the germ layers into the neural tube and the organisation of the body plan into the tailbud stage are developmentally significant. They give rise to the brain and spinal cord; the neural crest cells contribute to associated structures and the folding wraps the epidermis around the embryo.

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