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Sommario/riassunto

The brain functions within an internal environment that is determined and controlled by morphological structures and cellular mechanisms present at interfaces between the brain and the rest of the body. In vertebrates these interfaces are across cerebral blood vessels (blood-brain barrier) choroid plexuses (blood-cerebrospinal fluid barrier) and pia-arachnoid. There is a CSF-brain barrier in the neuroepithelium lining the ventricular system that is only present in embryos. There is now substantial evidence that many brain barrier mechanisms develop early and that in some cases they are functionally more active and even more specialized compared to adult barriers. Therefore barriers in developing brain should be viewed as adapted appropriately for the growing brain and not, as is still widely believed, immature. Considerable advances in our understanding of these barrier mechanisms have come from studies of the developing brain and invertebrates. A striking aspect, to be highlighted in this special edition, is that many of the molecular mechanisms in these very diverse species are similar despite differences in the cellular composition of the interfaces. This Frontiers Topic comprises articles in three sections: Original studies, Reviews and Myths & Misconceptions. Original articles provide new information on molecular and cellular barrier mechanisms in developing brains of primates, including human embryos (Brøchner et al., Ek et al., Errede et al.), rodents (Bauer et al., Liddelow, Strazielle & Ghersi-Egea, Saunders et al., Whish et al.), chick (Bueno et al.) and

zebrafish (Henson et al.) as well as studies in drosophila (Hindle & Bainton, De Salvo et al., Limmer et al.). The Reviews section includes evolutionary perspectives of the blood-brain and blood-CSF barriers (Bueno et al., Bill & Korzh). There are also detailed reviews of the current state of understanding of different interfaces and their functional mechanisms in developing brain (Bauer et al., Strazielle & Gjersi-Egea, Liddelow, Richardson et al., Errede et al., Henson et al., Brøchner et al.) and in invertebrates (Hindle & Bainton, De Salvo et al., Limmer et al). Different aspects of the relationship between properties of the internal environment of the brain and its development are discussed. (Stolp & Molnar, Johansson, Prasongchean et al.). A neglected area, namely barriers over the surface of the brain during development is also covered (Brøchner et al.). Clinically related perspectives on barrier disruption in neonatal stroke are provided by Kratzer et al. and other aspects of dysfunction by Morretti et al. and by Palmeta et al. on the continuing problem of bilirubin toxicity. Progress in this field is hampered by many prevailing myths about barrier function, combined with methodologies that are not always appropriately selected or interpreted. These are covered in the Misconceptions, Myths and Methods section, including historical aspects and discussion of the paracellular pathway, a central dogma of epithelial and endothelial biology (Saunders et al.) and a review of markers used to define brain barrier integrity in development and in pathological conditions (Saunders et al.). Use of inappropriate markers has caused considerable confusion and unreliable interpretation in many published studies. Torbett et al. deal with the complexities of the new field of applying proteomics to understanding blood-brain barrier properties as do Huntley at al. with respect to applying modern high throughput gene expression methods (Huntley et al.). The Editorial summarizes the contributions from all authors. This includes mention of some the main unanswered but answerable questions in the field and what the impediments to progress may be.