Respiratory Physiology & Neurobiology 173S (2010) S74–S82

Contents lists available at ScienceDirect

Respiratory Physiology & Neurobiology

journal homepage: www.elsevier.com/locate/resphysiol

Review

Evolution and development of gas exchange structures in Mammalia: The placenta and the lung☆

Andrea M. Mess*, Kirsten J. Ferner

Museum of Natural History, Leibniz Institute for Research on Evolution and Biodiversity at the Humboldt University Berlin,
Invalidenstr. 43, 10115 Berlin, Germany

ARTICLE INFO

Article history:
Accepted 9 January 2010

Keywords:
Placenta lung
Pre- and postnatal phases
Mammals
Chorioallantoic
Eutheria
Ruminants
Rodents

ABSTRACT

Appropriate oxygen supply is crucial for organisms. Here we examine the evolution of structures associated with the delivery of oxygen in the pre- and postnatal phases in mammals. There is an enormous structural and functional variability in the placenta that has facilitated the evolution of specialized reproductive strategies, such as precociality. In particular the cell layers separating fetal and maternal blood differ markedly: a non-invasive epitheliochorial placenta, which increases the diffusion distance, represents a derived state in ungulates. Rodents and their relatives have an invasive haemochorial placental type as optimum for the diffusion distance. In contrast, lung development is highly conserved and differences in the lungs of neonates can be explained by different developmental rates. Monotremes and marsupials have altricial stages with lungs at the early saccular phase, whereas newborn eutherians have lungs at the late saccular or alveolar phase. In conclusion, the evolution of exchange structures in the pre- and postnatal periods does not follow similar principles.

1. Introduction: mammalian respiration organs and reproduction

The class Mammalia is divided into three groups, each characterized by their specific mode of reproduction: Monotremata are egg-laying, Marsupialia are characterized by the dominance of the yolk sac placenta and in Eutheria chorioallantoic placentation is significant for fetomaternal exchange (Starck, 1975; Mossman, 1987). The associated reproductive strategies range from altricial neonates in ancestral mammals, monotremes, marsupials and the stem species of eutherians, towards intermediate and precocial forms that evolved in several eutherian taxa (Starck, 1975; Martin, 2003; Martin and McLarnon, 1985; see Novak, 1999 for data on the developmental conditions within mammals). An important aspect associated with the different reproductive strategies is the oxygen supply for the developing young and how this is facilitated in the pre- and postnatal phases. Primarily the placenta is providing oxygen for the fetus (Bartels, 1970; Schröder, 1995; Mess and Carter, 2006, 2007; Carter, 2009; Enders, 2009). In contrast to the lung, the placenta is a multi-functional organ; composed of the tissues of two individuals, with gas exchange representing only one of many functions (Enders, 2009). The gas exchange in the placenta is regarded to be less efficient than in the lung, because the minimum diffusion distance is larger and the permeability of the blood–blood barrier is lower than the permeability of the blood–gas barrier in the lung (Brandis, 2002). However, the intrauterine nourishment and placental gas exchange in mammals are efficient enough to enable different reproductive strategies. In particular, developmentally advanced fetuses require sufficient oxygen transfer across the placenta, whereas early stages tolerate anaerobic conditions—a fact that is regarded as a driving factor for the high degree of placental diversity in eutherians (Enders, 2009). After birth, the ability of the newborn animal to survive depends on the degree of maturation of the respiratory and circulatory systems. The newborn's respiratory apparatus must be sufficiently developed to take over the gas exchange function previously provided by the placenta (Mortola, 2001). The various reproductive strategies of mammals – ranging from altricial to precocial – request different metabolic capacities of the animal. Compared to altricial newborns, which remain in a nest, precocial species need to have a high metabolic performance, necessary for active locomotion immediately after birth.

Thus the question arises if the evolution of the exchange structures in the pre- and postnatal periods follows recognizable principles. The null-hypothesis is that pre- and postnatal strategies for gas exchange are independent. Therefore, we tested the hypothesis that similar patterns are present throughout ontogeny. We provide the first combined analysis on the evolution of gas exchange structures during ontogeny in regard to the associated reproductive strategies.

☆ This paper is part of the "ICRS Supplement", guest-edited by Dr. Steven F. Perry.

* Corresponding author. Tel.: +49 30 20938400; fax: +49 30 20938565.
E-mail addresses: andrea.mess@mfn-berlin.de, drandrmss@aol.com (A.M. Mess), kirsten.ferner@mfn-berlin.de (K.J. Ferner).

1569-9048/$ – see front matter © 2010 Elsevier B.V. All rights reserved.
doi:10.1016/j.resp.2010.01.005

2. Methodological approaches

The improved understanding of mammalian interrelationships as revealed by molecular phylogenetics and other systematics stimulated attempts to trace patterns of organ evolution in regard to the placenta of Eutheria (e.g., Vogel, 2005; Mess and Carter, 2006, 2007; Wildman et al., 2006; Elliot and Crespi, 2009) or Marsupialia (Freyer et al., 2003) as well as for the lung development (Szdzuy and Zeller, 2009). Here we provide the first combined analysis on the evolution of gas exchange structures in the pre- and postnatal phases and their relevance for associated reproductive strategies. In order to compare evolutionary events during ontogeny, we plotted available data on one of the most comprehensive super-trees of Mammalia (Bininda-Emonds et al., 2007). Since the database is most restricted for lung development, we chose those families for analysis for which at least one species has been investigated in this respect (Table 1). In a second step data on the placenta were added. If no data were available for the originally chosen species, substitutions were done by using better investigated species (see Table 1). We focused on the definitive placenta, i.e. near term of pregnancy, which marks the maximum potential for gas exchange and the developmental degree of the lung at birth. The data have been analysed by applying MacClade 4.0 (Maddison and Maddison, 2000) to the published tree topology (Fig. 1). The results are discussed in relation to the reproductive strategies with special reference to the developmental conditions of the newborn.

3. The placenta

A placenta is a structure for physiological exchange between mother and offspring (Starck, 1975; Mossman, 1987). It represents an interesting system of respiratory dynamics with a high degree of structural and physiological diversity (Mess and Carter, 2007). The mammalian placenta is derived from four extra-embryonic membranes evolved in amniotes: the amnion surrounding the embryo, the yolk sac and the allantois, which both could serve as a placenta in association with the chorion (Mossman, 1987; Mess et al., 2003). Umbilical vessels vascularized the chorioallantoic placenta, whereas vitelline vessels contribute to form a choriovitelline or yolk sac placenta. The chorioallantoic placenta, which acts as the main area for fetomaternal exchange in Eutheria (Mess and Carter, 2007), will be our primary frame of reference.

Several factors affect the oxygen transfer within the chorioallantoic placenta (e.g., Metcalfe et al., 1967; Bartels, 1970; Longo, 1987; Carter, 1989, 1999, 2009; Wilkening and Meschia, 1992; Schröder, 1995). However, physically gaining access to the placental complex for instrumentation is difficult and the evolutionary significance of this system is often not apparent. Most physiological features such as placental blood flow rates, hemoglobin concentration or blood oxygen affinity have continuous variables and do not allow tracing evolutionary trends (Carter, 2009). At present, morphology gives clues to factors with discontinuous variables, accessible for evolutionary analyses. Of special interest in this regard is the evolutionary history of the interhaemal barrier, i.e. the number of cell layers separating fetal and maternal blood (Mess and Carter, 2007; Carter, 2009). The interhaemal barrier is thought to influence the diffusion distance responsible for the oxygen diffusing capacity of the placenta (Carter, 2009). Originally recognized by Grosser (1909) and supported by electron microscopy, there are three principal types (Carter and Enders, 2004; Mess and Carter, 2006, 2007; Elliot and Crespi, 2009): in the *epitheliochorial* placenta the chorionic trophoblast is in contact with an intact uterine epithelium (Fig. 2A). In an *endotheliochorial* placenta the trophoblast is attached to the endothelium of the maternal capillaries because the uterine epithelium has been destroyed by the trophoblast (Fig. 2B). In a *haemochorial* placenta all the maternal tissues have been lost, including the capillary endothelium, and the maternal blood is directly in contact with the trophoblast (Fig. 2C). In contrast to quantitative or morphometric data (Baur, 1981; Mayhew, 2006), qualitative records including ultrastructural data are known for a broad cross-section of species.

Recent results indicate major evolutionary transformations within Eutheria. It has been shown that the last common ancestor of living Eutheria probably was characterized by endotheliochorial placentation (Vogel, 2005; Mess and Carter, 2006, 2007; Martin, 2008). An endotheliochorial placental type is also indicated by the present analysis based on a super tree (Fig. 1), but results may differ with a more complete taxon sampling (not done because of limited data on the lung). Other studies, differing in taxon sampling and using a range of statistical approaches for phylogenetic reconstructions, favor haemochorial placentation as ancestral for Eutheria (Wildman et al., 2006; Elliot and Crespi, 2009).

However, several transformations within the group have been indicated. There is broad agreement that a non-invasive epitheliochorial placenta represents a derived state in ungulates (Cetartiodactyla and Perissodactyla) and relatives (Vogel, 2005; Mess and Carter, 2006, 2007; Wildman et al., 2006; Klisch and Mess, 2007; Elliot and Crespi, 2009; Fig. 1). On the stem lineage to ungulates there was an evolutionary shift to precocial offspring. Even though the retention of an intact uterine epithelium increases the diffusion distance (Mess and Carter, 2006, 2007) an appropriate oxygen transfer must be provided. The perceived disadvantage of the epitheliochorial placenta for diffusion processes may have been countered by the increase in ambient oxygen during the Cenozoic era when large mammals radiated (see Mess and Carter, 2007). In ruminants the evolution of a cotyledonary placenta enlarges the exchange area by greater interdigitation of fetal and maternal tissues (Klisch and Mess, 2007). In contrast, rodents, lagomorphs and their relatives including humans possess the most invasive haemochorial placental type, representing the minimum number of layers as optimum for the diffusion distance (Mess, 2003; Vogel, 2005; Mess and Carter, 2006, 2009; Martin, 2008; Fig. 1). In particular, hystricognath rodents are characterized by numerous derived placental features. Transformations include a specialized placental architecture optimizing the area available for diffusion processes as judged from morphology, a fully countercurrent arrangement of the blood vessels, thinning of the trophoblast lining of the maternal blood spaces including surface extensions as well as a very effective mode of placental establishment and trophoblast invasion (Mess, 2001, 2003, 2007a,b,c,d). These evolutionary transformations on the stem lineage of Hystricognathi are thought to have positive effects on the oxygen supply of the fetus and certainly to contribute to their precocial reproductive strategy. In conclusion, the distinctive pattern of reproduction coincides with the successful radiation of hystricognaths (Mess et al., 2001; Mess, 2003).

Obviously, the enormous structural and functional plasticity of the chorioallantoic placenta enables the evolution of specialized reproductive strategies such as precociality in various ways. Indeed the placental types are associated with different developmental conditions: for instance, rodents possess a haemochorial type associated with either precocial or altricial strategies (Caviidae versus Muridae in Fig. 1). Endotheliochorial placentation occurs in elephants characterized by precocial newborns, in shrews with altricial offspring as well as in tupaids with intermediate forms (Fig. 1). The epitheliochorial placenta is associated mainly with precocial offspring as in ungulates (see Mess and Carter, 2006, 2007; Fig. 1), but also occurs in the American mole *Scalopus* with altricial reproduction (Carter, 2005). It is unlikely that transformations on the interhaemal barrier were driven by the respiratory need of the developing offspring only. In contrast, the evolution of the interhaemal barrier seems to be functionally associated with body mass (Elliot and Crespi, 2009). Moreover, divergent interests of mother