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Rat Homologues to the Human Post-Neonatal Period: Models for Vulnerability to the Sudden Infant Death Syndrome

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To the Editor

Re: Pendlebury JD, Yusuf K, Bano S, Lumb KJ, Schneider JM, Hasan SU. Prenatal cigarette smoke exposure and postnatal respiratory responses to hypoxia and hypercapnia. *Pediatr Pulmonol.* 2011 Published Online 25 October 2011.

I read with great interest this article describing the influences of prenatal cigarette smoke and temperature on postnatal respiratory control in rats. I have long followed and admired the work of this research group.

In this account, the authors describe their previous work conducted using 7 days old rat pups and compare data to experiments performed on 14 days old rat pups to determine if destabilizing effects of increased ambient temperature and prenatal cigarette smoke exposure persist in the older rats. The authors report selecting 7 days old rat pups to approximate the age of peak occurrence of the Sudden Infant Death syndrome (SIDS) in human infants (8–16 weeks), and 14 days old rat pups to represent a postnatal age beyond the analogous risk period for SIDS in humans. The authors cite Quinn¹ in calibrating postnatal age between rat and human.

SIDS is the leading cause of sudden unexpected infant death and of all deaths among infants aged 1–12 months, having a peak incidence between 2 and 4 months. I and many others investigate physiological parameters potentially contributing to the pathophysiology of SIDS, using rodent models. Of particular importance is the characterization of the developmental periods in rats that most closely approximate periods of vulnerability and peak incidence of SIDS in humans. Such equivalent periods in rats are as yet undefined.

Statements made by these authors suggest that 7 days old rat pups approximate the age of peak SIDS incidence, while 14 days old rat pups represent development beyond the analogous period of risk in humans. In so doing, these authors misinterpret even their chosen citation and inadvertently call into question the relevance to SIDS of models derived from rodents 14 days or older.

Quinn¹ is an editorial opinion considering the overall relationship between rat and human aging and should not be taken as an authoritative calibration of rat and human post-neonatal development. It is generally accepted that the first 10–12 days of rat postnatal development

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are homologous to human prenatal development during the final trimester, thus one “should not even consider the rat “born” until postpartum day 12”.¹ In evaluating lifespan, weaning, sexual and musculoskeletal maturity, and reproductive senescence in rats and humans one may generally equate an average of 16.7 subsequent rat days to a given human year. It is not prudent to rely solely on such broad generalization to identify specific periods in human post-neonatal development. However, were one to do so the traditionally accepted developmental period of human SIDS vulnerability (months 1–12) and the period of peak incidence (months 2 through 4) would equate to rat postnatal days 13–29, and days 15–18, respectively.

Estimating the period equivalent to that of human SIDS vulnerability must not be based solely on age correlation, and would be best derived from developmental aspects critical to SIDS vulnerability. Many of these, however, remain unknown. Respiratory dysfunction has been associated with SIDS, and neurochemical and physiological correlates suggest a critical period influencing respiratory control beginning on rat postnatal day P12 which may equate to the beginning of SIDS vulnerability at 1 month in humans.² A subsequent transitional phase with many factors contributing to respiratory instability, in rats continuing through P19, likely equates to a period within that of SIDS vulnerability in humans. There is no clear indication of why vulnerability to SIDS ends at 12 months in humans, nor when this equivalency would occur in rats. Rather than representing a developmental period beyond the analogous risk period for human SIDS, the 14 days old rats used by Pendlebury et al. likely illustrate animals approximating human infants well within the period of SIDS vulnerability.

It is important to prevent potential misconceptions regarding the developmental window appropriate for rodent models of SIDS pathophysiology. However, this does not impact the significance of findings described by these authors. To the contrary, this study’s documentation of profound respiratory destabilization with increased ambient temperature and prenatal cigarette smoke exposure within a period analogous to that of SIDS vulnerability in humans strengthens the linkage between maternal smoking and SIDS.

I thank you for your attention.

Regards,

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