Title: Effects of breastfeeding on body composition and maturational tempo in the rat

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Author's response to reviews: see over
Authors: The authors thank the reviewers for making important suggestions that would improve this report.

Changes are highlighted in the text in blue. Original text to be notified by Reviewers is in grey

Reviewer's report
Title: Effects of breastfeeding on rat and human development: A translational life-history perspective
Version: 1 Date: 3 October 2012
Reviewer: Peter Ellison

Reviewer's report:
This is an excellent report of an experimental study of the effect of weaning age on the subsequent development of rats, combined with an analysis of weaning age and pubertal development in a longitudinal human data set. The results are clearly reported, suggesting that early weaning is associated with significant differences in developmental tempo, body composition, and subsequent reproduction. The authors anchor their findings in the literature on life history theory and also draw important connections to the literature on developmental origins of health and disease.

The methods and analyses are all appropriate and well described. My only concern is with a matter of interpretation and inference. The authors interpret weaning age as a signal of the adequacy of social support, parental investment, and environmental quality, assuming that early weaning is associated with lower values of these variables relative to later weaning. This interpretation is consistent with much of the literature on humans associating poor or unstable conditions in childhood as predictors of the quality of future environments for the child. In the experimental protocol of this study, weaning was imposed by cross-fostering to non-lactating dams. But it seems quite possible to me that, under natural conditions, early weaning might well be associated with more robust nutritional conditions that lead to more rapid pup growth and an earlier attainment of an appropriate size for independence. Similarly, in humans living in subsistence ecological contexts, early weaning is associated with better nutritional conditions, not poorer. I think the authors should explicitly entertain and discuss this possibility and the different interpretation of their results that would flow from it. It would not diminish the value of their study in any way, but rather would enhance the value of the discussion and avoid premature conclusions.

Authors: This alternative interpretation is possible, and is now entertained as suggested in the Discussion, page 8.

Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests: I declare that I have no competing interests.
Reviewer's report
Title: Effects of breastfeeding on rat and human development: A translational life-history perspective
Version: 1 Date: 18 October 2012
Reviewer: Mark A Hanson

Reviewer's report:
This is an interesting paper which reports the results of a multigenerational study of the effects of the timing of weaning in rats, and also of breast vs. formula feeding and the quality of maternal care in humans, on subsequent development for phenotype in a life-history context. Whilst the authors make a good case for conducting the studies, and for lumping all the results together into one paper, the manuscript as it stands is far from adequate. There are major problems with the data presentation, analysis and interpretation which make it very hard to assess, and even to judge the adequacy of the study design itself. These are:

1. There is really no clear a priori hypothesis set out in the introduction. The paper is written in a somewhat anecdotal style, where the rationale shifts as it proceeds.

Authors: The working hypotheses are clearly indicated in the Introduction, page 3, last para. We admit to the style of a shifting rationale as the paper proceeds. We find it essential when as much data are presented in a single paper, and some of the most prestigious journals require this type of presentation.

2. The cross-fostering of pups to non-lactating dams, followed by subsequent separation, constitutes two distinct challenges. Thus the interpretation of timing of weaning is confounded by time spent with a foster mother.

Authors: We accept the comment, and a line with this notion was added in the rationale - last para of the Introduction

3. The data is extensive but is presented in a somewhat selective way, e.g. comparison with D26 or D21 data.

Authors: Every single figure and panel gives the results for all three groups, those weaned on d16, 21 and 26. It is only when the cross breeding in figure 5 that we bred each of the extreme groups (d16 and d26) with the control (d21). There deny any selection of data to have been shown (quite a severe allegation). When significance was evident for only one group, it is so said.

4. There is little information on statistical methods, so it is not possible to assess their validity. The n is not given, especially for subsequent generations; were litter effects controlled for?; use of repeated t tests across a time course is not appropriate because this assumes points are distinct, when of course the data at each time point are related; was connection for multiple comparisons made?
Authors: Statistical methods are given in the Material and Methods. The n is given clearly under Material and Methods – Animals, last sentence. Litter effects were not controlled for, and we added this statement in the Statistics paragraph. The use of repeated t tests across a time course was much entertained with our statistical consultant, who felt that the relatedness of time points is not a serious obstacle and connection for multiple comparisons makes the communication of results obscure.

5. The figures do not have adequate legends or labelling and units on the axis.

Authors: Figure legends were given immediately below the references, and we verified again that all have units on the axis.

6. The methodology of which animals were mated with which in F1/F2 is not clear. To give one example, what does “offspring of late weaned d16 parents, compared to d26 offspring had greater d10-body-fat mass …” (Page 6, lines ½) mean?

Authors: typo error corrected

7. The human studies are not really comparable, as they are a comparison between breast and non-breastfed infants, with the additional complexities of mother-infant attachment. These data cannot be presented adequately here and, if appropriate, merit a thorough and detailed presentation and analysis in a separate paper.

Authors: We decided to adopt this suggestion, removed all article parts related to human subjects, and as suggested, will report it separately.

8. The paper appears to have been hastily written or not proof-read, so that inaccuracies such as “rump-tale length) have crept in. Crown – rump length?

Authors: typo error corrected

Quality of written English: Needs some language corrections before being published

Authors: We do not object to publisher editing. Reviewer 1 was satisfied with the quality of written English.

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests: I declare that I have no competing interests.