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Letters to the Editor

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I would like to comment on the paper of Fosmire *et al.* (1) on "Some Effects of Postnatal Zinc Deficiency on Developing Rat Brain." It is well recognized that zinc deficiency results in a loss of appetite as acknowledged in the paper and as previously noted in children (2). It would thus seem likely that the pups of the zinc-deficient mothers had reduced appetite and ate even less than the pups of the pair-fed, adequate zinc-intake mothers. As generalized undernutrition can cause all of the findings the authors attribute to zinc deficiency, I believe it dangerous to attribute their findings to a lack of zinc.

The authors' main argument, that it is the zinc deficiency and not generalized undernutrition, is based on the difference in brain weights at 6 days in 12 pups from the zinc-deficient dams and 12 pups from the pair-fed dams, whereas body weights of 8 different pups from each maternal group did not differ. One wonders (*1*) why the authors did not combine body weights from the numerous groups studied rather than use just one group of 8 animals, and if this was to be done, why was this group not comprised of the same animals whose brains were studied at that age; (*2*) how the 12 animals were chosen for brain weights at 6 days; (*3*) whether the vertical lines in Figure 2 are SEM's as in Figure 3, and if so, are these really different at $P < 0.01$? No statistics are given for DNA values (Fig. 3), and although quantities are stated to be different in the three groups, one also wonders if these were "statistically" different at all ages.

Would not the proper experiment be to pair-feed pups from birth on diets identical in content other than in zinc, using artificial feeding methods such as described by Miller and the group from MIT? Until this is done it would seem dangerous to implicate zinc deficiency as a cause of poor brain growth, especially when Hambidge *et al.* (2) did not find this to be a problem in the children they studied.

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Dr. Lines has compared the observations we have reported in rats to studies in man by Hambidge *et al.* (1). In our opinion, such a comparison is inappropriate, because the two studies have no similarity whatsoever other than the zinc nutriture of the subjects. The speculations in our paper are speculations and nothing more. They seem appropriate in view of the important role of zinc in the molecular processes of growth.

We have reported effects of zinc deprivation in the rat dam during lactation, on the growth of pups, and on some aspects of the composition of the pups' brains. The effects on growth are confirmatory of our previous work (2, 6, 8) and observations of others (5). The effect of zinc deficiency on growth of suckling rats is similar to what occurs when weanling rats are deprived of zinc (3, 7, 9). Because the effects of zinc deficiency on nucleic acid and protein metabolism are indeed different from the effects of starvation as demonstrated by pair-feeding, we believe it can be concluded that the findings in the pups nursed by zinc-deprived dams were indeed due to zinc deficiency. That the nurslings were deprived of zinc is known from analysis of milk from zinc deprived nursing dams (5).

With regard to Dr. Lines' specific questions, representative growth curves were presented for the convenience of the reader. The curves presented were typical of this experiment and are reminiscent of our previous experience. The groups whose growth curves are presented were killed on *day 16* and the brains of pups nearest the median weights used for analysis.

To avoid bias, animals whose weight were nearest the mean for the litter were selected for analysis. Thus, at 6 days, four pups from each of three litters were analyzed.

In Figure 2, the vertical lines represent SEM's. The differences were different at the 0.01 level as is indicated in the text. The differences between the groups presented in Figure 3 were not significant at the 0.05 level, probably because so few pups were analyzed. Additional animals were not studied because we decided to change to a different strain of rat to improve husbandry. Additional studies are currently underway in our laboratory which confirm and extend the observations on 22-day fetal rats (4).

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