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Correspondence

Differences in maternal protein intake in pregnant rats alone alter the docosahexaenoic acid concentration in the fetal and adult offspring

To the Editor:

We read with interest the study by Rao et al [1] in a recent issue of *Metabolism*. Their study showed that feeding pregnant rats a diet containing 30% less protein and 4-fold more folic acid than controls was associated with reduced docosahexaenoic acid (22:6n-3) concentration in the brain of the adult male offspring, but not in females. There was no effect on 22:6n-3 concentration in the offspring when pregnant dams were fed a diet with reduced protein content, but an amount of folic acid equivalent to the control diet, or the protein-restricted diet without folic acid. This suggests that increased folic acid intake during pregnancy might adversely affect the amount of 22:6n-3 in the brain of male rats, which is of concern because this fatty acid is required for normal development and function of the central nervous system [2]. Unfortunately, Rao et al did not report whether this effect also occurred if animals were fed a diet with the control amount of protein (18%) but supplemented with folic acid.

It appears to have escaped the notice of Rao et al that we have published a series of reports on the effect of dietary protein restriction in rats on the concentration of 22:6n-3 in the pregnant dams, and in the fetal and adult offspring. In contrast to the observations of Rao et al, we found that feeding a diet containing 9% protein alone during pregnancy resulted in lower 22:6n-3 concentration in liver phospholipids, and in plasma phospholipids and triacylglycerol in the pregnant dams, and in fetal brain phosphatidylcholine and phosphatidylethanolamine [3]. The concentration of 22:6n-3 was also reduced in placental phospholipids and triacylglycerol [4]. This suggests that the protein-restricted diet constrained supply of 22:6n-3 from the dam to the placenta and developing fetal brain, possibly by limiting the pregnancy-associated physiological increase in 22:6n-3 concentration in plasma phospholipids [5]. This deficit in 22:6n-3 accumulation in brain persisted in the recently weaned offspring [6]. Interestingly, supplementation of the 9% protein diet with the methyl donor glycine did not alter the concentration of 22:6n-3 in maternal liver, plasma, or placental phospholipids compared with pregnancies where the 9% diet was fed without additional glycine, but was lower than in control pregnancies [4]. This suggests that modulation of 22:6n-3 concentration in pregnancy does not simply reflect the availability of 1-carbon donors.

Together these findings are of importance in understanding how interactions between maternal protein and methyl donors might influence the development and long-term function of the offspring. If our findings and those of Rao et al [1] were replicated in humans, this would be a source of substantial concern for the implementation of interventions to improve the nutritional status of women during pregnancy.

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