

Maternal Protein Malnutrition on Subsequent Generations in the Rat.

Beydoun, S.N., Cuenca, V., and Aubry, R.H.

In the rat, maternal dietary protein restriction contributes to both fetal and placental growth retardation with a significant reduction in brain cell number and cell size at term (2). The earlier the nutritional insult the more marked is the growth retardation, and less likely the recovery. In the rat, WINICK (1) concluded that a combination of prenatal and postnatal nutritional deprivation doubles the chance of long term brain underdevelopment.

Most of the studies evaluating the impact of malnutrition on fetal and neonatal growth were performed on one generation of animals. ZAMENHOF et.al. (3) however, in studying two generations of rats showed that the second generation (F<sub>2</sub>), to mothers (F<sub>0</sub>) who were subjected to undernutrition prior and during their (F<sub>1</sub>) pregnancy had also reduction in cerebral weight and cellularity although the (F<sub>1</sub>) generation was well nourished.

This study was undertaken to evaluate the effect of maternal protein malnutrition and subsequent nutritional rehabilitation in successive generations in the rat on: birth weight, neonatal brain weight, and neonatal brain cell size and cell number. Inbred rats on a normal protein diet (23% proteins) were mated. When pregnant, one group were kept on the same diet, while the rest were placed on a low protein diet (8% protein). The progeny of the malnourished group were kept on low protein and mated for several generations (F<sub>1M</sub>→F<sub>3M</sub>). The F<sub>3M</sub> generation were not able to reproduce. After placing them back on a normal protein diet for several weeks they could get pregnant, and their progeny were kept on the normal protein diet and mated for several generations (F<sub>4MW</sub>→F<sub>6MW</sub>). The birth weights, brain weights, brain wt./birth wt. ratios and the brain protein and DNA content of each generation at birth were compared statistically to the first normal protein diet progeny (F<sub>1M</sub>). The results are shown in the following table (± S.E.).

	F1W	F1M	F2M	F3M	F4MW	F5MW	F6MW
Fetal Wt. (g)	7.3±0.2	4.4±0.1 (P<.001)	5.1±0.1 (P<.001)	4.9±0.2 (P<.001)	5.9±0.2 (P<.001)	6.8±0.1 (NS)	8.0±0.5 (NS)
Brain Wt. (g)	0.3±0.01	0.21±.003 (P<.001)	0.23±.006 (P<.001)	0.19±.005 (P<.001)	0.22±.004 (P<.001)	0.21±.004 (P<.001)	0.28±.009 (NS)
Bt. Wt./ Bod/Wt.	4.2±0.1	4.5±0.1 (P<.05)	4.6±0.1 (P<.05)	4.3±0.1 (NS)	4.1±0.1 (NS)	3.2±0.1 (P<.001)	3.6±0.2 (P<.01)
Prot. Conc. (mg/g)	23.5±1.0	13.6±0.7 (P<.001)	14.3±0.3 (P<.001)	13.3±0.6 (P<.001)	20.0±0.5 (P<.01)	19.3±0.7 (P<.01)	18.3±0.8 (P<.02)
DNA Conc. (mg/g)	2.3±0.1	1.6±0.1 (P<.001)	2.0±0.1 (P<.05)	1.5±0.1 (P<.001)	1.9±0.1 (P<.01)	1.9±0.1 (P<.01)	2.0±0.1 (NS)
PROT/ DNA	10.0±0.4	12.0±0.4 (P<.02)	14.0±0.4 (P<.001)	11.4±0.9 (NS)	9.5±0.2 (NS)	9.9±0.3 (NS)	10.1±0.3 (NS)

There was no difference in the length of gestation, the number of fetuses in a litter or the dry/wet weight ratio in any of the groups studied. This study concludes that 1) maternal protein malnutrition in the rat leads to fetal growth retardation and brain underdevelopment 2) this effect persists for more than one generation even after nutritional rehabilitation 3) brain growth is compromised by both a reduction in cell size and cell number, the latter being in the earlier generations; and 4) it takes longer for the brain to recover than general body growth.

Bibliography:

- 1) WINICK, M: Fetal Malnutrition. Clin. Obstet. Gynecol. 13 (1970) 526.
- 2) ZAMENHOF, S., VAN MARTHENS, E., MARGOLIS, F.L.: DNA (cell number) and protein in neonatal brain, alteration by maternal dietary protein restriction. Science 160 (1968) 322.
- 3) ZAMENHOF, S., VAN MARTHENS, E., GRAVEL, L.: DNA (cell number) in Neonatal Brain: Second Generation (F2) Alteration by maternal (F0) dietary protein restriction. Science 172 (1971) 850.

Samir N. Beydoun, M.D.  
Associate Professor  
Department of Obstetrics & Gynecology (R-136)  
University of Miami  
School of Medicine  
P.O. Box 016960  
Miami, Florida 33101