Influence in Rats of Dietary Fats During the Perinatal Period: Effects Upon Development and Behavior of Dams and Offspring

Ya-Li Liu, MS, and Robert F. Borgman, DVM, PhD

SUMMARY

Female rats were fed purified rations containing 20% fat during gestation and lactation. The fat content was butter oil, an equal mixture of butter oil and lard, or safflower oil. Each litter size was reduced (at random) to 2 male and 2 female pups 1 day postpartum, and these offspring were fed a commercial ration after weaning and until they were 20 weeks of age.

When dams were fed safflower oil, fewer of them produced litters after mating, and their behavior during lactation was less than optimal. Litter size and birth weights were similar in all dams producing litters.

The type of fat fed to the dam in the perinatal period did not influence the growth, development, and spontaneous activity of the offspring. However, the offspring from the dams fed safflower oil exhibited poorer learning performance in a T-maze and sometimes had a longer time of inactivity following auditory stimulation than did the offspring from dams fed the other types of fats.

The lipid content of prepared formulas for human infants varies considerably from that in human milk.[7] Also, there have been increasing efforts by nutritionists to increase the unsaturated fat content of human diets of the United States in an effort to reduce the incidence of cardiovascular disease. Possibly, saturated fat reduction influences the brain of a human fetus if the mother consumes considerable quantities of unsaturated fat. Of particular interest in this regard is the influence of fat consumed during the perinatal period, when the fetal brain is experiencing its greatest growth, and its later influences on development and behavior. Many of the infant formulas available contain corn oil or safflower oil, potent sources of linoleic acid (a polyunsaturated fat).

In rats, the amount of lipid in the diet was found to influence the behavior of prematurely weaned rats.[8] When a ration containing considerable amounts of fat was fed from the 18th to 30th day of life, poor memory and learning ability caused by the early weaning was corrected.

Caffrey and Patterson[6] noticed that rats fed rations containing considerable amounts of saturated fat, as compared to those fed considerable amounts of polyunsaturated fat, performed better in a water maze and exhibited more emotionality. Feeding female rats cocoa butter (saturated fat) during gestation and lactation resulted in offspring that exhibited increased exploratory activity.[2]

The purpose in the present study was to determine whether a dietary fat containing relatively short-chain fatty acids (butter oil), a dietary fat containing a mixture of fatty acids somewhat resembling human milk (a mixture of butter oil and lard; human milk contains less short-chain fatty acids and more long-chain fatty acids than does bovine milk, and human milk is less saturated), or a dietary fat containing considerable linoleic acid (safflower oil, a polyunsaturated fat) would affect the rat dams or the behavior of their offspring.[a]

TABLE 1 – Purified Rat Ration

Ingredient	Percentage
Casein	20.0
Fat (*see* Table 2)	20.0
Dextrose	16.7
Sucrose	16.7
Cornstarch	16.7
Briggs salt mixture*	6.0
Cellulose	3.0
Choline Chloride	0.4
Magnesium oxide	0.5
Vitamin mixture**	nil

* Briggs salt mixture[5] contained the following ingredients by percentages: calcium carbonate, 25.0; dipotassium hydrogen phosphate, 15.0; disodium hydrogen phosphate, 12.17; tricalcium phosphate, 23.33; sodium chloride, 14.67; magnesium sulfate 7 H_2O, 8.33; managanese sulfate 7 H_2O, 0.53; potassium iodide, 0.066; zinc carbonate, 0.033; cupric sulfate, 0.033; and ferrous sulfate, 0.838. ** The vitamin mixture contained the following in mg/100 g of ration: vitamin A acetate, 0.60; vitamin D_3, 0.004; vitamin K, 0.20; alpha tocopherol acetate, 10.0; thiamine hydrochloride, 1.60; pyrodoxine hydrochloride, 1.60; riboflavin, 1.60; nicotinic acid, 20.0; calcium pantothenate, 4.0; biotin, 0.060; and vitamin B_{12}, 0.004.

Materials and Methods

General Methods – An inbred strain of rats[b] were maintained in quarters controlled to room temperature (24 to 26 C), a constant humidity (45 to 55%), and lighting 7:00 AM through 7:00 PM. Food and water were available ad libitum.

When the female rats attained a body weight of 220 to 240 g, they were mated for the first time to male rats of the same strain. Mating was confirmed by the presence of sperm in the female genital tract via daily vaginal lavage. During gestation and lactation, dams were maintained in maternity cages with solid bottoms and bedding of wood shavings. One day postpartum, each litter was reduced to 2 male and 2 female pups by random selection. Offspring were reared with 2 offspring of the same sex and litter per cage.

Received for publication Jan 17, 1977.

From the Department of Food Science, Clemson University, Clemson, SC 29631.

Published by permission of the director as Technical Contribution No. 1455, South Carolina Agricultural Experiment Station.

This work was performed in partial fulfillment of the requirements for the MS degree in nutrition by Miss Liu.

The authors thank Dr. Wilbert P. Byrd, Department of Experimental Statistics, for his assistance in the statistical analyses, and Pacific Vegetable Oil Corporation, Richmond, Ca, for the safflower oil.

[a] Liu, Ya-Li: The Effects of Perinatal Dietary Fats Upon Behavior and Development in the Rat. MS Thesis, Clemson University, Clemson, SC, 1974.

[b] Charles River Breeding Laboratories, Wilmington, Ma. CD F strain, inbred albino, derived from Fisher 344 rats.

Body weights were determined weekly on the dams and offspring, and 1 day postpartum on all neonates. Dams were observed until weaning, and the offspring were observed until they were 20 weeks of age. Development signs were observed daily in the offspring, as previously described.[1,4] After the rats were euthanatized by decapitation, brains of the dams and offspring were retained for analyses; the results are reported elsewhere.[3]

A purified ration, containing 20% fat and the necessary ingredients for an acceptable rate of growth (Table 1), was fed to the dams during gestation and lactation. The dietary fat (Table 2) was formulated by treatment groups as follows: group 1, butter oil; group 2, an equal mixture of butter oil and lard; and group 3, safflower oil. Oils were used within 6 months after obtaining them. The safflower oil was kept in sealed containers, and the butter oil and lard were stored in a freezer (−20 C). Rations were mixed in batches estimated to last 3 to 5 days and were kept refrigerated until used, to minimize deterioration. Food consumption was recorded for the dams during gestation and lactation. After weaning, the offspring were fed a commercial ration.[c]

Data were analyzed statistically.[10] The chi-square test was employed for the number of dams completing gestation, for the incidence of urination in the activity meter box, and for the maternal behavior during lactation. All other data were subjected to the analysis of variance technique.

Behavioral Observations—The maternal behavior during lactation was observed daily and judged as good, fair, or poor. The criteria used for the rating was the quality of nest construction and the incidence of maintaining pups in a nest rather than leaving them scattered about.

Behavioral testing of the offspring was initiated at 4 weeks of age; the schedule of testing is indicated (Table 3). Tests, using auditory stimulation were performed Monday through Friday; 5 times daily in the T-maze and once daily in the activity meter and open field box. The T-maze employed the aversive stimulation of a pulsating electrical current, as previously described.[2,4] The open field box was equipped with acoustical tile on the top and on all sides, with a one-way glass panel on 1 side for viewing purposes; a buzzer was sounded, and the time required for the rat to resume normal activity was recorded.[4]

[c] Purina Laboratory Chow, St Louis, Mo.

TABLE 2—Fatty Acids in Dietary Fats

Group	Dietary fat	Fatty acids* 10:0	12:0	14:0	16:0	16:1	18:0	18:1	18:2	18:3
1	Butter oil**	3	4	11	29	3	13	27	4	0
2	Butter oil** and lard	2	2	8	28	4	14	32	7	0
3	Safflower oil	0	0	trace	7	0	2	12	76	3

* Data are expressed as percentages. Determinations were not made for chains shorter than 10 carbons.
** Unsalted butter was extracted with hexane and the extract was dried to produce butter oil.

TABLE 3—Behavioral Testing of Offspring

Age (weeks)	Auditory stimulation	Activity meter	T-maze safe box position	Remarks for T-maze
0 to 3	No	No	No	Weaned at 3 weeks and rested 1 week
4 and 5	Yes	Yes	Yes, initial side	Initial learning
6	Yes	Yes	Yes, side reversed	Relearning
7 to 14	No	No	No	Rested 8 weeks
15	Yes	Yes	Yes, side reversed from 6th week	Memory retention and relearning
16	Yes	Yes	Yes, side reversed	Relearning
17 to 20	No	No	No	Terminated at 20 weeks

Results

The maternal dietary fat intake influenced the number of dams producing litters and the maternal behavior during lactation, but did not influence the growth rate of the offspring (Table 4). Those dams fed safflower oil (group 3) produced fewer litters after mating, and their behavior during lactation was less desirable than groups 1 and 2.

The feeding of safflower oil to dams (group 3) resulted in offspring which had a less desirable learning performance in the T-maze than noticed in the offspring fed butter oil and butter oil and lard (Table 5). The avoidance response was less and the escape response was greater in the group 3 offspring than in the groups 1 and 2 offspring during the 15th and 16th weeks. Resting for a period of 8 weeks did not appear to alter the responses of the offspring in the T-maze; that is the learning performance did not deteriorate during the rest period. Reversing the safe box between the 5th and 6th week increased the incidences of nonescape in all groups.

The exploratory activity of the offspring did not appear to be influenced by the dietary fat of the dams (Table 6); however, the female offspring were more active than the male offspring.

The period of inactivity following

TABLE 4—Maternal and Offspring Development as Influenced by Maternal Dietary Fats*

		Maternal behavior during lactation: No. of dams		Percentage of female rats			Offspring			
								Weight (av g)†		
Group	Dietary fat	Bred	Raising litters**	Good	Fair	Poor	Sex	Weight at 1 day	Gain/week	Weight at 20 weeks
1	Butter oil	17	11	64	36	0	Male	5.5	14.0	285
							Female	5.1	9.2	190
2	Butter oil and lard	17	11	64	27	9	Male	5.3	14.5	295
							Female	5.1	9.3	192
3	Safflower oil	17	6	17	33	50	Male	5.0	15.7	319
							Female	4.9	9.2	188

* Two male and 2 female offspring were retained per litter. ** Abortions occurred in 2 bred female rats in group 3. The reasons other bred female rats did not produce litters were not determined. This group had a significantly lower ($P < 0.5$) of bred female rats producing litters than did the other groups. † At the $P < 0.05$ level, there were no differences as to treatment, but the male offspring gained more rapidly and attained a greater weight than did the female offspring.

auditory stimulation of the offspring from dams fed safflower oil (group 3) was longer at 15 and 16 weeks of age than that of the offspring in groups 1 and 2 (Table 6). This finding would indicate poorer brain function organization in group 3 offspring.

Discussion

The effects of feeding safflower oil to dams during gestation and lactation were similar to results previously reported;[1] the number producing litters was reduced and the maternal attitude during lactation was less than optimal. Alteration in learning performance (in a T-maze) of offspring from dams fed safflower oil during the perinatal period was noticed in a previous study.[2] The total dietary content of vitamin E in group 3 dams, the content of the safflower oil plus the added vitamin E, provided an average of 2 mg/day per dam; an amount estimated to be sufficient to prevent a deficiency even with the content of polyunsaturated fat in the ration.[3]

The degree of saturation of fat consumed during the perinatal period might be expected to influence brain development, because brain tissue is predominately lipid and the major portion of brain development occurs during this period in rats.[11] Previous testing of rats indicated that increased amounts of saturated fats in the diet fed to dams in the perinatal period improved learning performance in their offspring[2] or improved observed performance if fed to young adult rats.[6]

TABLE 5—Behavioral Responses of Offspring in T-Maze*

Behavior response	Description of offspring: Sex	Group	Dietary fat of dams	Percentage of offspring with given behavior responses at various ages**: 4–5 Weeks	6 Weeks	15 Weeks	16 Weeks
Avoidance	Male	1	Butter oil	61	65	81	75
		2	Butter oil and lard	68	59	89	82
		3	Safflower oil	65	65	81	76
	Female	1	Butter oil	59	66	87	80
		2	Butter oil and lard	63	59	88	81
		3	Safflower	57	56	75	61
Escape	Male	1	Butter oil	39	29	19	24
		2	Butter oil and lard	31	32	11	17
		3	Safflower oil	34	22	19	24
	Female	1	Butter oil	40	26	13	15
		2	Butter oil and lard	36	28	12	18
		3	Safflower oil	42	38	25	38
Nonescape	Male	1	Butter oil	0	7	0	1
		2	Butter oil and lard	1	10	0	1
		3	Safflower oil	1	13	0	0
	Female	1	Butter oil	1	8	0	5
		2	Butter oil and lard	0	13	0	1
		3	Safflower oil	1	5	1	1

* There were 11 litters such in groups 1 and 2 and 6 litters in group 3. Each litter contained 2 male and 2 female offspring. The safe side of the T-maze was changed at the ends of the 5th, 6th, and 15th weeks, and the offspring were rested from the end of the 6th week until the 15th week. ** The avoidance response was lower and the escape response was higher in the group 3 female offspring ($P < 0.05$) during the 15th and 16th weeks.

TABLE 6—Exploratory Activity and the Inactivity Period Following Auditory Stimulation in Offspring*

Group	Dietary fat of dam	No. of litters	Sex	Exploratory period at various ages (av. No. of movements in 5 minutes/offspring)**: 4–6 Weeks	15–16 Weeks	Inactivity period at various ages auditory stimulation, av sec per offspring: 4–6 Weeks	15–16 Weeks†
1	Butter oil	11	Male	107	200	24	3
			Female	155	401	25	2
2	Butter oil and lard	11	Male	149	208	16	2
			Female	189	356	15	1
3	Safflower oil	6	Male	117	292	19	5
			Female	153	448	23	4

* Two male and 2 female offspring per litter. ** At the $P < 0.05$ level, there were no differences as to treatments, but the female offspring were more active than the male offspring. † At the $P < 0.05$ level, at 15 to 16 weeks, group 3 had a longer period of inactivity than did the other groups.

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