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Learning and Memory Impairment in Rats Fed a High Saturated Fat Diet

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At the age of 1 month, three separate groups of Long–Evans rats were placed on 20% (w/w) fat (40% of calories) diets high in either saturated fatty acids (lard-based) or polyunsaturated fatty acids (soybean oil-based) or standard laboratory chow (Purina, 4.5% (w/w) fat). After 3 months, all rats were administered three tests of learning and memory—Olton's radial arm maze, a variable-interval delayed alternation task, and the Hebb–Williams maze series. The lard-fed group was impaired on all tests. The soybean oil-fed group was slightly impaired on some measures, relative to the chow-fed group, but consistently perfomed better than the lard-fed group. The results indicate that a diet high in saturated fatty acids can impair a wide range of learning and memory functions and are in line with biochemical and physiological evidence showing widespread effects of such diets on brain function.

The importance of dietary (nutrient) adequacy in maintaining optimal brain function has been known for many years. While the majority of early studies focused on the need for adequate protein intake, there is substantive evidence that a dietary deficiency of the essential fatty acids (EFAs), linoleate (C18:2ω6) and α-linolenate (C18:3ω3), can lead to brain dysfunction resulting in impaired cognitive performance (Caffrey & Patterson, 1971; Paoletti & Galli, 1972; Galli, Messeri, Oliverio, & Paoletti, 1975; Borgman, Bursey & Caffrey, 1975; Lamptey & Walker, 1976, 1978; Morgan, Oppenheimer, & Winick, 1981; Ruthrich, Hoffman, Matthies, & Forster, 1984; Yamamoto, Saitoh, Moriuchi, Nomura, & Oduyama, 1987). Although these studies vary in design features such as types of fat fed, life stage studied, duration of feeding, and tests employed, they all have in common the finding that animals fed a diet deficient in at least one of the EFAs perform less well on tests of learning and memory

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than animals fed a diet containing higher levels of the EFAs. Most studies commenced diet manipulations during gestation or at birth. This reflects the fact that in the rat and mouse, the animals most often studied, the majority of brain lipid accretion occurs prior to weaning and it is generally believed that the brain is more sensitive to alterations in dietary fat during periods of rapid accretion (Matheson, Oei, & Roots, 1981).

While these studies provided valuable information with regard to the need for EFAs to support neuronal growth and function, they can not be extrapolatd to the human situation since EFA deficiency is rare and only observed in unusual circumstances. However, there is now evidence that brain may be sensitive to qualitative differences in dietary fat composition, in the absence of EFA deficiency, even when diet manipulation is commenced postweaning, and that functional consequences of dietary change can ensue. For example, our studies indicate that feeding young, rapidly growing rats 20% (w/w) fat diets high in saturated fatty acids (SFAs; lard-based diet) resulted in increased pain sensitivity (Yehuda, Leprohon-Greenwood, Dixon, & Coscina, 1986), *d*-amphetamine-induced hypothermia in a cold environment (Yehuda et al., 1986), and altered protein/carbohydrate selection, a component of feeding behavior (Crane & Greenwood, 1987; McGee & Greenwood, 1989) relative to rats fed a diet rich in polyunsaturated fatty acids (PUFAs; soybean oil (SBO)-based diet). Equally important is the observation that motor activity in an open field is not affected (Yehuda et al., 1986), suggesting that these effects are not nonspecific responses to the dietary manipulation. In these studies the level of dietary fat (20% w/w or 40% of calories) was chosen to represent present North American human consumption patterns and the fat sources (lard and SBO) are commonly consumed fats and oils in the human diet.

In a subsequent series of experiments, the Morris water maze (Coscina, Yehuda, Dixon, Kish, & Leprohon-Greenwood, 1986) and Olton's radial arm maze (RAM) (Winocur & Greenwood, 1987) were used to test spatial memory in rats fed SBO and lard diets. The results indicated superior performance by the SBO-fed rats. The purpose of this study was to replicate our original observations using the RAM and to conduct a more systematic investigation of cognitive performance following dietary fat manipulation using additional tasks, including the Hebb–Williams maze (HWM) and a variable-interval delayed alternation (VIDA) task. The HWM provided a good test of general learning ability (Rabinovitch & Rosvold, 1951) and the VIDA task was included because of its sensitivity to different types of learning and memory function. The latter test has been shown to differentiate between short-term and long-term memory, as well as between memory for specific events and memory for non-specific information. Moreover, this test has proven to be extremely useful in differentiating between the effects of damage to specific brain

regions, as well as being sensitive to effects of normal aging (Winocur, 1985, 1986).

MATERIALS AND METHODS

Animals and Diets

Male Long–Evans hooded rats (n = 8/group) 1 month of age and weighing 60–80 g were fed *ad libitum* 20% (w/w) fat diets, described previously (Coscina et al., 1986; Yehuda et al., 1986), containing (g/100 g diet) 20 g lard (supplemented with 5% SBO and safflower oil) or SBO, 27 g casein, 40.2 g cornstarch, 5 g nonnutritive fiber, 2.5 g vitamin mixture (Teklad Test Diets, Madison, WI), 5.1 g Bernhart-Tomarelli mineral mixture, and 0.25 g methionine. No effect of these diets on either caloric intake or growth is observed (Coscina et al., 1986; Yehuda et al., 1986). A third group of animals received standard laboratory chow (Ralston Purina, Longueuil, P. Q., Canada) to serve as a comparative control to previous behavioral testing. After 2.5 months of feeding, food consumption was reduced for an additional 2 weeks and throughout the behavioral testing to maintain rats at 80% of their normal body weight. Diet formulation of the semisynthetic diets was verified by determining protein content (micro-Kjeldahl) and fatty acid profile after mixing. Fat was extracted from the diets, and fatty acid methyl esters were prepared and analyzed by gas–liquid chromatography using flame ionization detection as described previously (Crane & Greenwood, 1987). The fatty acid profile of the diets is provided below (Table 1). Supplementation of the lard with SBO and safflower oil prior to mixing the diet was to ensure adequacy of EFA intake.

TABLE 1
Fatty Acid Composition of Diets (% Fatty Acids)

Fatty acid	Lard diet	Soybean oil diet	Laboratory chow
C14:0	1.6	—	—
C16:0	21.9	10.6	15.7
C16:1	1.9	—	1.3
C18:0	11.5	3.1	4.3
C18:1	34.2	16.2	19.9
C18:2ω6	16.3	52.1	41.7
C18:3ω3	2.5	5.9	4.6
C20:5ω3	—	—	1.4
C22:6ω3	—	—	1.4

Note. Lipid was extracted from premixed diets and analyzed for fatty acid content by gas–liquid chromatography using flame-ionization detection.

Behavioral Procedures

Behavioral testing began 3 months after rats were placed on their respective diets. The three tasks, RAM, HWM, and VIDA, were administered in the same order to all rats with a 2-week interval between each task (during which time they were maintained on their food restriction schedule).

Radial arm maze (RAM). Testing procedures for the RAM were based on those developed by Olton and Samuelson (1976) and modified by Winocur (1982). This maze consists of eight arms (85 × 7 cm) radiating horizontally from a central cylindrical platform (34 cm in diameter). Food cups, with rims to hide the contents of the cup from the animal's sight, are fixed to the floor at the end of each arm. Food-deprived rats received 3 days of preliminary training in which several 45-mg Noyes food pellets were placed throughout the appparatus, including the center platform, each arm, and the food cups. Rats were placed in pairs and allowed to explore the apparatus for about 15 min. After preliminary training, rats received one test trial per day for 10 consecutive days. A trial consisted of baiting each food cup with two pellets and individually placing the rat on the center platform. The rat was removed after all eight arms had been entered or after 10 min had elapsed. An arm was recorded as having been entered if all four feet were in the arm. Records were kept of the arms entered and the order. Errors were indicated as reentered arms.

Hebb–Williams maze (HWM). Administration of this test conformed closely to the well-standardized procedures developed by Rabinovitch and Rosvold (1951). The test consists of 12 different maze problems in which the rats must learn to reach a goal box without entering blind alleys. Initially, food-restricted rats were handled and allowed to habituate to the apparatus. After 3 days, when the rats were exploring freely and eating well (rats were fed 45-mg Noyes food pellets in the apparatus), they individually received preliminary training on practice problems to become familiar with the procedures that apply during the testing trials. Preliminary training was continued until the rat ran from the start to goal box in a total of 70 s over a 10-trial daily session. At this point, testing began in which rats received 10 trials per day on each of the 12 mazes. During testing, records were kept of the total number of errors made. An error was scored when the rat's two forefeet crossed into an error zone within a blind alley. See Rabinovitch and Rosvold (1951) for a more detailed description of testing and scoring procedures.

Variable-interval delayed alternation (VIDA) task. This test was conducted in a Skinner box with a single retractable lever (Winocur, 1985, 1986). Food-restricted rats were initially shaped to press the lever for food according to a continuous reinforcement (CRF) schedule. Shaping was discontinued when a response rate of 75 responses per 15-min session

was achieved. For VIDA testing, each daily session consisted of 12 reinforced (Go) trials alternating with 12 nonreinforced (No-Go) trials. The lever was always present during the Go and No-Go trials, each of which was 20 s long. Each lever press during the Go trials produced a single 45-mg Noyes food pellet, whereas lever presses during the No-Go trials were not rewarded. The Go and No-Go trials were separated by a variable intertrial interval (ITI), during which the lever was retracted. ITIs were 0, 5, 10, 20, 40, or 80 s long, with each delay occurring twice after the Go trials and twice after the No-Go trials, for a total of four times per session. The sequence of ITIs was varied for each session, which always began with a Go trial. Testing was conducted daily for 15 consecutive days.

The results were analyzed in terms of Go/No-Go latency ratios. Ratios were calculated at each ITI by dividing mean latency to first response in the Go trials by mean latency to first response in the No-Go trials. A low ratio would result from shorter latencies in the Go than No-Go trials. Thus, the lower the latency ratio, the better the rat's performance. Successful performance on this task depends on the rat's ability to learn the alternation rule and to remember specific events of the preceding trial. Remembering a successful lever press on a preceding Go trial becomes a signal for the onset of a No-Go trial for which no response is required. By isolating ITI_0, where the need to remember specific events of the preceding trial are minimal, one can track rate of learning of the basic response alternation rule.

Statistical Analysis

Statistical analyses were done using SAS 6.03 (SAS Institute, Inc., Cary, NC) for the microcomputer. Data were analyzed using analysis of variance (ANOVA) incorporating a factorial design to measure main effects and interactions when appropriate.

RESULTS

RAM

The measure of performance reported here is the total number of alleys reentered before all eight alleys were entered at least once on a given trial and the food was consumed. As can be seen in Table 2, the mean number of reentered alleys per trial (errors) differed between the groups ($F(2, 22) = 3.41$, $p < .05$). Subsequent analysis showed that this significant effect was due to the difference in error scores between the lard and SBO groups ($t(14) = 2.30$, $p < .05$). The difference between the lard and chow groups approached significance ($t(15) = 1.67$, $p < .10$) whereas the chow and SBO groups did not differ ($t < 1$).

TABLE 2
Influence of Dietary Fat on Performance on Olton's Radial Arm Maze

	Lard	Soybean oil	Chow
Errors	1.65^{a}	0.78^{b}	0.95^{ab}
SEM	0.37	0.09	0.22

Note. Means and SEM of total errors per trial in all groups over 10 days of testing on the RAM test. Means with different superscripts are significantly different ($p < .05$).

HWM

Figure 1 provides the mean number of errors for the various groups across the 12 mazes. For ease of presentation, the mazes were blocked in pairs. An ANOVA applied to the data indicated a significant diet × block interaction ($F(10, 110) = 2.62$, $p < .01$) as well as significant diet ($F(2, 22) = 6.74$, $p < .005$) and block ($F(5, 110) = 79.10$, $p < .001$) main effects. The significant interaction is due mainly to the disproportionately poor performance of the lard group, relative to the chow groups, on the first 6 mazes (p's $< .01$). The SBO group generally performed better than the lard group ($t(14) = 2.24$, $p < .05$), although on two blocks (3 and 5) the SBO group was worse than the chow group (both p's $< .02$).

VIDA

There was no effect of diet on acquiring the lever pressing response, as all rats achieved stable CRF responding within 5–8 days of the be-

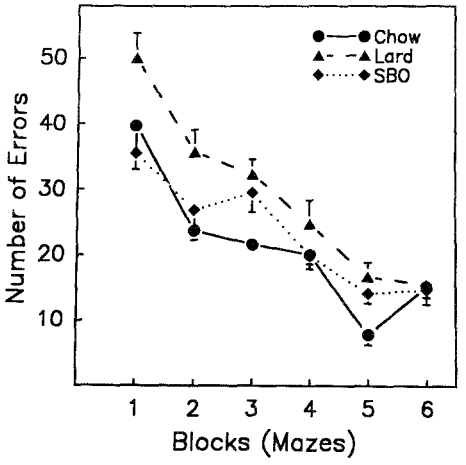

FIG. 1. Means ± 1 SD of errors for all groups on the Hebb–Williams mazes blocked in pairs.

ginning of training. An ANOVA performed on the number of days to reach a response rate of 75 responses per session yielded no significant difference between groups ($F < 1$). An ANOVA was also performed on the response output for each rat's last CRF session and here again there was no significant difference between groups ($F < 1$).

For ease of presentation, latency ratios for each test trial were collapsed into two time delays—short (0, 5, and 10 s) and long (20, 40, and 80 s). Figure 2 shows the performance of all groups at the two delays over the 15 test days, collapsed into five blocks of 3 days each. The results indicate differences between the groups that varied over blocks of trials. This was confirmed by an ANOVA that yielded a significant diet × block ($F(8, 84) = 2.76$, $p < .01$) interaction and a significant diet effect ($F(2, 21) = 12.25$, $p < .001$). None of the interactions involving

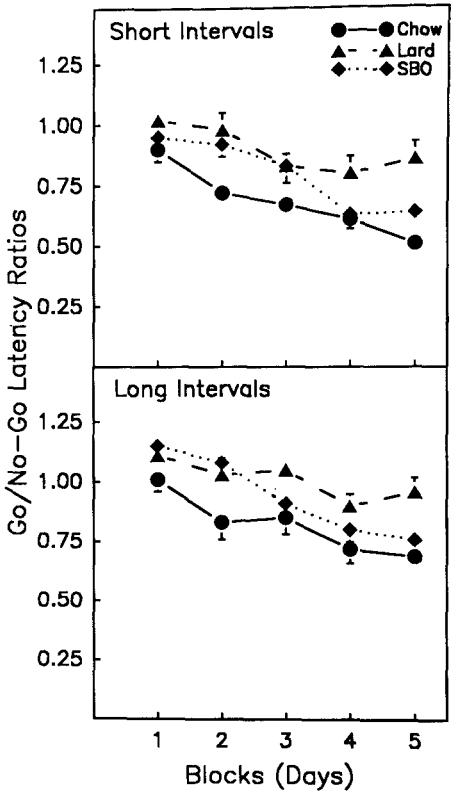

FIG. 2. Means ± 1 SD of latency ratios for all groups at short and long delays over five blocks of 3 test days on the VIDA task. Go/No-Go latency ratios at each ITI were calculated by dividing mean latency to first response in the Go trials by mean latency to first response in the No-Go trials.

ITI were significant (F's < 1) although there was an overall main effect of ITI ($F(1, 21) = 54.07$, $p < .001$).

It is clear from Figure 2 that the lard-fed animals were consistently impaired relative to the chow and SBO groups. An interesting feature of the results is that the SBO-fed animals also had difficulty, relative to the chow group, during the early stages of testing. Significant differences between the SBO and chow groups were observed in block 2 at the short and long ITI's (both p's $< .05$).

The results indicate that the lard group and, to a lesser extent, the SBO group were impaired in performing the delayed alternation task when it was necessary to recall events of the preceding trial. The question arises whether the deficits extend to ITI_0 where demands on working memory are minimal and where successful performance depends exclusively on having learned the alternation rule. A separate analysis performed on the ITI_0 data (Fig. 3) revealed significant diet ($F(2, 21) = 3.97$, $p < .005$) and block ($F(4, 84) = 12.36$, $p < .001$) effects, but the diet $\times$ block interaction was not significant ($F < 1$). Further analysis showed that the main effect of diet was due entirely to the lard group whose overall performance was significantly worse than that of the chow group ($t(14) = 2.86$, $p < .02$). The SBO group fell between the other two groups but differed significantly from neither (both p's $> .05$).

DISCUSSION

The results of this study demonstrate that rats fed a diet high in SFAs (lard diet) for 3 months were consistently impaired, relative to rats fed standard laboratory rat chow, on three tests of learning and memory.

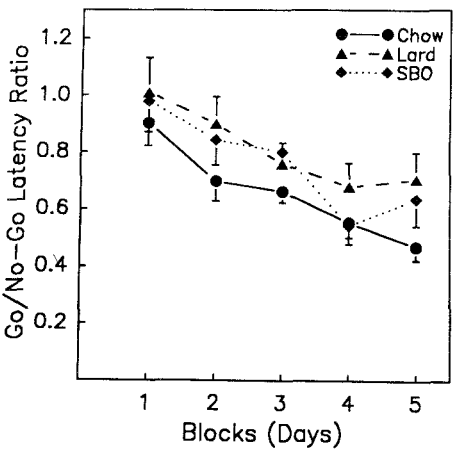

FIG. 3. Means $\pm$ 1 SD of latency ratios for all groups at ITI_0 over five blocks of 3 test days on the VIDA task.

On Olton's RAM, the lard-fed rats displayed a slight but significant deficit in spatial memory. Their temporal memory over short and long intervals was severely impaired on the VIDA test and, on the HWM test, they were deficient in learning various maze problems. Rats fed a diet high in PUFAs (SBO diet) showed some impairment on the VIDA and HWM tests but, generally, their performance was superior to that of the lard-fed group.

On each of the tests, the lard group failed to remember specific features of the task. In the RAM and HWM tests, this was indicated by an increased tendency to reenter incorrect arms and alleys and, on the VIDA test, as poor memory for events of the preceding trial. There was also evidence that the deficit extended to measures of implicit memory. For example, the lard group's impaired performance in the ITI_0 condition of the VIDA test, where memory for specific events was minimally challenged, indicated a deficit in learning a response alternation rule. Indeed, the lard-fed rats' overall behavior suggested that they learned very little about the VIDA task. Their level of performance, which was equally impaired in the short and long delay conditions, remained virtually constant over 15 days of testing. The widespread deficits of the lard group on the VIDA test contrast with the more selective performance deficits seen in populations of brain-damaged (Winocur, 1985) and normal aged (Winocur, 1986) rats tested under identical conditions.

The HWM data also point to a generalized deficit in the lard-fed rats. Not only did they make more errors on most mazes than the SBO and chow groups but, over the first six mazes at least, their rate of improvement was slower than that of the other groups. This finding suggests difficulty in acquiring maze-learning skills and/or transferring relevant information that could facilitate performance on the various mazes. The failure to learn specific mazes in the HWM series has been related to the type of learning and memory deficits caused by damage to hippocampus and related structures, whereas the general skill of maze learning appears to be controlled primarily within the frontal lobes (Winocur & Moscovitch, in press). To the extent that these functions can be identified with different neural systems (Squire, 1987; Moscovitch, in press), it appears that the adverse effects of a high SFA diet are nonselective with respect to these systems.

It may be significant that, relative to the other groups, the lard group was least impaired on the RAM. This may simply represent the fact that animals were tested on this task first and impairment continued to increase with continual exposure to the diets. This is an unlikely explanation since the degree of impairment of the lard-fed rats on both the VIDA and HWM tests was similar despite the fact that testing on the HWM preceded that of the VIDA task. The RAM is used primarily to assess spatial memory and is regarded by some (Olton, 1983; Kesner,

1986) as a regionally specific test of hippocampal dysfunction. The VIDA and HWM tests assess a wider range of functions that require the participation of several brain regions. The more robust deficits observed in the lard group on these tasks may be seen as evidence that the effects of high SFA diets on brain function are quite general and most likely to impact on those behaviors that depend on the integrity of multiple neural systems.

The present results differ somewhat from those previously reported on the Morris water maze (Coscina et al., 1986), in which performance of the SBO-fed rats was superior to that of both the lard- and the chow-fed groups. The reason for this disparity is not clear, although the studies did differ in at least three important ways. First, the Morris water maze is a much more stressful test than the ones used in the present study, where only positive reinforcement was used. The possible interaction of stress response and dietary fat cannot be eliminated as a confounding variable in the previous work. Second, the present study incorporated a food restriction paradigm, with food serving as the positive reinforcer in all tests. Conceivably, motivation to eat may have differed among the groups and influenced the outcome. On the other hand, observations of the rats' food intake behavior did not suggest any differences. The fact that all groups reached asymptotic levels of bar pressing at the same time during CRF training in the VIDA test would argue against motivational differences. Finally, duration of the feeding trial was longer in the present study. That is, rats were tested on the Morris water maze after 3 weeks of exposure to the diets in the previous study, whereas testing only began after 3 months of exposure to the diets in this study. The degree to which this longer exposure to the diets may have influenced metabolic outcome, and subsequent behavior, is presently not known.

At present, neither the mechanism of action, nor the important characteristic of the fat source mediating the functional changes can be identified. Direct comparison of results of the SBO and lard diets with chow is complicated by the fact that chow differs from these two diets in most respects. Hence, it is impossible to isolate a single dietary factor responsible for the alterations in performance. However, the SBO and lard diets differ only in the fat source used in their formulation. Thus the comparison between these two diets allows for the conclusion that the quality of dietary fat fed impacts on brain function in rats. The overall superior performance of the chow-fed animals in comparison to both the lard- and the SBO-fed groups also opens the possibility that the level of dietary fat was an important variable since chow contains proportionately less fat (4.5% w/w) than the other two diets and a similar fatty acid composition to that of the SBO diet. Further studies are necessary for this to be substantiated owing to the other differences in diet formulation not controlled for in this experiment.

Previous studies on dietary fat and cognitive performance (Caffrey & Patterson, 1971; Paoletti & Galli, 1972; Galli et al., 1975; Borgman et al., 1975; Lamptey & Walker, 1976, 1978; Morgan et al., 1981; Ruthrich et al., 1984; Yamamoto et al., 1987) concentrated on the role of the EFAs in the central nervous system. These 18-carbon fatty acids, which must enter the body via the diet, are elongated and desaturated in the body to 20- and 22-carbon fatty acids with additional double bonds. These longer chain polyenoic metabolites are preferentially localized in electrically active tissue (Tinoco et al., 1979; Bernsohl & Cohen, 1972) where they are felt to play an as yet undefined but essential role (Dratz & Dreese, 1986; Salem, Kim, & Yergery, 1986; Neuringer, Anderson, & Connor, 1988). To assess the physiological need for these fatty acids, diets either were deficient in one or both of the EFAs or had ratios of the EFAs which would interfere with their elongation and desaturation. Collectively these studies demonstrated that as the profile of fatty acids in the central nervous system was altered, performance in cognitive tasks declined. These results clearly demonstrate that brain is sensitive to dietary availability of EFAs and point to the plausible hypothesis that as membrane composition is altered, the metabolic characteristics of the neuron may be influenced.

Whether more modest alterations in dietary fat composition could impact on membrane composition to a degree which would alter neuronal function and overall performance is unknown at present. However, we (Dyer & Greenwood, 1988, manuscripts submitted) and others (Foot, Cruz, & Clandinin, 1982) have previously demonstrated that the membrane phospholipid fatty acid profile of a number of subcellular membranes is altered within 4 weeks of feeding either the SBO and lard diets or similar diet combinations. Furthermore, our results demonstrate that the magnitude of change in membrane fatty acid composition increased with continual exposure (up to 12 weeks) to the fat source. In general, while the total proportion of membrane PUFAs as well as the overall unsaturation index is not influenced by dietary fat, the proportion of the long-chain polyenoic fatty acids is especially sensitive to dietary fat composition. While the magnitude of change in membrane phospholipid fatty acid profile associated with these dietary manipulations, especially when commenced postweaning, is small, there is evidence that it is physiologically relevant to the animal. That is, changes in the activities of membrane-bound enzymes, acetylcholine esterase (Foot, Cruz, & Clandinin, 1983) and monoamine oxidase (Crane & Greenwood, 1987), are observed in association with the altered fat intakes. The magnitude of change in enzyme activity, however, is small and was insufficient to influence steady-state concentrations of either serotonin or its metabolite 5-hydroxy indole acetic acid (Crane & Greenwood, 1987). At present, it is not known whether alterations in acetylcholine turnover are observed

with alterations in dietary fat composition. Limited studies on the binding of ligands to CNS receptors suggest that only slight differences would be expected and would vary depending upon the receptor of interest. For example, increased ligand binding to cardiac β-adrenergic (Wince & Rutledge, 1981) and brain opiate (Tsujii et al., 1986), but not striatal D_2-dopamine (Leprohon-Greenwood & Cinader, 1987), binding sites are observed following dietary fat manipulation. Differences in electrical membrane properties of dorsal root ganglion isolated from mice fed either 20% (w/w) SBO or beef tallow diets (Scott, Lew, Clandinin, & Cinader, 1989), however, provide further evidence that neuronal function is sensitive to dietary fat intake.

It is interesting to note that brain regional response to dietary fat manipulation is similar, such that no brain region (cortex, hippocampus, hypothalamus, cerebellum, and striatum) by diet interaction is observed (Greenwood, Leiberman, & Winocur, submitted). This is consistent with our behavioral findings, suggesting that the impact of dietary fat on performance is not confined to one region; rather as tasks require increased integration from a number of regions, performance is altered to a greater extent. Collectively, these results suggest that dietary fat has a modest impact on neuronal function, perhaps mediated via alterations in membrane composition, such that more complex skills requiring greater integration from a number of brain regions are more sensitive to the dietary manipulation. The future challenge will be to integrate the psychological and biochemical data sets in order to more fully understand the relationship between fat intake and cognitive performance.

REFERENCES

Bernsohl, J., & Cohen, S. R. (1972). Polyenoic fatty acid metabolism of phosphoglycerides in developing brain. *In* K. Elliott & J. Knight (Eds.), *Lipids, malnutrition & the developing brain* (pp. 159–178). New York: Elsevier Excerpta Medica North-Holland.

Borgman, R. F., Bursey, R. G., & Caffrey, B. C. (1975). Influence of maternal dietary fat upon rat pups. *American Journal of Veterinary Research,* **35,** 799–805.

Caffrey, B., & Patterson, M. Y. (1971). Effects of saturated and unsaturated fats on learning, emotionality, and reaction to stress. *Psychology Reports,* **29,** 79–86.

Coscina, D. V., Yehuda, S., Dixon, L. M., Kish, S. J., & Leprohon-Greenwood, C. E. (1986). Learning is improved by a soybean oil diet in rats. *Life Sciences,* **38,** 1789–1794.

Crane, S. B., & Greenwood, C. E. (1987). Dietary fat source influences neuronal mitochondrial monoamine oxidase activity and macronutrient selection in rats. *Pharmacology, Biochemistry and Behavior,* **27,** 1–6.

Dratz, E. A., & Dreese, A. J. (1986). The role of docosahexaenoic acid (22:6ω3) in biological membranes: Examples from photoreceptors and model membrane bilayers. *In* A. P. Simopoulos, R. R. Kifer, & R. E. Martin (Eds.), *Health effects of polyunsaturated fatty acids in seafoods* (pp. 319–351). New York: Academic Press.

Dyer, J. R., & Greenwood, C. E. (1988). Neural fatty acid profile in weaned rats is susceptible to short-term changes in dietary fat composition. *Society for Neuroscience Abstracts,* **14,** 406.1. (abstract)

Foot, M., Cruz, T. F., & Clandinin, M. T. (1982). Influence of dietary fat on the lipid composition of rat brain synaptosomal and microsomal membranes. *Biochemical Journal,* **208,** 631–640.

Foot, M., Cruz, T. F., & Clandinin, M. T. (1983). Effect of dietary lipid on synaptosomal acetylcholinesterase activity. *Biochemical Journal,* **211,** 507–509.

Galli, C., Messeri, P., Oliverio, A., & Paoletti, R. (1975). Deficiency of essential fatty acids during pregnancy and avoidance learning in the progeny. *Pharmacology Research Communications,* **7,** 71–80.

Kesner, R. P. (1986). Neurobiological views of memory. *In* J. C. Martinez & R. P. Kesner (Eds.), *Learning and memory: A biological view* (pp. 399–438). New York: Academic Press.

Lamptey, M. S., & Walker, B. L. (1976). A possible essential role for dietary linolenic acid in the development of the young rat. *Journal of Nutrition,* **106,** 86–93.

Lamptey, M. S., & Walker, B. L. (1978). Learning behavior and brain lipid composition in rats subjected to essential fatty acid deficiency during gestation, lactation and growth. *Journal of Nutrition,* **108,** 358–367.

Leprohon-Greenwood, C. E., & Cinader, B. (1987). Variations in age-related decline in striatal D_2-dopamine receptors in a variety of mouse strains. *Mechanisms of Ageing and Development,* **38,** 199–206.

Matheson, D. F., Oei, R., & Roots, B. I. (1981). Effect of dietary lipid on the acyl group composition of glycerophospholipids of brain endothelial cells in the developing rat. *Journal of Neurochemistry,* **36,** 2073–2079.

McGee, C. D., & Greenwood, C. E. (1989). Effects of dietary fatty acid composition on macronutrient selection and synaptosomal fatty acid composition in rats. *Journal of Nutrition,* in press.

Morgan, B. L. G., Oppenheimer, J., & Winick, M. (1981). Effects of essential fatty acid deficiency during late gestation on brain *N*-acetyl-neuramic acid metabolism and behaviour in the progeny. *British Journal of Nutrition,* **46,** 223–230.

Moscovitch, M. (in press). Confabulation and the frontal system: Strategic versus associative retrieval in neuropsychological theories of memory. *In* H. L. Roediger III & F. I. M. Craik (Eds.), *Festschrift for Endel Tolving.* Hillsdale, NJ: Erlbaum.

Neuringer, M., Anderson, G. J., & Connor, W. E. (1988). The essentiality of n-3 fatty acids for the development and function of the retina and brain. *In* R. E. Olson, E. Beutler, & H. P. Broquist (Eds.), *Annual reviews of nutrition.* (Vol. 8, pp. 517–541). Palo Alto, CA: Annual Reviews.

Olton, D. S. (1983). Memory functions and the hippocampus. *In* W. Seifert (Ed.), *Neurobiology of the hippocampus* (pp. 335–373). New York: Academic Press.

Olton, D. S., & Samuelson, R. J. (1976). Remembrance of places passed: Spatial memory in rats. *Journal of Experimental Psychology,* **2,** 97–116.

Paoletti, R., & Galli, C. (1972). Effects of essential fatty acid deficiency on the central nervous system in the growing rat. *In* K. Elliot & J. Knight (Eds.), *Lipids, malnutrition & the developing brain* (pp. 121–140). New York: Elsevier Excerpta Medica North-Holland.

Rabinovitch, M. S., & Rovsold, H. E. (1951). A closed-field intelligence test for rats. *Canadian Journal of Psychology,* **5,** 122–128.

Ruthrich, H. L., Hoffman, P., Matthies, H., & Forster, W. (1984). Perinatal linoleate deprivation impairs learning and memory in adult rats. *Behavioral and Neural Biology,* **40,** 205–212.

Salem, N., Kim, H. Y., & Yergery, J. A. (1986). Docosahexaenoic acid: Membrane function and metabolism. *In* A. P. Simopoulos, R. R. Kifer, & R. E. Martin (Eds.), *Health effects of polyunsaturated fatty acids in seafoods* (pp. 263–317). New York: Academic Press.

Scott, B., Lew, J., Clandinin, M. T., & Cinader, B. (1989). Dietary fat influences electric

membrane properties of neurons in cell culture. *Journal of Cellular and Molecular Biology,* **9,** 105–113.

Squire, L. R. (1987). *Memory and brain.* New York: Oxford Univ. Press.

Tinoco, J., Babcock, R., Hincenbergs, I., Medwadowski, B., Miljanich, P., & Williams, M. A. (1979). Linolenic acid deficiency. *Lipids,* **14,** 166–173.

Tsujii, S., Nakai, Y., Fukata, J., Koh, T., Takahashi, H., Usui, T., & Imura, H. (1986). Effects of food deprivation and high fat diet on opioid receptor binding in rat brain. *Neuroscience Letters,* **72,** 169–173.

Wince, L. C., & Rutledge, C. O. (1981). The effect of dietary lipid on the binding of [^{3}H]-dihydroalprenolol and adenylate cyclase activity in rat atria. *Journal of Pharmacology and Experimental Therapeutics,* **219,** 625–631.

Winocur, G. (1982). Radial arm maze behaviour by rats with hippocampal lesions: Effects of cueing. *Journal of Comparative and Physiological Psychology,* **96,** 155–169.

Winocur, G. (1985). The hippocampus and thalamus: Their roles in short and long-term memory and the effects of interference. *Behavioral Brain Research,* **16,** 135–152.

Winocur, G. (1986). Memory decline in aging rats: A neuropsychological interpretation. *Journal of Gerontology,* **41,** 758–763.

Winocur, G., & Greenwood, C. E. (1987). Polyunsaturated fat diets improve spatial memory in rats. *Society for Neuroscience Abstracts,* **13,** 184.1. (abstract)

Winocur, G., & Moscovitch, M. (in press). Hippocampal and frontal lobe contributions to learning and memory: An analysis of lesion and aging effects on maze-learning in rats. *Behavioral Neuroscience.*

Yamamoto, N., Saitoh, M., Moriuchi, A., Nomura, M., & Oduyama, H. (1987). Effect of dietary alpha-linolenate/linoleate balance on brain lipid composition and learning ability of rats. *Journal of Lipid Research,* **28,** 144–151.

Yehuda, S., Leprohon-Greenwood, C. E., Dixon, L. M., & Coscina, D. V. (1986). Effects of dietary fat on pain threshold, thermoregulation and motor activity in rats. *Pharmacology Biochemistry and Behaviour,* **24,** 1775–1777.