The role of diet in the correction of learning defect due to hypercholesterolemia

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In order to investigate the role of the reduced the cholesterol content in the diet on the learning defect produced by hypercholesterolemia, we carried out an experimental study.

Thirty-two male albino rats weighing 200-220 g. were divided in three groups. Ten of them were used as control group and kept on normal diet and tap water for 24 weeks. Twenty-two rats firstly received normal diet containing 1 % of cholesterol for 12 weeks then the cholesterol was withdrawn from their diet of 9 of 22 animals and they were kept on normal diet and tap water for another 12 weeks.

At the end of the feeding period the learning capacity of all animals were measured using a T maze and their blood and tissue cholesterol levels were analysed.

When compared with control group, a significant impairement in learning capacity was found in hypercholesterolemic rats ($p<0.01$). The control animals reached to the diet placed at the exit of T maze in 28.17±3.40 second while reaching time was 134±32.65 second in hypercholesterolemic rats. Replacement of the hypercholesterolemic diet with normocholesterolemic one, corrected the impairement in the learning capacity as parallel to the decrease in the plasma and tissue cholesterol in ra ts. [Turk J Med Res 1993; 11(4): 176-178]

Keywords: Cholesterol, Learning, Hypercholesterolemia

It has been shown by many reports that cholesterol impaires the neuronal functions by disturbing membrane fluidity (4,5,13). Among the other complicated brain functions, learning is also influenced by the increased membrane cholesterol. Learning induced reduction in membrane cholesterol and learning disability due to high cholesterol in membrane indicated the importance of cholesterol in learning process (7,8). Our previous study showed that diet induced hypercholesterolemia also produces learning defect in rats (11).

However it is not certain whether the impairement of learning due to diet induced hypercholesterolemia is permanent or is reversible by the withdrawal of cholesterol from the diet.

For this reason the present experimental study was carried out to isvestigate the effect of the restricted dietary cholesterol on hypercholesterolemia induced learning defect in rats.

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MATERIALS AND METHODS

Thirty-two male albino rats were used in this experimental study. Ten animal received normal rat diet and tap water for 24 weeks and used as control group. Twenty-two animals were divided into two groups and 13 rats fed with a diet containing 1% cholesterol were exposed to a T-maze and given them a two hours chance to get familiar with this maze as well as to find the food placed at the exit at the and of 12 weeks following 16 hours fasting period.

The next day fasted animals placed again into the same T-maze and the time required to find the exit was recorded using a stopwatch. The mean of four measurements was accepted the value of each animal.

Nine of 22 animals in group 3 received 1% of cholesterol containing diet, for 12 weeks. Then their diet was replaced with a normocholesterol one for another 12 weeks.

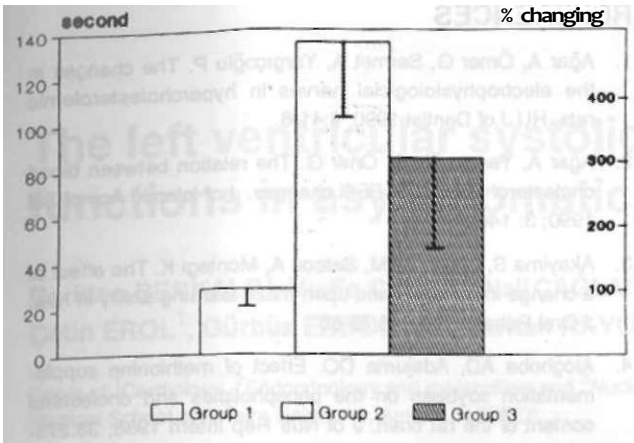

Figure 1. Learning index (reaching to the food).

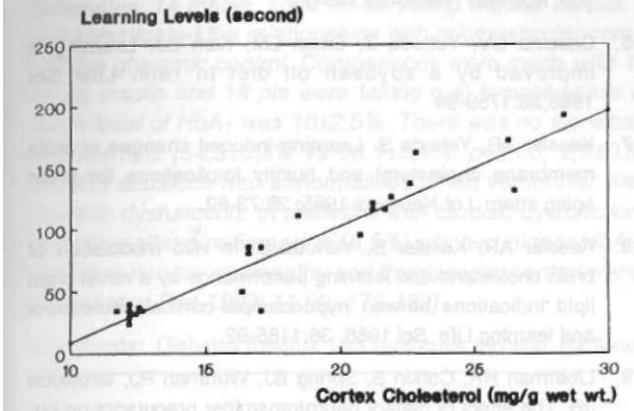

Figure 2. Correlation between learning index and cortex cholesterol (y= -84.72+9.38x, r= 0.954, p<0.01).

At the end of 24 weeks the same T-maze test were done for the rats of control and group 3 by the same observer. The mean time require to reach the food place at the exit was accepted as memory and learning index.

After the maze task all animals were anesthetized with urethane (1g/kg, ip) and their blood, cerebellum, cerebral cortex as well as liver were removed. After elimination of tissue blood with ice-cold saline they were used for cholesterol- analysis using Sclavo Cholest-cinet enzymatic kit in Pointe 180 chemistry analyzer.

" Students's t" test was used for the evaluation of statistics.

RESULTS

The mean total cholesterol levels of 8 month old control rats was 70.66±10.0 mg/dL this value increased to 141.29±34.5 mg/dL in the rats receiving a diet rich in cholesterol for 12 weeks (p<0.01). When the hypercholesterolemic diet was replaced with a normocholesterolemic one for another 12 week, the mean total cholesterol value in the plasma of group 3 decreased to 114.05± 16.27 mg/dl and this decline was found to be significant (p<0.05).

As seen in Table 1 increased blood cholesterol was associated with elevated cholesterol in liver and brain tisues in the second group. However increased tissue cholesterol decreased near to normal value with the removal of cholesterol from the diet for another 12 weeks.

The mean time required to reach the exit of T-maze was 28.17±3.4 second in normocholesterolemic control rats. This time was 134.42±36.65 second in rats fed with cholesterol rich diet for 12 weeks. Withdrawal of cholesterol from the diet partially restored the delay of reaching time to the food placed at the exit in the 3 rd group. (84.56±37.98 sec, p<0.01, Figure 1).

There was a significant correlation between the time required to reach the exit and cortex (r-0.954, p<0.01, Figure 2) and blood cholesterol (r-0.862, p<0.01).

DISCUSSION

Previous studies is our laboratory showed that feeding rats with a diet containing 1% of cholesterol for 12 weeks produces hypercholesterolemic state associated with imparled learning (11) as well as decreased electrophysiological activities in rat brain (1,2,10,15).

It has been reported that an increase in membrane cholesterol decreases its fluidity and impaires neuronal functions (4,5,13). Kessler and Yehuda (7) who study the relationship between learning and cholesterol level, showed that learning produces a decrase in the cholesterol level of both hippocampus and brain cortex. Many investigators reported that nutrients such as iron deficient diet, special type fatty acids, niacin, folic acid, magnesium, zinc can modify learning and memory (3,6,9,14).

The repport of Kessler et al (8) who indicate an increase in learning ability with feeding a diet rich in

Table-1: Cholesterol levels of tissues (mg/g wet.wt). Group 2 vs, Group 1 and, Group 3 vs. Group 2 (*p<0.05,**p<0.01),

	GROUP 1	GROUP 2	GROUP 3
U VER	1.36±0.24	2.23±0.28"	1.85±0.20"
CEREBELLUM	16.78±3.72	30.69±3.94"	23.58±2.94"
CORTEX	12.78±1.59	21.94±4.75**	16.9±3.69*

plant lipids and the results of Coscina (6) showing the benefical effect of temporary changes in the fat levels of diet on learning revealed that diet composition influences deeply learning ability.

Our previous study (11) showed that among the above mentioned nutriet factors, diet induced hypercholesterolemia is also involved in the impairement of learning ability. However there is no information in the literature whether this dietary cholesterol induced learning deficit is corrected by the removal of cholesterol from the diet. Our present data clearly suggest that withdrawal of cholesterol restores both the delay of memory consolidation, learning and tissue cholesterol levels.

The lack of complete correction of impaired learning may be explained by the insufficient decrease in both tissue and blood cholesterol levels. The presence of negative and significant correlation between blood as well as tissue cholesterol and learning supports this explanation.

The restoration of dietary cholesterol induced learning disability by the withdrawal of cholesterol from the diet for 12 weeks is a strong evidence of reversibility of diet induced changes in brain functions and gives a clue for clinician.

Hiperkolesterolemiye bağlı öğrenme bozukluğunun düzeltilmesinde diyetin rolü

Diyete bağlı hiperkolesteroleminin neden olduğu öğrenme bozukluğunun, diyetin normale çevrilmesi ile düzeltilip düzeltilemeyeceğini saptamak amacıyla bu deneysel çalışma tertiplendi.

Ağırıığı 200-220 gram arasında 32 erkek albino sıçan 3 gruba ayrılarak 10 tanesi kontrol grubu olarak 24 hafta boyunca normal diyet aldılar. Sıçanların 22'sine ise 12 hafta boyunca %1 kolesterol içeren diyet verilmesini takiben 9 tanesinin diyetinden kolesterol uzaklaştırılıp 12 hafta süre ile tekrar normal diyetle beslendiler.

Beslenme periyodu sonunda T-tipi labirentte öğrenme kapasiteleri ölçülen hayvanların kan ve dokularında kolesterol düzeyleri saptandı.

Kontrolla karşılaştırıldığında hiperkolesterolemik grupta anlamlı öğrenme bozukluğu saptandı ($p<0.01$). Labirentin çıkışına konulan besine kontrol grubu 28.17±3.40 saniyede ulaşırken, hiperkolesterolemik grup 134.42±32.65 saniyede ulaştı. Hiperkolesterolemik diyeti takiben normal diyete alınan hayvanların öğrenme düzeyleri plazma ve doku kolesterollerindeki düşmeye paralel olarak düzelme gösterdi ise de tam olarak kontrol değerlere dönmedi.

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REFERENCES

1. Ağar A, Ömer G, Sermet A, Yargıçoğlu P. The changes in the electrophysiologicial nerves in hypercholesterolemic rats. HU J of Dentist 1990; 8:41-6.
2. Ağar A, Yargıçoğlu P, Öner G. The relation between blood cholesterol levels and EEG changes. J of Islamic Aca of Sci 1990;3:146-50.
3. Akayima S, Shikimori M, Satocu A, Montegi K. The effect of a change in dietary habit upon maze learning ability in rats. J Oral Rehabil 1991; 18:75-80
4. Aloghoba AD, Adejuma DO. Effect of methionine supplementation soybean on the phospholipids and cholesterol content of the rat brain. J of Nutr Rep Intern 1988; 38:275-81.
5. Berdanier CD. Role of membrane lipids in metabolic regulation. Nutr Rev 1988;456:145-50.
6. Coscina DV, Yehuda Z, Dixon LM, Kish SJ. Learning is improved by a soybean oil diet in rats. Life Sci 1986;38:1789-94.
7. Kessler AR, Yehuda S. Learning induced changes in brain membrane cholesterol and fluidity implications for brain aging intern J of Neurosci 1985; 28:73-82.
8. Kessler AR, Kessler B, Yehuda S. In vivo modulation of brain cholesterol and learning performance by a novel plant lipid indications betwen hypoccampal-cortical cholesterol and learning Life. Sci 1986; 38:1185-92.
9. Liberman HR, Corkin S, Spring BJ, Wurtman RJ, Growdon JH. The effect of dietary neurotransmitter precursors on human behavior. Am J Clin Nutr 1985; 42: 366-70.
10. ÖnerG, Ağar A, Yargıçoğlu P. The effect of hypercholesterolemia on brain electrical activities recorded from rats. Turkish J of Resecarch in Medical Sci 1990;8:41-6.
11. Öner G. Kızılırmak F, Şentürk ÜK. The effect of cholesterol on learning ability of rats. Doğa -Tr J of Medical Sci 1992;16:145-9.
12. Radin NS. Extraction of tissue lipids with a solvent of low toxicity. Meth Enzymol 1981; 72:5-7.
13. Shinitzky M. Patterns of lipid changes in membranes of the aged brain. Gerontology 1987;33:149-54.
14. Yamamoto N, Hashimoto A, Takemoko Y, Okuyama H, Nomura M, Kitajima R, Togahi T, Tamai Y. Effect of the dietary alpha-linolenate/linoleate balance onlipid compositions and learning ability of rats. Il. Discrimination process, and extinction process, and glycolipid composition. J Lipid Res 1989:29:1013-21.
15. Yargıçoğlu P, Ağar A, Oğuz Y, Öner G. The effect of hypercholesterolemia on SEPS recorded from rats. Intern J Neurosci 1991; 61:93-99.