# Chapter 3

# Dehydroepiandrosterone treatment alters lipid/phospholipid profiles of rat brain and liver mitochondria

## Introduction

In previous chapter we saw that treatment with DHEA affects mitochondrial respiration rates in dose dependent and tissue-specific manner. It also influenced other important mitochondrial parameters lilke cytochrome content and activity of ATPase, GDH, SDR and MDH. The dependence of mitochondrial membrane-bound enzymes on specific phospholipid classes of membrane is well recognized (Daum, 1985; Fry and Green, 1981; Mc Millin and Dowhan, 2002). Hence it would be interesting to study whether DHEA treatment also affects the lipid/phospholipid profile.

It is also known that DHEA decreases dietary fat consumption and body fat content. It alters lipid profiles in Zucker rats (Abadie et al., 2000). In case of mice fed the DHA diet, the content of the essential fatty acid, arachidonate, was decreased in plasma cholesteryl esters and liver and kidney phospholipids (Miller et al., 1988). Also, stress-induced lipid peroxidation levels in the liver and heart reversed after DHEA administration (Hu et al., 2000). Like exercise, DHEA protects against excess fat accumulation and development of insulin resistance in rats (Han et al., 1998).

There are studies which showed treatment of experimental animals with DHEA resulted in hypertrophy of the hepatocytes due to increased proliferation of mitochondria and peroxisomes (Bellei et al., 1992). DHEA treatment also stimulated the mitochondrial electron transport functions (Song et al., 1989; Swiercynski et al., 2001). Treatment with DHEA significantly influenced respiratory parameters of brain as well as liver mitochondria (Song et al., 1989; Mohan and Cleary, 1991; Bellei et al., 1992; Swiercynski et al., 2001) which supports results of chapter 2.

We therefore examined the effect of DHEA treatment on membrane lipid/phospholipid profiles of rat brain and liver mitochondria.

## Materials and methods

### Chemicals

3β-Hydroxy-5-androsten-17-one (+)-dehydroisoandrosterone (DHEA) was purchased from Sigma–Aldrich, USA. Bovine serum albumin fraction V (BSA), 4-morpholinopropanesulfonic acid (MOPS), disodium salt of ethylenediaminetetraacetic acid (EDTA), 1-6 diphenyl-1,3,5-hexatriene (DPH), were purchased from Sigma Chemical Co. USA. Silica gel G was from E. Merck, Darmstadt, Germany. All other chemicals were of analytical-reagent grade and were purchased locally.

### Animals and treatment with DHEA

Adult male albino rats (8-10 week old) of Charles-Foster strain weighing between 200-250 g were used. The animals received daily injections of 0.1, 0.2, 1.0 or 2.0 mg DHEA /Kg body weight subcutaneously (s.c.) for 7 consecutive days. Daily records of body weight were maintained. Suspension of DHEA was prepared fresh in saline prior to injection. The controls received equivalent volume of saline. The animals were killed on the $8^{th}$ day. The experimental protocol was approved by the Departmental Animal Ethics Committee.

### Isolation of mitochondria

Isolation of brain and liver mitochondria was essentially according to the procedures described previously in chapter 2.

### Lipid analysis

#### Extraction of lipids

Extraction of lipids, separation of phospholipids classes by thin layer chromatography (TLC) and determination of membrane fluidity were carried out essentially according

to the procedures described previously (Folch and Lees, 1957; Pandya, Dave and Katyare, 2004b). Aliquots of mitochondrial suspension (4-8 mg protein) were extracted with 4 ml of freshly prepared chloroform: methanol mixture (2:1 V/v). The samples were vortexed vigorously and centrifuged at 3000 rpm for 10 min and the organic phase was carefully removed with the help of a broad gauge needle. The samples were re-extracted with 3 ml of chloroform: methanol mixture as above. The pooled organic phase was treated with 0.1 volume of 0.017% $MgCl_2$ by vortexing vigorously. The tubes were than centrifuged as described above to achieve phase separation. The organic phase was carefully removed with care being taken to avoid the protein/proteolipid layer present between organic and aqueous phases (Folch and Lees, 1957; Pandya, Dave and Katyare, 2004b). The solvent was completely evaporated under the stream of nitrogen after which the extracted lipids were redissolved in known volume of chloroform: methanol mixture. Suitable aliquots were taken for the estimation of phospholipids phosphorus (Bartlett, 1954) and cholesterol (Zlatkis, Zak and Boyle, 1953), and for TLC.

**Separation of phospholipids by TLC**

Separation of phospholipids classes was carried out by one dimensional TLC using silica gel G. The conditions for chamber saturation were according to Stahl (1969). Aliquots of the reconstituted samples containing 8-10 µg of phospholipids phosphorous were spotted on TLC plate in a way such that the diameter of the spot was minimum. The solvent system used for separation of phospholipid classes was as described by Skipski et al. (1967) and consisted of chloroform: methanol: acetic acid: water (25:15:4:2 V/v). After the run was completed, the solvent was allowed to evaporate completely and the plates were briefly exposed to iodine vapor to visualize the individual phospholipid spots and the spots were marked. The areas corresponding to marked spots were carefully scraped and the silica gel was transferred to clean test tubes. To each tube 0.5ml of 10N $H2SO_4$ was added and the samples were heated on a sand bath for 8-10 hour. The tubes were allowed to cool after which a drop of 70% perchloric acid was added. The tubes were again heated for

3-4 hours till the solution in the tubes was clear and smell of chlorine was undetectable (Pandya, Dave and Katyare, 2004b). The analysis of phosphorus content was according to the procedure of Bartlett (1954).

Contents of individual phospholipids were computed by multiplying total phospholipid by the % fraction of the said phospholipid (Pandya, Dave and Katyare, 2004b).

**Determination of membrane fluidity**

Membrane fluidity measurements were carried out spectroflourophotometrically at 25 °C using DPH as the probe in a Shimadzu spectroflourophotometer model RF 5000 (Pandya, Dave and Katyare, 2004b).

Protein estimation was according to the method of Lowry et al. (1951) using bovine serum albumin as the standard.

All results are given as mean ± SEM.

Statistical evaluation of the data was by Students' t-test.

## Results

### Effects on Brain Mitochondria

Data in Table 1 show that treatment with DHEA (0.1 mg and 0.2 mg) resulted in about 13% increase in the total phospholipids content and 62% to 66% increase in the cholesterol (CHL) content of the brain mitochondria; the effect declined at higher doses of DHEA. The TPL: CHL ratio (mole:mole) decreased only in the animals treated with 0.2 mg DHEA. The membrane fluidity was, in general, unchanged (Table 1).

Examination of phospholipid profile revealed that treatment with 1.0 mg DHEA resulted in about 70% increase in the lysophospholipid (Lyso) component. The sphingomyelin (SPM) component increased progressively up to 1.0 mg DHEA (1.30 to 2.01 fold increase) after which the effect diminished and became comparable to that noted for animals treated with 0.2 mg dose. The phosphatidylcholine (PC) component increased marginally only in those animals treated with 0.1 mg dose. The composition of acidic phospholipid phosphatidylinositol (PI) and phosphatidylserine (PS) was unaltered except for lowering of PI at the highest dose (2.0 mg) of DHEA. DHEA treatment also had a Phosphatidylethnolamine (PE) lowering effect which was evident up to the dose of 1.0 mg; the effect declined at the higher dose. DHEA treatment also resulted in decrease in the diphosphatidylglycerol (DPG) component at 1.0 mg dose (Table 2).

Since the TPL contents and phospholipid composition changed significantly (Tables 1 and 2), it was important to find out the extent to which the content of individual phospholipid class was altered by DHEA treatment. Data in Table 3 detail the contents of individual phospholipid classes. Thus, the content of Lyso increased progressively (42 to 104%) up to the dose of 1.0 mg; the effect was abolished at higher dose. The content of PC also increased following DHEA treatment with maximum increase (52%) being seen at the lowest dose (0.1 mg) of DHEA after which the effect declined and at the highest dose the value became comparable to untreated controls. A 38% decrease in PI content at 2.0 mg dose and 55% increase in PS content at 0.2 mg dose were other interesting features. A similar 31% increase in DPG content was noted in animals treated with 0.2 mg DHEA. The content of PE was not affected under these conditions (Table 3).

**Effects on Liver Mitochondria**

As can be noted (Table 1) DHEA treatment did not influence the TPL content of liver mitochondria. However, the CHL content increased by 30% in animals treated with 1.0 mg DHEA regimen. This was also reflected in the lowering of the molar ratio of TPL:

CHL. Consequently the membrane fluidity decreased in groups treated with 1.0 and 2.0 mg DHEA. Analysis of phospholipid composition revealed that DHEA treatment in general had tendency to increase acidic phospholipids namely PI and PS. The effect was evident in animals receiving DHEA dose of up to 1.0 mg; at higher dose of 2.0 mg the effect was abolished. DHEA treatment up to 1.0 mg dose also had a PE lowering effect. Once again even in this case, at higher dose of 2.0 mg the effect was abolished (Table 4).

The observed changes were also reflected in the contents of the two acidic phospholipids PI and PS which increased by 1.44 to 1.94 fold. Interestingly, the content of Lyso increased 1.71 fold in animals receiving 0.1 mg DHEA. There was a generalized tendency of increase in the content of SPM up to the dose of 1.0 mg. However, the content of SPM decreased by 11% in animals treated with 2.0 mg dose of DHEA. The contents of other phospholipid classes were unchanged (Table 5).

**Table1: Effect of DHEA treatment on total phospholipids (TPL) and cholesterol (CHL) content of rat brain and liver mitochondria**

| Tissue | Treatment | TPL (μg/mg protein) | CHL (μg/mg protein) | TPL/CHL (mole:mole) | Fluorescence polarization, p |
|---|---|---|---|---|---|
| Liver | Untreated (12) | 178.0 ± 13.87 | 51.59 ± 2.16 | 1.79 ± 0.20 | 0.203 ± 0.009 |
| | 0.1 mg DHEA (12) | 172.9 ± 7.80 | 56.22 ± 3.95 | 1.61 ± 0.12 | 0.209 ± 0.005 |
| | 0.2 mg DHEA (12) | 185.2 ± 15.35 | 59.05 ± 5.08 | 1.62 ± 0.12 | 0.208 ± 0.005 |
| | 1.0 mg DHEA (12) | 187.1 ± 8.88 | 66.98 ± 4.51[c] | 1.43 ± 0.07[a] | 0.228 ± 0.007[a] |
| | 2.0 mg DHEA (8) | 166.8 ± 12.29 | 53.24 ± 2.36 | 1.57 ± 0.20 | 0.231 ± 0.004[b] |
| Brain | Untreated (12) | 410.0 ± 33.96 | 383.2 ± 10.23 | 0.54 ± 0.05 | 0.279 ± 0.006 |
| | 0.1 mg DHEA (12) | 532.2 ± 46.23[a] | 621.0 ± 43.92[d] | 0.43 ± 0.03 | 0.263 ± 0.008 |
| | 0.2 mg DHEA (12) | 534.4 ± 44.51[a] | 634.8 ± 48.30[d] | 0.42 ± 0.02[a] | 0.261 ± 0.008 |
| | 1.0 mg DHEA (12) | 507.0 ± 9.91[b] | 532.2 ± 33.31[d] | 0.50 ± 0.04 | 0.273 ± 0.007 |
| | 2.0 mg DHEA (8) | 416.9 ± 37.57 | 456.6 ± 27.67[d] | 0.44 ± 0.02 | 0.284 ± 0.003 |

Experimental details are as given in the text. Results are given as mean ± SEM of the number of observations indicated in the parentheses. a, $p < 0.05$; b, $p < 0.02$; c, $p < 0.01$ and d, $p < 0.001$ compared with the corresponding untreated group.

**Table 2: Effect of DHEA treatment on phospholipids composition of rat brain mitochondria**

| Phospholipid Class | Composition, (% of Total) | | | | |
|---|---|---|---|---|---|
| | Untreated (12) | 0.1 mg DHEA (14) | 0.2 mg DHEA (10) | 1.0 mg DHEA (12) | 2.0 mg DHEA (10) |
| Lyso | 3.43 ± 0.33 | 3.76 ± 0.34 | 3.81 ± 0.61 | 5.87 ± 0.27[c] | 3.42 ± 0.28 |
| SPM | 5.80 ± 0.36 | 7.54 ± 0.47[a] | 8.68 ± 0.23[c] | 11.71 ± 0.83[c] | 8.16 ± 0.33[c] |
| PC | 40.99 ± 0.79 | 44.85 ± 0.71[b] | 42.35 ± 0.70 | 42.35 ± 0.82 | 39.14 ± 0.81 |
| PI | 2.49 ± 0.11 | 2.62 ± 0.08 | 2.93 ± 0.29 | 2.29 ± 0.11 | 1.88 ± 0.17[a] |
| PS | 2.50 ± 0.08 | 2.76 ± 0.12 | 2.84 ± 0.18 | 2.32 ± 0.12 | 2.46 ± 0.21 |
| PE | 40.27 ± 0.59 | 34.60 ± 0.68[c] | 34.97 ± 0.99[c] | 32.64 ± 1.33[c] | 40.52 ± 0.60 |
| DPG | 4.53 ± 0.09 | 3.87 ± 0.20 | 4.42 ± 0.32 | 2.83 ± 0.47[b] | 4.43 ± 0.40 |

Experimental details are as given in the text. Results are given as mean ± SEM of the number of observations indicated in the parentheses. a, $p < 0.01$; b, $p < 0.002$; and c, $p < 0.001$ compared with untreated group.

**Table 3: Effect of DHEA treatment on phospholipids content of rat brain mitochondria**

| Phospholipid Class | Content, (µg/ mg protein) | | | | |
|---|---|---|---|---|---|
| | Untreated (12) | 0.1 mg DHEA (14) | 0.2 mg DHEA (14) | 1.0 mg DHEA (12) | 2.0 mg DHEA (10) |
| Lyso | 14.54 ± 1.30 | 20.60 ± 2.08[b] | 21.92 ± 1.69[d] | 29.68 ± 1.33[e] | 13.09 ± 1.11 |
| SPM | 24.03 ± 1.69 | 41.27 ± 3.56[e] | 47.16 ± 2.81[e] | 59.21 ± 3.99[e] | 31.78 ± 2.77[a] |
| PC | 166.55 ± 12.69 | 253.81 ± 22.39[b] | 233.89 ± 17.70[c] | 214.43 ± 4.88[d] | 152.43 ± 12.57 |
| PI | 10.30 ± 1.01 | 14.42 ± 0.99[c] | 16.71 ± 1.60[c] | 11.56 ± 0.56 | 6.34 ± 0.54[d] |
| PS | 10.35 ± 1.04 | 15.29 ± 1.18[c] | 16.11 ± 1.16[d] | 11.74 ± 0.68 | 8.50 ± 0.67 |
| PE | 165.81 ± 14.52 | 194.77 ± 15.92 | 192.27 ±13.75 | 165.99 ± 8.08 | 154.09 ± 10.17 |
| DPG | 18.37 ± 1.38 | 21.30 ± 1.67 | 24.11 ± 2.17[a] | 14.42 ± 2.45 | 15.91 ± 1.29 |

Experimental details are as given in the text. Results are given as mean ± SEM of the number of observations indicated in the parentheses. a, $p < 0.05$; b, $p < 0.02$; c, $p<0.01$; d, $p < 0.002$ and e, $p < 0.001$ compared with the untreated group.

**Table 4: Effect of DHEA treatment on phospholipids composition of rat liver mitochondria**

| Phospholipid Class | Composition, (% of Total) | | | | |
|---|---|---|---|---|---|
| | Untreated (12) | 0.1 mg DHEA (14) | 0.2 mg DHEA (10) | 1.0 mg DHEA (12) | 2.0 mg DHEA (10) |
| Lyso | 1.54 ± 0.08 | 1.76 ± 0.19 | 1.74 ± 0.12 | 1.69 ± 0.17 | 1.54 ± 0.18 |
| SPM | 3.00 ± 0.10 | 3.85 ± 0.30[b] | 3.32 ± 0.26 | 3.44 ± 0.33 | 3.33 ± 0.56 |
| PC | 46.91 ± 0.56 | 46.50 ± 0.82 | 46.71 ± 1.65 | 46.31 ± 1.18 | 45.97 ± 1.49 |
| PI | 1.76 ± 0.07 | 3.18 ± 0.28[d] | 3.26 ± 0.15[d] | 3.19 ± 0.52[b] | 2.19 ± 0.12 |
| PS | 1.87 ± 0.08 | 2.80 ± 0.19[d] | 2.99 ± 0.22[d] | 3.43 ± 0.44[c] | 2.31 ± 0.35 |
| PE | 33.20 ± 0.57 | 30.40 ± 0.39[d] | 29.24 ± 1.54[a] | 29.57 ± 1.65[b] | 31.27 ± 0.86 |
| DPG | 11.76 ± 0.44 | 10.51 ± 0.51 | 12.73 ± 0.59 | 12.38 ± 0.75 | 13.61 ± 0.63[a] |

Experimental details are as given in the text. Results are given as mean ± SEM of the number of observations indicated in the parentheses. a, $p < 0.05$; b, $p < 0.02$; c, $p < 0.002$ and d, $p < 0.001$ compared with the untreated group.

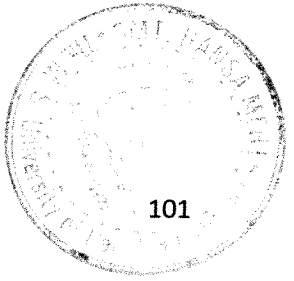

**Table 5: Effect of DHEA treatment on phospholipids content of rat liver mitochondria**

| Phospholipid Class | Content, (µg/ mg protein) | | | | |
|---|---|---|---|---|---|
| | Untreated (12) | 0.1 mg DHEA (14) | 0.2 mg DHEA (10) | 1.0 mg DHEA (12) | 2.0 mg DHEA (10) |
| Lyso | 2.79 ± 0.29 | 4.78 ± 0.52[b] | 3.31 ± 0.25 | 3.16 ± 0.23 | 2.28 ± 0.16 |
| SPM | 5.44 ± 0.55 | 6.59 ± 0.53 | 6.26 ± 0.46 | 6.47 ± 0.56 | 4.84 ± 0.30[a] |
| PC | 83.17 ± 6.29 | 79.84 ± 3.02 | 90.32 ± 7.69 | 86.33 ± 4.02 | 73.12 ± 6.24 |
| PI | 3.15 ± 0.29 | 5.54 ± 0.56[c] | 6.10 ± 0.57[c] | 6.07 ± 0.50[c] | 3.30 ± 0.24 |
| PS | 3.36 ± 0.35 | 4.84 ± 0.41[a] | 5.79 ± 0.47[c] | 6.52 ± 0.34[c] | 3.19 ± 0.27 |
| PE | 59.32 ± 4.98 | 52.35 ± 2.23 | 55.29 ± 5.43 | 55.21 ± 4.03 | 49.13 ± 3.25 |
| DPG | 20.72 ± 1.64 | 18.18 ± 1.24 | 24.59 ± 2.01 | 23.36 ± 2.10 | 20.77 ± 1.07 |

Results are given as mean ± SEM of the number of observations indicated in the parentheses.
a, $p < 0.02$; b, $p < 0.01$ and c, $p < 0.001$ compared with the untreated group.

## Discussion

The present study were undertaken to examine the possible effect(s) of DHEA treatment on lipid/phospholipid profile on rat brain and liver mitochondria. From the data presented (Table 1-5) it is clear that DHEA treatment influenced differently the lipid/phospholipid profiles of the mitochondria from the two tissues. Also, in general, in both the tissues the effects were evident at doses of DHEA of up to 1.0 mg and the effects diminished at the highest dose (2.0 mg) of DHEA. The differential effects of DHEA treatment became manifest with respect to contents of TPL and CHL, and the composition and contents of the individual phospholipid components.

Thus, DHEA treatment significantly increased the TPL and CHL contents of brain mitochondria while it was without any effect on TPL content in the liver mitochondria; in the liver mitochondria only the CHL content increased marginally (Table 1). The contents of Lyso and SPM increased substantially in the brain mitochondria in a dose-dependent manner with marginal effects being seen in the liver mitochondria. Under these conditions the content PI and PS increased in mitochondria from both the tissues with maximum effect being seen for the liver mitochondria. The content of PC, PE and DPG were generally not affected in either of the tissues except for a small but reproducible increase in DPG content of brain mitochondria from animals receiving 0.2mg dose of DHEA (Tables 3 and 5). These differential effects resemble the known tissue-specific effects of hormones. Interestingly, however, there is no known receptor of DHEA (Natawa et al., 2002).That the effects diminished at the highest dose (2.0 mg) is not really surprising since adverse catabolic effects of pharmacologic doses of hormones such as thyroid hormones have been well documented (Satav and Katyare, 1981; 1982).

Increased content of CHL in the brain mitochondria following DHEA treatment deserves some comment. It has been reported that the brain synthesizes its own cholesterol (Bjorkhem and Meaney, 2004). The increased content of CHL which we observe here resembles the similar increase in the brain mitochondria from developing animals (Pandya, Dave and Katyare, 2004b). It has been reported that the

content of CHL in the brains of Alzheimer's patients increases significantly which may have a role in β amyloid plaque formation (Kalman and Janka, 2005). Interestingly, however, the DHEA content in the brains of Alzheimer's patients is known to be significantly low compared to the age-matched controls (Weill-Engerer et al., 2002). Apparently, this increase occurs due to decrease in brain specific CYP46A1 enzyme responsible for the degradation of cholesterol to a water soluble metabolite 24S-hydroxycholesterol rather than decreased synthesis (Kalman and Janka, 2005). The increased content of Lyso which we note in the present study is suggestive of increased turnover. It may hence be suggested that DHEA treatment may selectively stimulate the biosynthesis of CHL in the brain. Important to no note in this context is the fact that the brain itself synthesizes DHEA, DHEA-S and pregnenolone (Racchi, Balduzzi and Corsini, 2003). These three steroids are considered to be the neurosteroids and may possibly have a role in cerebral metabolism (Baulieu and Paul, 1998).

The increased content of PS is another interesting feature. It has been shown that in experimental animals and in human trials nutritional supplementation of PS improved memory and cognitive functions while PC was ineffective in this respect (McDaniel, Maier and, Einstein, 2003). This observation assumes importance in the context of the fact that DHEA has been reported to have beneficial effects in improving memory and cognitive functions in elderly population (Buvat, 2003). Our results also show that while DHEA can influence the synthesis of PS and PI, apparently it has no or only marginal effect on synthesis of PC, PE and DPG. As pointed out above, the increased levels of Lyso which are suggestive of increased turnover rule out the possibility that the content of these phospholipids could have increased due to selective synthesis rather than due to decreased catabolism.

Changes in the fatty acid composition of serum, hepatic and adipose lipids in lean and obese Zucker rats, following treatment with DHEA have been reported by Abadie et al. (2000). Mc Intosh et al. (1999) reported decreased serum and liver lipid contents following DHEA treatment. Mohan and Cleary (1991) observed that the liver mitochondria in rats maintained on diet supplemented with DHEA had decreased

levels of DPG and PE and increase in the content of PC. Our results on decrease in PE are consistent with the observations of Mohan and Cleary (1991). However, it may be pointed out that Mohan and Cleary (1991) fed the experimental animals diet containing 0.6% DHEA. In our studies the animals received DHEA by s.c. route. It is possible that the differences in the dose regimen and route of administration may be responsible for the observed differences in our results.

Treatment with DHEA has been reported to lower the carbohydrate metabolism with simultaneous increase in metabolism of lipids (Miller et al., 1988; Song et al., 1989; Su and Lardy, 1991). Abadie et al. 2000 reported that treatment with DHEA for 30 days resulted in significant alteration of fatty acid profiles of serum, hepatic and adipose lipid components in lean and obese Zucker rats. DHEA feeding also resulted in increased proportion of arachidonic acid in total lipids and decreased oleic acid in soleus as well as cardiac muscle (Abadie et al., 2001; Imai et al., 1999) reported that the increase in hepatic content of oleic acid induced by DHEA in the rat was attributable to the induction of stearoyl-CoA desaturase. McIntosh et al. (1999) observed that DHEA treatment reduced serum and hepatic lipids. Mohan and Cleary (1991) observed that the mitochondria from rats treated with DHEA for 7 days had lower levels of cardiolipin and phosphatidylethanolamine and an increase in phosphatidylcholine. Also, changes in fatty acid composition of these phospholipids occurred after 7 days and 24 h of DHEA treatment (1991). However, as far as we are aware, the detailed tissue-specific effects of DHEA treatment on compositional changes in the lipid/phospholipid profiles have not been reported thus far.

The compositional changes in the phospholipids which we observe here may lead to altered charge distribution across the mitochondrial inner membrane, which in turn could modulate the function of the components of the electron transport chain. Dependence of electron transport chain components of specific lipid/phospholipid components is well documented (Daum, 1985). The changes in lipid/phospholipids profiles which we report here would complement the function of these components. Abnormalities in lipid/phospholipid profiles are known to affect cerebral and mitochondria functions in pathological conditions such as Parkinson's disease, neural

trauma, neurodegenerative disease and Alzheimer disease (Farooqui, Ong and Horrocks, 2004).

In conclusion, the results of this study suggested that treatment with DHEA alters the lipid/phospolipid profile in both brain and liver mitochondria in tissue-specific and dose dependent manner and so respiratory rates in young adult rats. So it is interesting to role of exogenous DHEA in development and aging which leads to further studies.

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