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# Altered lipid concentrations of liver, heart and plasma but not brain in HIV-1 transgenic rats

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**Keywords**

HIV-1 transgenic rat; fatty acid; brain; liver; heart; plasma; arachidonic; docosahexaenoic; polyunsaturated fatty acids (PUFA); concentration; composition; metabolism

## 1. Introduction

Human immunodeficiency virus-1 (HIV-1) infection is a risk factor for cardiovascular disease [1–3], hepatic fibrosis and non-alcoholic steatohepatitis [4] and neuropathological co-morbidities such as HIV neurocognitive disorders, depression and psychosis [5–7]. In these conditions, disturbed lipid metabolism associated with systemic expression of the viral proteins is common. In antiretroviral-naive HIV-1-infected patients, lipid disturbances are characterized by elevated plasma triglyceride and cholesterol concentrations, reduced plasma lipoprotein clearance [4, 8–12] and altered plasma and liver fatty acid composition [4, 13–17], suggesting a possible role of the viral proteins on lipid metabolism. These disturbances in lipid metabolism have been linked to the development or progression of cardiovascular, hepatic and neurocognitive disorders in HIV-infected patients, reflecting the role of lipids in HIV-related co-morbidities [4, 18, 2, 19].

*In vitro* studies suggest that the effects of the virus on lipid metabolism can be caused by direct induction of genes involved in lipogenesis and association of viral proteins with membrane lipid rafts. In this regard, transfection of lymphocytes with HIV-1 was reported to induce protein expression of lipogenic genes such as the lipoprotein receptor [20, 21], to increase cholesterol concentrations in lipid rafts [22, 23], and to selectively increase unsaturated fatty acid composition in lymphocyte membranes [24]. In cell culture, certain elements of the retroviral protein (*gag, pol, Env, Nef, gp120*) were reported to associate with membrane lipid rafts and to cause localized changes in membrane cholesterol and sphingolipid concentrations [25–29]. The in vivo effect of the virus on lipid (including fatty acid) concentrations is not known, except for one study that reported abnormal lipid metabolism in a transgenic mouse model of the replicative (R) element of the HIV protein [30].

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The HIV-1 Tg rat demonstrates pathological and behavioural abnormalities at 7–9 months of age, and is a model at this age for human HIV-1 dementia, skeletal and cardiac muscle myopathy and liver inflammation [31–36]. The virus in the non-infectious HIV-1 Tg rat lacks *gag* and *pol* replicative genes, but contains other HIV-1 proteins including glycoprotein 120 (gp120) and protein trans-activator of transcription (Tat), which can induce peripheral and central cytokine production [37, 32, 19, 34, 35], and changes in plasma and tissue lipid metabolism. In agreement with this suggestion, we recently reported an increased plasma unesterified arachidonic acid (AA, 20:4n-6) concentration, and increased brain AA metabolism, measured using quantitative autoradiography following the intravenous infusion of radiolabeled AA, in unanesthetized 7–9 month old male HIV-1 Tg compared with control rats [31].

In view of in vitro evidence of altered expression of genes involved in lipid metabolism and fatty acid profiles of HIV-infected cells [24, 22, 23, 20, 21], of clinical evidence of disturbed plasma and tissue lipid concentrations in antiretroviral-naive HIV-1-infected patients [4, 13, 8, 14, 15, 9, 10, 16, 12], and of an increased plasma unesterified AA concentration and brain AA metabolism in 7–9 month old HIV-1 Tg rats [31], we hypothesized that lipid concentrations in different organs and plasma will be altered in drug-free HIV-1 Tg rats compared to wildtype controls. To test this hypothesis, in the present study we measured concentrations of different lipids (including fatty acids) in liver, plasma, heart and brain of 7–9 month old wildtype and HIV-1 Tg rats fed a polyunsaturated fatty acid (PUFA)-sufficient diet free of AA and docosahexaenoic acid (DHA, 22:6n-3) [31, 32]. We measured concentrations in the different organs because of their interdependence on each other for lipid synthesis, secretion or utilization. In this regard, the liver is the main site of long-chain PUFA (AA and DHA) synthesis from their respective shorter-chain nutritionally essential PUFAs, linoleic acid (LA, 18:2n-6) and α-linolenic acid (α-LNA, 18:3n-3) and their secretion when esterified within lipoproteins into the plasma [38, 39], whereas brain and heart PUFA synthesis is much less; these organs largely derive long-chain PUFAs (AA and DHA) from plasma [40–42]. Understanding the potential impact of the HIV-1 virus on organ and plasma lipid concentrations using the HIV-1 Tg rat model is clinically relevant for i) determining whether a direct, isolated effect of the virus on in vivo lipid metabolism exists, and ii) addressing fatty acid nutritional requirements of individuals with HIV-1 infection.

## 2. Materials and Methods

### 2.1. Materials

Fatty acid standards were purchased from NuChek Prep (Elysian, MN, USA) or Avanti® Polar Lipids (Alabaster, AL, USA). Other chemicals and reagents were purchased from Sigma-Aldrich, Fisher Scientific or Acros Organics.

### 2.2. Animals

Procedures were performed under an approved animal protocol (#09-027) in accordance with the NIH Guidelines on the Care and Use of Laboratory Animals. Male HIV-1 Tg (7 to 9 months old) derived from Fischer 344/NHsd Sprague-Dawley rats, and age-matched prenatal control inbred Fischer 344 rats, were housed under a constant 12-h dark-light cycle with *ad libitum* access to water and the Teklad global 2018S (2018 sterilized) for control and 2918 (2018 irradiated) for HIV-1 Tg rats (Harlan Teklad, Madison, WI). The 2018 diet contained 5% soybean oil as the source of fat, which consisted of 16.7% saturated, 21.8% monounsaturated, 54.8% LA, 6.2% α-LNA, 0.03% AA, 0.02% eicosapentaenoic (EPA, 20:5n-3) and 0.06% DHA [31].

Lipid concentrations were determined in liver, heart and brain of HIV-1 Tg and control rats (n = 7 per group) following microwaving. The rats were anesthetized with Nembutal (50 mg/kg i.p.) and then subjected twice to high-energy microwave fixation, once at 5.5 kW (Cober Electronics, Norwalk, CT, USA) for 4.4 s to stop brain fatty acid metabolism, and a second time at 5.5 kW for 4.8 s to stop peripheral fatty acid metabolism [43]. Esterified plasma fatty acids were quantified from frozen arterial plasma in another set of non-microwaved HIV-1 Tg and control rats (n = 8 per group) that had been subjected to radiotracer (14C-AA) infusion following surgical implantation of a catheter into the right femoral artery and vein [31]. Unesterified plasma fatty acid concentrations have been reported [31].

### 2.3. Plasma and tissue lipid extraction and separation of lipid classes

Total lipids were extracted from plasma, liver, heart and brain samples by the Folch method [44], and were separated into neutral lipid cholesteryl esters, triacylglycerol, unesterified fatty acids, and total phospholipids) or phospholipid subclasses (ethanolamine glycerophospholipid (EtnGpl), phosphatidylinositol (PtdIns), phosphatidylserine (PtdSer) and choline glycerophospholipid (ChoGpl)) using thin layer chromatography (TLC) on silica gel-60 plates (EM Separation Technologies, Gibbstown, NJ, USA) [40]. The TLC bands were scraped into test tubes and methylated with 1% $H_2SO_4$-methanol for 3 h at 70°C after adding appropriate amounts of an internal standard (di-17:0 PC for phospholipids or 17:0 for unesterified fatty acids), and were quantified by gas-chromatography (GC) as previously described [40].

### 2.4. Tissue and plasma phospholipid, triglyceride and cholesteryl ester concentrations

Liver, heart, brain and plasma phospholipids and triglycerides were determined by dividing the sum of all fatty acids within each separated fraction by 2 and 3, the number of fatty acids per molecule, respectively. The sum of all fatty acids within the separated cholesteryl ester fraction was used calculate the cholesteryl ester concentration, which has one fatty acid per molecule.

### 2.5. Cholesterol

Total cholesterol in liver, heart and brain was determined in the total lipid extract by GC following saponification and trimethylsilylchloride derivatization as previously described [45].

### 2.6. Statistical analysis

Data are presented as mean ± SD (n = 7–8 per group). Differences between means were determined by an unpaired t-test and were considered significant at $P < 0.05$.

## 3. Results

### 3.1 Body and organ weights

HIV-1 Tg rats weighed significantly less (27%) than controls (307 ± 21 g vs. 426 ± 19 g, n = 7, $P < 0.001$), as reported [31, 32, 34]. The liver weight was significantly lower in HIV-1 Tg rats than controls by 41% (8.2 ± 1.3 g vs. 14.1 ± 1.7 g, n = 6, $P < 0.001$), but did not differ significantly when expressed as percent body weight (2.7 ± 0.5 % vs. 3.3 ± 0.5 %, $P = 0.053$). Heart weight was significantly lower (0.79 ± 0.06 g vs. 0.94 ± 0.15 g, n = 7, $P < 0.05$), but was higher significantly when expressed as percent of body weight (0.25 ± 0.01 % vs. 0.22 ± 0.04 %, n = 7, $P < 0.05$), as reported [46]. Brain weight also was lower in HIV-1 Tg rats than controls (1.3 ± 0.2 g vs. 1.7 ± 0.1 g, n = 7, $P < 0.01$), but was not significantly

changed when expressed as percent of body weight (0.43 ± 0.06 % vs. 0.39 ± 0.04 %, P = 0.14).

### 3.2. Concentration of lipid classes and individual phospholipids

As shown in Table 1, total phospholipid (nmol/g wet wt) was significantly reduced in the heart of HIV-1 Tg rats. ChoGpl and EtnGpl concentrations were reduced in liver and heart of HIV-1 Tg rats, respectively. Total cholesterol and cholesteryl ester concentrations (nmol/g wet wt) were significantly higher (33%) in HIV-1 Tg liver, as were triglycerides, an effect that approached statistical significance (P = 0.06). In plasma, total triglycerides were significantly higher (33%) in HIV-1 Tg than control rats, but no significant difference in plasma cholesteryl ester or phospholipid was seen.

### 3.3. Plasma fatty acid concentrations

The main changes in esterified fatty acids in plasma occurred within triglycerides, and corresponded to the n-3 and n-6 PUFA changes seen in liver (Table 2). Concentrations of monounsaturated fatty acids and n-3 and n-6 PUFAs were increased significantly by 24–175% in HIV-1 Tg rats compared to controls. The greatest changes were seen in LA, n-6 docosapentaenoic acid (DPA), AA, EPA and DHA, whose concentrations were increased by 88%, 77%, 88%, 175% and 101%, respectively (P < 0.05). As reported elsewhere (Supplementary Table 1) [31], only the plasma AA concentration differed significantly between groups, being 33% higher in HIV-1 Tg than in control rats [31].

### 3.4. Liver fatty acid concentrations

In liver (Table 3-A), concentrations of several n-3 and n-6 PUFAs were increased in total lipids and in triglyceride, cholesteryl ester and unesterified lipid fractions, but were decreased in phospholipids, in HIV-1 Tg rats, whereas decreases and increases were significant in minor saturated and monounsaturated fatty acids such as myristic (14:0), arachidic (20:0), palmitoleic (16:1n-7) and eicosanoic (20:1n-9) acid. LA and AA concentrations were significantly increased in total liver lipids, triglycerides, cholesteryl esters and unesterified fatty acids of HIV-1 Tg rats. Other n-6 PUFA intermediates such as docosatetraenoic acid (DTA, 22:4n-6) and docosapentaenoic acid (n-6 DPA, 22:5n-6) were significantly higher in total lipids, triglycerides and cholesteryl esters. n-6 DPA, however, was reduced by 2.6-fold in phospholipids of HIV-1 Tg rats, as was α-LNA (18:3n-6; 1.7 fold). n-3 PUFAs including α-LNA, n-3 DPA (22:5n-3) and DHA were significantly higher in liver total lipids, triglycerides and cholesteryl esters of HIV-1 Tg rats than controls. EPA also was significantly increased in total lipids and triglycerides, but was reduced in phospholipids, whereas α-LNA and n-3 DPA were increased significantly in phospholipids only. Significant changes in unesterified n-3 PUFA concentrations were not seen in the liver.

Fatty acid changes in liver phospholipid subfractions (EtnGpl, ChoGpl, PtdIns, PtdSer; Table 3-B) corresponded to changes in total phospholipids, particularly for the PUFAs. The n-6 PUFAs DTA and n-6 DPA were decreased in ChoGpl and PtdIns and in all subfractions, respectively, consistent with the changes in total phospholipids (P < 0.05). α-LNA was increased in EtnGpl, ChoGpl and PtdSer, whereas EPA was reduced in all subfractions of HIV-1 Tg rats, also consistent with the changes in total phospholipids. Oleate was significantly increased by 34% in ChoGpl.

### 3.5. Heart fatty acid concentrations

Fatty acid concentration changes in total lipids and esterified and unesterified lipid subfractions of heart were similar to changes in liver and plasma. As shown in Table 4-A, AA and n-3 DPA concentrations in total heart lipids were significantly higher in HIV-1 Tg

rats than controls, whereas the n-6 DPA concentration was lower ($P < 0.05$). In phospholipid, myristate, palmitate, oleate, LA, AA and n-6 DPA were significantly reduced, whereas n-3 DPA was increased. AA, n-3 DPA and DHA were significantly increased in heart triglycerides. AA and myristate were significantly increased in heart unesterified fatty acids and cholesteryl esters, respectively.

The major fatty acid changes in heart phospholipid subfractions occurred within EtnGpl and ChoGpl (Table 4-B). Stearate, AA and n-3 DPA were significantly reduced in EtnGpl, but were increased in ChoGpl of HIV-1 Tg rats. Palmitoleate, oleate, vaccinate (18:1n-7) and linoleate were consistently reduced in both fractions, whereas n-6 DPA was decreased in EtnGpl only. DTA was significantly higher in ChoGpl of HIV-1 Tg rats than controls.

### 3.6. Brain fatty acid concentrations

In brain, changes occurred in minor fatty acids (Tables 5-A and 5-B). LA and n-3 DPA were significantly higher by 5–28% in total lipids, phospholipids and triglycerides of HIV-1 Tg rats (Table 5-A). Lignocerate (24:0), arachidate, erucate and LA concentrations were increased significantly in some brain phospholipid subfractions of HIV-1 Tg rats (Table 5-B).

## 4. DISCUSSION

Lipid concentrations in liver, heart, brain and plasma of wildtype 7–9 month old rats were similar to previous reports in adult rats [40, 41, 47, 42]. In comparison, 7– 9 month old HIV-1 Tg rats showed multiple disturbances in lipid concentrations, including increased accumulation of total cholesterol and cholesteryl esters in liver and hypertriglyceridemia in plasma. HIV-1 Tg rats also had increased n-3 and n-6 PUFA concentrations in triglyceride, cholesteryl ester and unesterified fatty acids of liver, heart and plasma, but not of brain. Concentrations of several fatty acids including PUFAs were decreased in liver and heart total phospholipids, but increased or decreased within individual liver and heart phospholipids (ChoGpl, EtnGpl, PtdIns and PtdSer), suggesting membrane phospholipid remodeling. Overall, these findings suggest a profound change of peripheral but not brain lipid metabolism, due to the presence of the transgenic HIV-1 virus (20–25 copies) in each cell [35].

Previous studies have attributed HIV-1 related disturbances in lipid composition to the replicate *gag* and *pol* elements of the virus, which associate with lipid rafts and cause localized increases in membrane cholesterol concentrations that facilitate viral invasion of host cells [25–27]. Because HIV-1 Tg rats lack these replicative elements, this study demonstrates that non-replicative viral elements also profoundly change tissue lipid concentrations as well as membrane phospholipid composition. This is in agreement with studies that reported that the *gp120, Env and nef* non-replicative elements of the HIV-1 protein interact with plasma membranes, cause localized changes in lipid composition and disrupt cell protein trafficking and signaling [26, 48, 49, 28, 29], consistent with in vitro evidence of increased N-methyl-D-aspartate receptor clustering in lipid microdomains caused by the gp-120 element of the virus [50]. Identifying and targeting non-replicative viral elements that cause membrane lipid disruptions may improve the clinical efficacy of antiretroviral drugs, particularly those that interfere with the membrane phospholipid clustering assembly of the virus and its entry into the host cell [51].

Antiretroviral medications are reported to produce hyperlipidemia in humans by increasing liver triglyceride secretion and reducing its clearance from plasma [11, 12]. The increases in plasma triglyceride and liver cholesterol and cholesteryl ester concentrations in HIV-1 Tg rats (Table 1) suggest a role for the virus alone in lipogenesis. HIV-1 transfection of T-

lymphocytes induced protein expression of lipogenic genes and reduced expression of proteins involved in lipid clearance, such as the high-density lipoprotein receptor [20, 21]. Mechanisms related to the induction of lipogenic enzymes by the HIV-1 proteins likely operate at the transcriptional level, consistent with the reported activation of sterol regulatory-element binding protein-2 transcription (SREBP-2) in HIV infected $CD4^+$ T cells [52].

The accumulation of triglycerides, cholesterol and cholesteryl esters in liver of HIV-1 Tg rats (Table 1) suggests the presence of fatty liver syndrome, which has been reported in humans with HIV-1 infection [4]. Increased liver and plasma lipids in patients have been described in association with reduced clearance of circulating lipoproteins [4, 9, 11], possibly due to insulin resistance [8, 53]. Unlike humans, however, HIV-1 Tg rats do not show insulin resistance at 7 months of age [34], suggesting that the lipid changes observed in this study were not secondary to insulin-related abnormalities.

Liver, heart and plasma concentrations within total lipids, phospholipid, triglyceride, cholesteryl ester and unesterified fatty acid were altered in the HIV-1 Tg rats. These changes were characterized mainly by increased n-3 and n-6 PUFA concentrations in total lipid, triglyceride, cholesteryl ester and unesterified fatty acids, and a reduction in some PUFAs within total phospholipids (Tables 2, 3-A and 4-A), suggesting disturbed PUFA metabolism. Changes in saturated and monounsaturated fatty acids occurred only in minor fatty acids such as myristate (14:0), eicosanoate (20:1n-9), behenate (22:0), and palmitoleate (16:1n-7). The effects of the virus on liver and plasma triglyceride and cholesteryl ester long-chain PUFA concentrations (AA, n-6 DPA, EPA and DHA) in particular, suggest changes in liver enzymes involved in their synthesis (elongases and desaturases) and secretion (acyl transferases) into plasma. Because rat heart synthesis of long-chain PUFAs is limited [42], the increases in heart likely reflect uptake from plasma following increased liver secretion. The reductions in liver and heart phospholipid PUFA concentrations were opposite to changes seen in triglyceride, cholesteryl and unesterified fatty acids, and suggest disturbances in enzymes regulating long-chain PUFA turnover within phospholipids (phospholipases, acyl-CoA synthetases and acyl-CoA transferases [54]).

Notable changes in liver total lipids and several lipid compartments were the increases (> 2-fold) in diet-derived α-LNA and LA concentrations in the HIV-1 Tg rats (Table 3-A). The increases cannot be attributed to changes in dietary α-LNA and LA composition, because both control and HIV-1 Tg rats received the same diets with the minimum recommended amounts of α-LNA and LA for rodents [55]. Thus, the increases in liver α-LNA and LA were likely due to adipose tissue mobilization. Adipose tissue hormone sensitive lipase selectively hydrolyzes PUFAs including α-LNA and LA from triglycerides [56–59] when stimulated by reduced food intake [58], which was reported in HIV-1 Tg rats [60, 34]. Increased long-chain n-3 and n-6 PUFA concentrations in liver may also be due to adipose mobilization, in addition to increased synthesis-secretion by the liver and reduced plasma clearance. The contribution of adipose tissue lipolysis and reduced food intake to the changes in liver PUFA concentrations can be addressed in future studies with pair-feeding.

The changes in heart fatty acid concentrations (Table 4) may significantly affect cardiac function, because fatty acids and their metabolites, particularly AA, EPA and DHA, have been implicated in regulating cardiac excitability [61, 62]. Concentrations of AA were increased in total lipids, phospholipids, triglycerides and unesterified fatty acids, whereas EPA and DHA concentrations did not change. The preferential increase of AA over EPA and DHA is consistent with the selective increase in plasma unesterified AA concentration, from which the heart partly derives its AA, and with one report that suggested preferential uptake of AA by heart over DHA [63]. An increase in AA plasma availability and heart

concentration may be associated with increased pro-arrhythmic AA-metabolites [61] or cardiac inflammation [34]. It is not known, however, whether such changes contribute to the reported 61% increase in cardiovascular disease risk in drug-free HIV-infected patients compared with age-matched controls [2].

There was no major difference in brain fatty acid concentrations between groups (Table 5), despite reported upregulation of AA metabolism and of AA and DHA metabolizing enzymes (i.e. $cPLA_2$ and $iPLA_2$) in association with neuroinflammatory markers [31, 64]. This demonstrates that under pathological conditions of inflammation and upregulated AA and DHA metabolism, the brain remains resilient to changes in fatty acid composition, consistent with what has been reported in postmortem frontal cortex of bipolar disorder and schizophrenic patients [65–67].

One limitation of this study is that we did not measure the expression of enzymes involved in lipid metabolism (e.g. desaturase, elongase, lipoprotein lipase, synthetase and transferase enzymes) in the heart or liver, which limits our ability to derive possible mechanistic pathways that account for the changes in tissue lipid concentrations. Enzyme expression was not measured because the rats were subjected to head-focused and whole-body microwave fixation to stop lipid metabolism by rapidly denaturing brain and tissue enzymes and other proteins [43]. In brain, despite the limited change in lipid concentrations, the HIV-1 Tg rat compared with control was reported to show significantly higher protein and mRNA levels of the inflammatory cytokines IL1-β and TNFα, and of AA-selective $cPLA_2$-IVA, $sPLA_2$-IIA, COX-2, membrane prostaglandin E2 synthase, 5-lipoxygenase (LOX), 15-LOX and cytochrome p450 epoxygenase, and decreased levels of brain-derived neurotrophic factor (BDNF) and drebrin, a marker of post-synaptic excitatory dendritic spines[64]. It would be worthwhile to investigate in future studies, whether similar changes in lipid-metabolizing enzymes occur in liver or heart, in which lipid concentrations were markedly altered (Tables 3 and 4).

In conclusion, 7–9 month old HIV-1 Tg rats demonstrated evidence of hyperlipidemia, membrane remodeling and preferential changes in PUFA concentrations in liver, plasma and heart, but not brain, in association with systemic expression of the non-replicative HIV-1 proteins. Since comparable changes may contribute to the reported lipodystrophy and inflammation in humans with HIV-1 infection, future studies might explore drug or dietary treatments with statins, mood stabilizers, low n-6 PUFA diets or n-3 long-chain PUFA supplementation [68], which may reduce plasma and liver lipid accumulation, and target central and peripheral inflammation associated with increased AA metabolism or tissue concentrations.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Abbreviations

| | |
|---|---|
| **AA** | arachidonic acid |
| **α-LNA** | alpha-linolenic acid |

| | |
|---|---|
| **COX** | cyclooxygenase |
| **ChoGpl** | choline glycerophospholipid |
| **cPLA$_2$** | cytosolic phospholipase A$_2$ |
| **DHA** | docosahexaenoic acid |
| **DPA** | docosapentaenoic acid |
| **DTA** | docosatetraenoic acid |
| **EtnGpl** | ethanolamine glycerophospholipid |
| **EPA** | eicosapentaenoic acid |
| **FAME** | fatty acid methyl ester |
| **GC** | gas chromatography |
| **gp-120** | glycoprotein-120 |
| **iPLA$_2$** | calcium-independent phospholipase A$_2$ |
| **LA** | linoleic acid |
| **MUFAs** | monounsaturated fatty acids |
| **PtdIns** | phosphatidylinositol |
| **PtdSer** | phosphatidylserine |
| **PUFA** | polyunsaturated fatty acid |
| **SFAs** | saturated fatty acids |
| ***sn*** | stereospecifically numbered |
| **Tg** | transgenic |
| **tat** | trans-activator of transcription protein |
| **TLC** | thin layer chromatography |

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**Table 1**

Phosphorous, cholesterol, cholesteryl ester and triglyceride concentration in liver, heart, brain and plasma of control and HIV-1 Tg rats (μmol/g wet tissue or μmol/ml plasma)

| | Liver | | Heart | | Brain | | Plasma | |
|---|---|---|---|---|---|---|---|---|
| | **Control** | **HIV-1 Tg** | **Control** | **HIV-1 Tg** | **Control** | **HIV-1 Tg** | **Control** | **HIV-1 Tg** |
| Total phospholipid | 29.1 ± 2.9 | 28.4 ± 2.6 | 25.4 ± 0.8 | 24.2 ± 1.3* | 54.8 ± 2.5 | 55.3 ± 1.9 | 1.3 ± 0.2 | 1.5 ± 0.3 |
| EtnGpl | 5.6 ± 0.8 | 5.8 ± 1.4 | 10.0 ± 0.5 | 8.9 ± 0.5*** | 16.2 ± 1.0 | 16.7 ± 0.8 | | |
| ChoGpl | 13.6 ± 1.2 | 11.9 ± 0.9 * | 10.0 ± 0.3 | 9.9 ± 0.4 | 21.3 ± 0.8 | 21.6 ± 0.7 | | |
| PtdIns | 2.0 ± 0.3 | 1.8 ± 0.9 | 0.7 ± 0.1 | 0.7 ± 0.1 | 2.5 ± 0.4[1] | 2.4 ± 0.1 | | |
| PtdSer | 0.7 ± 0.1 | 0.8 ± 0.1 | 0.5 ± 0.1 | 0.5 ± 0.1 | 7.2 ± 0.5 | 7.3 ± 0.5 | | |
| Total cholesterol | 2.0 ± 0.3 | 3.0 ± 1.0 * | 1.0 ± 0.2 | 1.0 ± 0.5 | 24 ± 6 | 26 ± 5 | | |
| Cholesteryl ester | 1.0 ± 0.2 | 2.0 ± 0.9 * | 0.30 ± 0.05 | 0.3 ± 0.04 | 0.2 ± 0.1 | 0.2 ± 0.1 | 1.6 ± 0.2 | 1.7 ± 0.5 |
| Triglyceride | 15.7 ± 3.3 | 27.1 ± 14.2 | 4.7 ± 1.6 | 5.2 ± 1.8 | 0.20 ± 0.05 | 0.20 ± 0.04 | 0.07 ± 0.03 | 0.10 ± 0.02* |

ChoGpl, choline glycerophospholipids; EtnGpl, ethanolamine glycerophospholipids; PtdIns, Phosphatidylinositol; PtdSer, phosphatidylserine. Values are mean ± SD of n= 7–8 per group.

[1] Values are mean ± SD of n=5–6 per group for brain PtdIns.

* P<0.05,

*** P<0.001 by unpaired t-test.

**Table 2**

Esterified fatty acid concentrations (nmol/ml) in plasma phospholipids, cholesteryl esters and triglycerides of control and HIV-1 Tg rats

| | Phospholipids | | Cholesteryl esters | | Triglycerides | |
|---|---|---|---|---|---|---|
| | Control | HIV-1 Tg | Control | HIV-1 Tg | Control | HIV-1 Tg |
| 14:0 | 3 ± 4 | 2 ± 2 | 9 ± 2 | 15 ± 11 | 12 ± 8 | 11 ± 5 |
| 16:0 | 555 ± 107 | 678 ± 160 | 157 ± 26 | 178 ± 68 | 49 ± 26 | 63 ± 24 |
| 18:0 | 738 ± 121 | 738 ± 192 | 40 ± 19 | 53 ± 36 | 27 ± 10 | 30 ± 10 |
| 20:0 | 3 ± 2 | 5 ± 1 | 2 ± 1 | 13 ± 18 | 2 ± 1 | 2 ± 1 |
| 16:1n-7 | 21 ± 28 | 13 ± 3 | 37 ± 9 | 32 ± 12 | 3 ± 3 | 3 ± 1 |
| 18:1n-9 | 64 ± 20 | 81 ± 22 | 34 ± 5 | 50 ± 20* | 17 ± 10 | 26 ± 6* |
| 18:1n-7 | 83 ± 13 | 82 ± 17 | 16 ± 3 | 22 ± 10 | 7 ± 5 | 10 ± 3 |
| 20:1n-9 | 2 ± 1 | 2 ± 1 | 1 ± 0.2 | 6.2 ± 11.2 | 1 ± 1 | 1 ± 0 |
| 22:1n-9 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 7 ± 1 | 9 ± 2* |
| 24:1n-9 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 18:2n-6 | 335 ± 80 | 459 ± 105* | 248 ± 54 | 296 ± 70 | 33 ± 25 | 62 ± 16* |
| 18:3n-6 | 0 ± 0 | 0.0 ± 0.0 | 2 ± 1 | 1 ± 1 | 1 ± 1 | 1 ± 0.4 |
| 20:3n-6 | 0 ± 0 | 0.0 ± 0.0 | 11 ± 3 | 14 ± 12 | 7 ± 2 | 7 ± 1 |
| 20:4n-6 | 720 ± 117 | 704 ± 159 | 990 ± 180 | 1006 ± 246 | 32 ± 14 | 60 ± 11*** |
| 20:2n-6 | 7 ± 2 | 8.0 ± 1.9 | 0 ± 0 | 9 ± 15 | 2 ± 1 | 1 ± 1 |
| 22:4n-6 DTAn-6 | 17 ± 7 | 20 ± 7 | 13 ± 1 | 19 ± 20 | 5 ± 1 | 8 ± 3* |
| 22:5n-6 DPAn-6 | 6 ± 3 | 8 ± 2 | 1 ± 0 | 7 ± 2 | 0.5 ± 0.2 | 0.8 ± 0.3 |
| 18:3n-3 | 1 ± 1 | 1.9 ± 1.7 | 2 ± 1 | 8 ± 13 | 3 ± 3 | 2 ± 1 |
| 20:3n-3 | 16 ± 4 | 12 ± 5 | 5 ± 1 | 4 ± 4 | 1 ± 1 | 1 ± 0 |
| 20:5n-3 EPA | 3 ± 2 | 4 ± 1 | 6 ± 4 | 7 ± 5 | 2 ± 1 | 7 ± 2*** |
| 22:5n-3 DPAn-3 | 20 ± 4 | 28 ± 6** | 1 ± 0 | 1 ± 0 | 1 ± 0.2 | 2 ± 1 |
| 22:6n-3 DHA | 83 ± 13 | 91 ± 23 | 20 ± 3 | 22 ± 7 | 2 ± 1 | 4 ± 1** |
| Total SFAs | 1314 ± 220 | 1442 ± 346 | 208 ± 46 | 256 ± 117 | 89 ± 42 | 106 ± 36 |
| Total MUFAs | 170 ± 58 | 178 ± 41 | 89 ± 18 | 110 ± 45 | 26 ± 18 | 40 ± 9 |
| Total n-6 PUFAs | 1086 ± 191 | 1198 ± 266 | 1253 ± 230 | 1323 ± 312 | 71 ± 35 | 132 ± 26** |
| Total n-3 PUFAs | 120 ± 20 | 134 ± 32 | 27 ± 5 | 33 ± 17 | 5 ± 5 | 9 ± 3 |

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| | Phospholipids | | Cholesteryl esters | | Triglycerides | |
|---|---|---|---|---|---|---|
| | **Control** | **HIV-1 Tg** | **Control** | **HIV-1 Tg** | **Control** | **HIV-1 Tg** |
| Total fatty acids | 2693 ± 465 | 2957 ± 679 | 1593 ± 230 | 1740 ± 452 | 209 ± 98 | 309 ± 68 * |
| Ratio of n-6/n-3 | 9.0 ± 0.4 | 9.0 ± 0.5 | 46.8 ± 2.6 | 44.5 ± 9.9 | 25.2 ± 25.0 | 16.2 ± 5.7 |
| Ratio of AA to DHA | 8.7 ± 0.3 | 7.8 ± 0.7 ** | 48.8 ± 3.1 | 47.7 ± 5.7 | 20.4 ± 17.3 | 15.6 ± 2.2 |

Values are mean ± SD of n=8 per group.

SFAs, saturated fatty acids; MUFAs, monounsaturated fatty acids; PUFAs, polyunsaturated fatty acids.

* P<0.05,

** P<0.01,

*** P<0.001 by unpaired t-test.

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**Table 3-A**

Fatty acid concentrations (nmol/g) in liver total lipids, phospholipids, cholesteryl esters, triglycerides and unesterified fatty acid compartment of control and HIV-1 Tg rats

| | Total lipids | | Phospholipids | | Cholesteryl esters | | Triglycerides | | Unesterified fatty acids | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | HIV-1Tg | Control | HIV-1Tg | Control | HIV-1Tg | Control | HIV-1Tg | Control | HIV-1Tg |
| 14:0 | 1180± 363 | 560± 189 ** | 172 27 | 86 ± 22 *** | | | 976 ± 332 | 472 ± 175 ** | | |
| 16:0 | 34450± 6957 | 34232± 11545 | 11865 ± 1143 | 10977 ± 700 | 318± 83 | 469± 168 | 19678 ± 5704 | 20428 ± 10622 | 433 ± 119 | 376 ± 115 |
| 18:0 | 15148± 2008 | 15195± 3328 | 13735 ± 1870 | 13367 ± 2495 | 97± 26 | 129± 41 | 926 ± 208 | 1387 ± 862 | 110 ± 20 | 117 ± 23 |
| 20:0 | 94 ± 5 | 163 ± 38 *** | 43 ± 5 | 49 ± 11 | | | 41 ± 6 | 104 ± 44 * | | |
| 16:1n-7 | 6227± 2239 | 1467± 601 *** | 1120 ± 340 | 270 ± 104 *** | 53± 11 | 60± 22 | 5006 ± 1990 | 1224 ± 551 ** | 15 ± 5 | 6 ± 3 ** |
| 18:1n-9 | 12212± 4213 | 16737± 8307 | 1508 ± 278 | 1405 ± 146 | 62± 11 | 302± 237 * | 9358 ± 2395 | 12797 ± 6331 | 39 ± 10 | 52 ± 9 * |
| 18:1n-7 | 4222± 1897 | 2670± 2520 | 2286 ± 166 | 1818 ± 267 ** | 22± 4 | 71± 38 ** | 2322 ± 358 | 2158 ± 233 | 27 ± 9 | 28 ± 8 |
| 20:1n-9 | 117± 14 | 227± 45 *** | 36 ± 4 | 48 ± 16 | | | 69 ± 11 | 164 ± 51 *** | | |
| 18:2n-6 | 14777± 1652 | 40109± 17857 ** | 7080 ± 940 | 7852 ± 514 | 124± 17 | 440± 282 * | 6930 ± 1698 | 30893 ± 17828 ** | 55 ± 17 | 112 ± 22 *** |
| 20:4n-6 | 15882± 1036 | 20990± 4720 * | 14401 ± 1033 | 15252 ± 1785 | 188± 43 | 368± 131 ** | 545 ± 171 | 4794 ± 3064 ** | 26 ± 15 | 46 ± 10 * |
| 22:4n-6 | 653± 51 | 1795± 633 *** | 305 ± 50 | 330 ± 27 | 10± 2 | 17± 6 ** | 149 ± 50 | 1203 ± 601 ** | 12 ± 6 | 16 ± 12 |
| 22:5n-6 | 556± 109 | 413± 135 * | 442 ± 99 | 171 ± 47 *** | 3± 2 | 2± 1 | 38 ± 11 | 214 ± 136 ** | 4 ± 6 | 2 ± 1 |
| 18:3n-3 | 404± 119 | 1640± 781 ** | 47 ± 8 | 81 ± 17 ** | 6± 4 | 31± 18 ** | 339 ± 113 | 1479 ± 776 ** | 7 ± 6 | 13 ± 10 |
| 20:3n-3 | 958± 421 | 695± 76 | 758 ± 334 | 209 ± 54 ** | 72± 13 | 62± 23 | 85 ± 30 | 443 ± 100 *** | 5 ± 4 | 9 ± 14 |
| 20:5n-3 | 372± 87 | 675± 267 * | 256 ± 76 | 79 ± 20 *** | 11± 5 | 12± 5 | 72 ± 22 | 560 ± 281 ** | 5 ± 2 | 11 ± 11 |
| 22:5n-3 | 1045± 73 | 2278± 692 *** | 789 ± 105 | 887 ± 33 * | 0.5± 0.1 | 1.5± 1.0 * | 122 ± 46 | 1244 ± 737 ** | 4 ± 4 | 6 ± 2 |
| 22:6n-3 | 3498± 276 | 4760± 1426 * | 3043 ± 334 | 3570 ± 739 | 6± 2 | 20± 9 ** | 96 ± 38 | 916 ± 717 * | 7 ± 4 | 8 ± 2 |
| Total SFAs | 51193± 9198 | 50480± 14937 | 25969 ± 2912 | 24716 ± 3067 | 416± 107 | 598± 202 | 21634 ± 6206 | 22403 ± 11615 | 544 ± 138 | 492 ± 124 |
| Total MUFAs | 22873± 5190 | 21115± 7042 | 4950 ± 639 | 3541 ± 471 *** | 137± 25 | 434± 293 * | 16842 ± 4464 | 16353 ± 6889 | 81 ± 21 | 86 ± 15 |
| Total n-6 PUFAs | 32436± 2056 | 64533± 23397 ** | 22522 ± 1862 | 23930 ± 1873 | 325± 54 | 828± 402 ** | 7887 ± 1905 | 37896 ± 21822 ** | 98 ± 35 | 176 ± 32 *** |
| Total n-3 PUFAs | 5905± 577 | 9373± 2886 ** | 4630 ± 558 | 4746 ± 662 | 84± 16 | 114± 49 | 641 ± 214 | 4082 ± 2304 ** | 23 ± 18 | 36 ± 22 |
| Total fatty acids | 112779± 15824 | 146176± 48196 | 58204 ± 5813 | 56801 ± 5183 | 973± 190 | 1986± 892 * | 47067 ± 10027 | 81293 ± 42650 | 749 ± 182 | 802 ± 179 |
| Ratio of n-6/n-3 | 5.5± 0.4 | 6.8± 0.5 *** | 4.9 ± 0.3 | 5.1 ± 0.5 | 3.9± 0.8 | 7.3± 1.3 *** | 12.7 ± 1.6 | 9.2 ± 0.6 *** | 5.0 ± 1.1 | 5.7 ± 1.5 |

| | Total lipids | | Phospholipids | | Cholesteryl esters | | Triglycerides | | Unesterified fatty acids | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | HIV-1Tg | Control | HIV-1Tg | Control | HIV-1Tg | Control | HIV-1Tg | Control | HIV-1Tg |
| Ratio of AA to DHA | 4.5± 0.2 | 4.5± 0.5 | 4.8 ± 0.3 | 4.3 ± 0.5 | 33.9± 4.8 | 19.4± 2.7*** | 5.9 ± 0.6 | 5.8 ± 1.1 | 3.8 ± 0.4 | 5.8 ± 1.8* |

Values are mean ± SD of n=7 per group.

SFAs, saturated fatty acids; MUFAs, monounsaturated fatty acids; PUFAs, polyunsaturated Fatty acids.

*P<0.05,

**P<0.01,

***P<0.001 by unpaired t-test.

**Table 3-B**

Fatty acid concentrations (nmol/g) in liver glycerophospholipids of control and HIV-1 Tg rats

| | EtnGpl | | ChoGpl | | PtdIns | | PtdSer | |
|---|---|---|---|---|---|---|---|---|
| | **Control** | **HIV** | **Control** | **HIV** | **Control** | **HIV** | **Control** | **HIV** |
| 14:0 | 16 ± 4 | 16 ± 18 | 83 ± 12 | 38 ± 12*** | 6 ± 4 | 4 ± 1 | 2 ± 0.4 | 1 ± 0.3** |
| 16:0 | 2055 ± 283 | 1956 ± 424 | 5804 ± 463 | 5060 ± 447** | 381 ± 51 | 282 ± 133 | 112 ± 20 | 106 ± 21 |
| 18:0 | 1968 ± 344 | 2214 ± 886 | 6321 ± 807 | 5562 ± 927 | 1634 ± 314 | 1422 ± 733 | 555 ± 116 | 583 ± 102 |
| 20:0 | 10 ± 3 | 9 ± 1 | 21 ± 1 | 19 ± 6 | 3 ± 0.1 | 2 ± 1 | 2 ± 0.2 | 3 ± 0.5 |
| 16:1n-7 | 282 ± 108 | 68 ± 14*** | 449 ± 125 | 110 ± 51*** | 27 ± 11 | 7 ± 4*** | 10 ± 3 | 4 ± 1*** |
| 18:1n-9 | 252 ± 35 | 338 ± 77* | 777 ± 144 | 606 ± 93* | 69 ± 51 | 46 ± 25 | 25 ± 4 | 27 ± 4 |
| 18:1n-7 | 546 ± 72 | 443 ± 75* | 960 ± 127 | 713 ± 173* | 95 ± 55 | 61 ± 27 | 43 ± 9 | 37 ± 8 |
| 20:1n-9 | 9 ± 1 | 11 ± 2 | 15 ± 0 | 13 ± 12 | 2 ± 0.2 | 1 ± 0.1* | 1 ± 0.2 | 2 ± 0.3* |
| 18:2n-6 | 1850 ± 380 | 2102 ± 295 | 3033 ± 446 | 2545 ± 1055 | 196 ± 44 | 271 ± 124 | 87 ± 16 | 98 ± 20 |
| 18:3n-6 | | | 79 ± 20 | 41 ± 17** | | | 2 ± 0.6 | 2 ± 0.5 |
| 20:2n-6 | 40 ± 6 | 63 ± 11*** | 72 ± 3 | 109 ± 42* | 12 ± 2 | 6 ± 3** | 3 ± 1 | 4 ± 1** |
| 20:4n-6 | 2422 ± 290 | 2563 ± 694 | 7156 ± 425 | 7098 ± 859 | 1331 ± 238 | 1283 ± 659 | 359 ± 69 | 423 ± 58 |
| 22:4n-6 | 106 ± 17 | 111 ± 15 | 93 ± 10 | 79 ± 12* | 49 ± 6 | 25 ± 11*** | 24 ± 2 | 26 ± 3 |
| 22:5n-6 | 121 ± 24 | 45 ± 11*** | 190 ± 42 | 58 ± 23*** | 23 ± 5 | 5 ± 2*** | 20 ± 5 | 8 ± 2*** |
| 18:3n-3 | 16 ± 3 | 23 ± 3** | 14 ± 2 | 27 ± 6*** | 2 ± 0.2 | 3 ± 1 | 1 ± 0.2 | 1 ± 0.3* |
| 20:3n-3 | 105 ± 43 | 51 ± 22* | 373 ± 161 | 88 ± 30*** | 101 ± 46 | 27 ± 15** | 10 ± 4 | 5 ± 1** |
| 20:5n-3 | 49 ± 14 | 20 ± 2*** | 139 ± 45 | 33 ± 10*** | 7 ± 1 | 2 ± 0*** | 6 ± 2 | 3 ± 1*** |
| 22:5n-3 | 251 ± 20 | 288 ± 41 | 304 ± 35 | 310 ± 38 | 74 ± 20 | 61 ± 28 | 21 ± 3 | 25 ± 9 |
| 22:6n-3 | 1011 ± 88 | 1225 ± 450 | 1293 ± 114 | 1375 ± 226 | 75 ± 18 | 71 ± 34 | 134 ± 26 | 156 ± 32 |
| Total SFAs | 4074 ± 615 | 3905 ± 1835 | 12236 ± 1197 | 10685 ± 1230* | 2047 ± 358 | 1725 ± 849 | 683 ± 129 | 705 ± 111 |
| Total MUFAs | 1090 ± 203 | 862 ± 95* | 2191 ± 254 | 1433 ± 295*** | 192 ± 98 | 114 ± 54 | 79 ± 14 | 69 ± 12 |
| Total n-6 PUFAs | 4538 ± 660 | 4884 ± 954 | 10623 ± 755 | 9931 ± 918 | 1631 ± 245 | 1590 ± 779 | 495 ± 74 | 562 ± 74 |
| Total n-3 PUFAs | 1381 ± 119 | 1587 ± 495 | 1984 ± 234 | 1799 ± 214 | 251 ± 68 | 161 ± 73* | 165 ± 30 | 187 ± 36 |
| Total fatty acids | 11115 ± 1553 | 11555 ± 2778 | 27155 ± 2348 | 23876 ± 1851* | 4082 ± 648 | 3581 ± 1729 | 1418 ± 212 | 1517 ± 215 |

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| | EtnGpl | | ChoGpl | | PtdIns | | PtdSer | |
|---|---|---|---|---|---|---|---|---|
| | **Control** | **HIV** | **Control** | **HIV** | **Control** | **HIV** | **Control** | **HIV** |
| Ratio of n-6/n-3 | 3 ± 0.3 | 3 ± 0.4 | 5 ± 0.4 | 6 ± 0.7 | 6.8 ± 1.4 | 10 ± 2** | 3 ± 0.4 | 3 ± 0.3 |
| Ratio of AA/DHA | 2 ± 0.3 | 2 ± 0.3 | 6 ± 0.2 | 5 ± 0.4 | 18.1 ± 2.4 | 18 ± 2 | 3 ± 0.4 | 3 ± 0.3 |

Values are mean ± SD of n=7 per group.

SFAs, saturated fatty acids; MUFAs, monounsaturated fatty acids; PUFAs, polyunsaturated Fatty acids.

* P<0.05,

** P<0.01,

*** P<0.001 by unpaired t-test.

**Table 4-A**

Fatty acid concentrations (nmol/g) in heart total lipids, phospholipids, cholesteryl esters, triglycerides and unesterified fatty acid compartment of control and HIV-1 Tg rats

| | Total lipids | | Phospholipids | | Cholesteryl esters | | Triglycerides | | Unesterified fatty acids | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | HIV-1 Tg | Control | HIV-1 Tg | Control | HIV-1 Tg | Control | HIV-1 Tg | Control | HIV-1 Tg |
| 14:0 | 313 ± 114 | 272 ± 155 | 87 ± 11 | 51 ±9** | 3 ± 1 | 8 ± 4* | 156 ± 89 | 154 ± 119 | 9 ± 2 | 8 ± 1 |
| 16:0 | 11815 ± 1515 | 11291 ± 1869 | 7665 ± 353 | 6879 ±476** | 64 ± 8 | 60 ± 27 | 3897 ± 1429 | 4000 ± 1460 | 182 ± 50 | 153 ± 47 |
| 18:0 | 13137 ± 620 | 13003 ± 453 | 12021 ± 437 | 11983 ±731 | 47 ± 5 | 52 ± 10 | 700 ± 195 | 750 ± 258 | 85 ± 13 | 88 ± 18 |
| 16:1n-7 | 736 ± 306 | 452 ± 238 | 251 ± 25 | 157 ±118 | 5 ± 2 | 4 ± 3 | 411 ± 282 | 314 ± 212 | 9 ± 3 | 5 ± 1* |
| 18:1n-9 | 4791 ± 1052 | 4863 ± 1580 | 1651 ± 397 | 1247 ±151* | 15 ± 5 | 14 ± 6 | 2729 ± 975 | 2915 ± 1107 | 45 ± 22 | 34 ± 16 |
| 18:1n-7 | 3602 ± 347 | 3293 ± 372 | 2323 ± 282 | 2116 ±115 | 6 ± 2 | 7 ± 3 | 721 ± 242 | 752 ± 299 | 17 ± 8 | 13 ± 8 |
| 20:1n-9 | 67 ± 11 | 69 ± 21 | 30 ± 2 | 30 ±4 | | | 35 ± 11 | 38 ± 16 | 1.7 ± 0.8 | 1.0 ± 0.4 |
| 18:2n-6 | 17970 ± 2224 | 15874 ± 2607 | 11853 ± 604 | 9029 ±558*** | 40 ± 11 | 43 ± 7 | 4738 ± 1469 | 5521 ± 1823 | 69 ± 37 | 68 ± 29 |
| 18:3n-6 | | | 19 ± 3 | 12 ±2*** | 1.9 ± 0.3 | 2.8 ± 1.1 | 26 ± 7 | 28 ± 9 | 2 ± 0.4 | 4 ± 3 |
| 20:2n-6 | 146 ± 16 | 187 ± 27** | 95 ± 6 | 121 ±13*** | | | 39 ± 13 | 53 ± 17 | 1.4 ± 0.8 | 4 ± 4 |
| 20:4n-6 | 10457 ± 502 | 11827 ± 351*** | 9294 ± 269 | 10640 ±595*** | 78 ± 27 | 94 ± 21 | 247 ± 67 | 346 ± 61* | 16 ± 3 | 19 ± 2* |
| 22:4n-6 | 756 ± 94 | 824 ± 75 | 570 ± 24 | 618 ±57 | 7 ± 1 | 8 ± 1 | 75 ± 20 | 114 ± 19** | 24 ± 3 | 49 ± 49 |
| 22:5n-6 | 514 ± 22 | 411 ± 44*** | 457 ± 14 | 367 ±45*** | | | 17 ± 4 | 20 ± 4 | | |
| 18:3n-3 | 340 ± 89 | 365 ± 123 | 84 ± 5 | 80 ±10 | 0.8 ± 0.2 | 1.5 ± 0.8 | 216 ± 79 | 238 ± 88 | 5 ± 3 | 5 ± 2 |
| 20:3n-3 | 191 ± 22 | 177 ± 23 | 148 ± 13 | 128 ±11* | | | 31 ± 10 | 41 ± 11 | 1.1 ± 0.5 | 1.1 ± 0.7 |
| 20:5n-3 | 45 ± 6 | 42 ± 10 | 36 ± 5 | 32 ±6 | | | 12 ± 3 | 15 ± 1 | 0.5 ± 0.1 | 1.1 ± 0.7 |
| 22:5n-3 | 1247 ± 91 | 1876 ± 133*** | 1057 ± 67 | 1555 ±113*** | | | 61 ± 14 | 138 ± 29*** | 2 ± 1 | 2 ± 1 |
| 22:6n-3 | 3668 ± 438 | 3669 ± 456 | 3185 ± 361 | 3211 ±508 | 2 ± 1 | 3 ± 2 | 52 ± 12 | 86 ± 17*** | 2 ± 1 | 2 ± 1 |
| Total SFAs | 25387 ± 1985 | 24686 ± 2203 | 19822 ± 665 | 18975 ±1090 | 115 ± 11 | 119 ± 34 | 4761 ± 1710 | 4917 ± 1834 | 284 ± 64 | 262 ± 69 |
| Total MUFAs | 9206 ± 1614 | 8678 ± 2162 | 4265 ± 263 | 3565 ±275*** | 26 ± 6 | 24 ± 4 | 3901 ± 1419 | 4023 ± 1549 | 73 ± 33 | 54 ± 24 |
| Total n-6 PUFAs | 29843 ± 2477 | 29123 ± 2593 | 22289 ± 672 | 20788 ±994** | 126 ± 38 | 146 ± 20 | 5139 ± 1577 | 6081 ± 1914 | 112 ± 41 | 143 ± 83 |
| Total n-3 PUFAs | 5446 ± 466 | 6087 ± 515* | 4475 ± 404 | 4974 ±603 | 4 ± 1 | 5 ± 2 | 361 ± 111 | 504 ± 127* | 9 ± 5 | 10 ± 4 |
| Total fatty acids | 69927 ± 5979 | 68591 ± 6983 | 50886 ± 1587 | 48334 ±2637* | 279 ± 46 | 300 ± 35 | 14180 ± 4768 | 15522 ± 5386 | 492 ± 150 | 483 ± 185 |
| Ratio of n-6/n-3 | 5.5 ± 0.6 | 4.8 ± 0.5* | 5.0 ± 0.5 | 4.2 ±0.4** | 33.7 ± 3.9 | 35.0 ± 11.2 | 14.3 ± 0.9 | 12.0 ± 1.8* | 14.3 ± 3.9 | 14.2 ± 2.1 |

| | Total lipids | | Phospholipids | | Cholesteryl esters | | Triglycerides | | Unesterified fatty acids | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | HIV-1 Tg | Control | HIV-1 Tg | Control | HIV-1 Tg | Control | HIV-1 Tg | Control | HIV-1 Tg |
| Ratio of AA to DHA | 2.9 ± 0.3 | 3.3 ± 0.4 | 2.9 ± 0.3 | 3.4 ±0.4 | 32.4 ± 7.1 | 31.3 ± 8.7 | 4.8 ± 0.7 | 4.1 ± 0.8 | 9.7 ± 3.9 | 10.6 ± 2.7 |

Values are mean ± SD of n=7 per group.

SFAs, saturated fatty acids; MUFAs, monounsaturated fatty acids; PUFAs, polyunsaturated fattyacids; ND, not detected. P<0.05,

** P< 0.01,

*** P<0.001 by unpaired t-test.



*Prostaglandins Leukot Essent Fatty Acids*. Author manuscript; available in PMC 2013 October 01.

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**Table 4-B**

Fatty acid concentrations (nmol/g) in heart glycerophospholipids of control and HIV-1 Tg rats

| | EtnGpl | | ChoGpl | | PtdIns | | PtdSer | |
|---|---|---|---|---|---|---|---|---|
| | **Control** | **HIV** | **Control** | **HIV** | **Control** | **HIV** | **Control** | **HIV** |
| 14:0 | | | 37 ± 8 | 20 ± 6*** | | | | |
| 16:0 | 1768 ± 95 | 1666 ± 129 | 5342 ± 324 | 4868 ± 263* | 126 ± 30 | 135 ± 31 | 63 ± 13 | 56 ± 9 |
| 18:0 | 4371 ± 275 | 3593 ± 212*** | 5128 ± 196 | 5881 ± 309*** | 728 ± 58 | 701 ± 58 | 623 ± 54 | 593 ± 33 |
| 16:1n-7 | 59 ± 11 | 36 ± 6*** | 83 ± 16 | 28 ± 5*** | | | | |
| 18:1n-9 | 443 ± 22 | 379 ± 34** | 572 ± 47 | 407 ± 45*** | 41 ± 8 | 41 ± 6 | 42 ± 7 | 40 ± 6 |
| 18:1n-7 | 813 ± 53 | 733 ± 50* | 1088 ± 125 | 835 ± 56*** | 23 ± 4 | 23 ± 3 | 17 ± 3 | 17 ± 4 |
| 18:2n-6 | 7176 ± 450 | 6199 ± 547** | 3119 ± 417 | 1481 ± 190*** | 134 ± 20 | 137 ± 20 | 47 ± 13 | 52 ± 26 |
| 20:4n-6 AA | 2878 ± 233 | 2535 ± 197* | 3896 ± 141 | 5239 ± 462*** | 312 ± 36 | 286 ± 51 | 77 ± 12 | 87 ± 11 |
| 22:4n-6 | 218 ± 26 | 223 ± 10 | 109 ± 9 | 131 ± 20* | 23 ± 7 | 25 ± 2 | 44 ± 5 | 46 ± 4 |
| 22:5n-6 | 211 ± 19 | 156 ± 12*** | 40 ± 4 | 35 ± 6 | | | 16 ± 3 | 13 ± 1* |
| 18:3n-3 | 38 ± 3 | 37 ± 6 | 15 ± 1 | 14 ± 2 | | | | |
| 22:5n-3 | 378 ± 24 | 517 ± 35*** | 213 ± 11 | 354 ± 51*** | 5 ± 1 | 9 ± 1*** | 17 ± 3 | 23 ± 5* |
| 22:6n-3 DHA | 1617 ± 98 | 1555 ± 203 | 304 ± 40 | 368 ± 95 | 7 ± 2 | 7 ± 2 | 79 ± 13 | 78 ± 11 |
| Total SFAs | 6138 ± 363 | 5259 ± 332** | 10508 ± 327 | 10769 ± 348 | 857 ± 76 | 837 ± 65 | 690 ± 65 | 652 ± 39 |
| Total MUFAs | 1316 ± 70 | 1147 ± 76** | 1743 ± 174 | 1270 ± 100*** | 121 ± 19 | 133 ± 20 | 125 ± 25 | 123 ± 22 |
| Total n-6 PUFAs | 10518 ± 695 | 9154 ± 738** | 7189 ± 363 | 6920 ± 508 | 465 ± 60 | 441 ± 79 | 183 ± 23 | 198 ± 38 |
| Total n-3 PUFAs | 2080 ± 104 | 2158 ± 216 | 564 ± 45 | 757 ± 145** | 17 ± 6 | 19 ± 4 | 102 ± 17 | 105 ± 13 |
| Total fatty acids | 20053 ± 1016 | 17718 ± 1002*** | 20005 ± 697 | 19715 ± 900 | 1462 ± 140 | 1422 ± 133 | 1100 ± 115 | 1077 ± 101 |
| Ratio of n-6/n-3 | 5.1 ± 0.4 | 4.3 ± 0.5** | 12.8 ± 1.4 | 9.4 ± 1.6** | 32.7± 11.9 | 26.6± 5.4 | 1.8 ± 0.2 | 1.9 ± 0.3 |
| Ratio of AA/DHA | 1.8 ± 0.2 | 1.7 ± 0.3 | 13.0 ± 1.6 | 14.9 ± 3.3 | 46.4± 6.9 | 46.8± 9.6 | 1.0 ± 0.1 | 1.1 ± 0.2 |

Values are mean ± SD of n=7 per group.

SFAs, saturated fatty acids; MUFAs, monounsaturated fatty acids; PUFAs, polyunsaturated fattyacids; ND, not detected. P<0.05,

** P< 0.01,

*** P<0.001 by unpaired t-test.

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**Table 5-A**

Fatty acid concentrations (nmol/g) in brain total lipids, phospholipids, cholesteryl esters, triglycerides and unesterified fatty acid compartment of control and HIV-1 Tg rats

| | Total lipids | | Total phospholipids | | Cholesteryl ester | | Triglyceride | | Unesterified fatty acid | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | HIV | Control | HIV | Control | HIV | Control | HIV | Control | HIV |
| 14:0 | | | 151 ± 8 | 295 ± 396 | 15.4± 11.7 | 9.8 ± 7.8 | 9.8 ± 4.7 | 11.7 ± 3.8 | 2.3 ± 1.5 | 1.5 ± 1.5 |
| 16:0 | 24384 ± 901 | 24616± 916 | 23445 ± 1004 | 23538 ± 1238 | 45.1± 21.3 | 39.3 ± 16.9 | 201.9 ± 40.1 | 218.1 ± 34.5 | 35.4 ± 7.6 | 45.9 ± 35.4 |
| 18:0 | 27097 ± 1116 | 27163± 870 | 24815 ± 1052 | 24575 ± 998 | 25.9± 8.1 | 27.2 ± 10.2 | 93.8 ± 13.3 | 101.6 ± 10.5 | 36.0 ± 14.3 | 58.1 ± 72.9 |
| 20:0 | 584 ± 78 | 651± 115 | 534 ± 86 | 609 ± 86 | 6.6± 8.0 | 2.3 ± 1.7 | | | 1.0 ± 0.4 | 1.1 ± 0.7 |
| 22:0 | 510 ± 69 | 593± 85 | 484 ± 72 | 554 ± 38 | | | 5.1 ± 1.5 | 5.8 ± 2.0 | | |
| 24:0 | 568 ± 70 | 633± 88 | 506 ± 79 | 540 ± 64 | | | | | | |
| 16:1n-7 | 577 ± 56 | 564± 30 | 541 ± 47 | 613 ± 236 | 8.2± 5.7 | 6.4 ± 4.3 | 11.7 ± 4.2 | 9.9 ± 3.3 | | |
| 18:1n-9 | 23564 ± 1464 | 24359± 1559 | 21758 ± 1227 | 22014 ± 1430 | 11.2± 3.9 | 8.1 ± 1.6 | 82.6 ± 22.6 | 101.0 ± 23.0 | 7.4 ± 2.0 | 6.9 ± 1.2 |
| 18:1n-7 | 6501 ± 815 | 6812± 760 | 5528 ± 572 | 5651 ± 555 | 5.7± 3.8 | 6.1 ± 2.5 | 43.8 ± 9.5 | 49.8 ± 8.4 | 2.9 ± 1.0 | 2.6 ± 0.6 |
| 20:1n-9 | 2703 ± 430 | 3155± 561 | 850 ± 129 | 966 ± 154 | | | 5.5 ± 0.6 | 5.8 ± 0.7 | 0.3 ± 0.003 | 0.4 ± 0.1 |
| 22:1n-9 | | | | | 17.5± 4.6 | 19.9 ± 4.9 | 17.1 ± 4.3 | 19.2 ± 3.6 | 8.7 ± 3.2 | 9.3 ± 2.3 |
| 24:1n-9 | 3804 ± 157 | 3694± 190 | | | | | | | | |
| 18:2n-6 | 943 ± 87 | 1261± 137*** | 778 ± 75 | 989 ± 131** | 7.8± 3.9 | 4.9 ± 1.8 | 58.4 ± 33.7 | 109.2 ± 30.2* | 1.3 ± 0.5 | 1.8 ± 0.5 |
| 18:3n-6 | | | | | 4.7± 4.6 | 2.5 ± 1.8 | 3.8 ± 0.7 | 4.2 ± 0.6 | | |
| 20:2n-6 | 189 ± 17 | 231± 29** | 164 ± 12 | 195 ± 21** | | | 1.7 ± 0.6 | 2.4 ± 0.5* | | |
| 20:3n-6 | | | | | 7.3± 5.3 | 6.2 ± 0.9 | | | 3.7 ± 1.6 | 6.5 ± 0.6** |
| 20:4n-6 | 12148 ± 383 | 12090± 571 | 10830 ± 513 | 10637 ± 518 | 11.2± 5.8 | 8.3 ± 4.6 | 27.2 ± 3.1 | 28.7 ± 3.3 | 3.0 ± 1.2 | 2.4 ± 0.5 |
| 22:4n-6 | 1484 ± 196 | 1734± 256 | 4322 ± 291 | 4326 ± 214 | 29.7± 30.0 | 15.7 ± 10.7 | 24.4 ± 15.1 | 19.2 ± 7.5 | 18.5 ± 14.7 | 13.4 ± 11.1 |
| 22:5n-6 | 497 ± 21 | 476± 28 | 428 ± 30 | 393 ± 24 | | | 1.8 ± 0.4 | 1.5 ± 0.2 | | |
| 18:3n-3 | 23 ± 6 | 29± 3 | 2425 ± 364 | 2792 ± 486 | | | 3.1 ± 2.0 | 4.7 ± 1.3 | 0.7 ± 0.1 | 0.7 ± 0.1 |
| 20:3n-3 | 330 ± 26 | 325± 16 | 284 ± 16 | 309 ± 94 | | | 1.8 ± 0.5 | 1.8 ± 0.3 | | |
| 20:5n-3 | 35 ± 12 | 42± 15 | 25 ± 5 | 28 ± 5 | | | | | | |
| 22:5n-3 | 258 ± 20 | 325± 16*** | 217 ± 16 | 259 ± 15*** | | | 1.1 ± 0.3 | 1.8 ± 0.4* | | |
| 22:6n-3 | 12966 ± 274 | 13116± 660 | 11264 ± 516 | 11122 ± 615 | 1.3± 0.9 | 1.1 ± 0.5 | 30.7 ± 4.6 | 28.5 ± 3.7 | 2.4 ± 0.7 | 1.9 ± 0.5 |
| Total SFAs | 53142 ± 2032 | 53629± 1637 | 49871 ± 2117 | 50086 ± 1632 | 91.9± 39.6 | 78.2 ± 33.3 | 309.8 ± 53.1 | 337.3 ± 45.5 | 74.5 ± 20.5 | 106.1 ± 107.8 |
| Total MUFAs | 33346 ± 2509 | 34890± 2170 | 28677 ± 1819 | 29245 ± 1789 | 26.3± 10.3 | 20.0 ± 4.8 | 142.8 ± 36.4 | 166.6 ± 34.7 | 10.4 ± 2.8 | 9.7 ± 0.9 |

| | Total lipids | | Total phospholipids | | Cholesteryl ester | | Triglyceride | | Unesterified fatty acid | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Control** | **HIV** | **Control** | **HIV** | **Control** | **HIV** | **Control** | **HIV** | **Control** | **HIV** |
| Total n-6 PUFAs | 15261 ± 524 | 15791± 489 | 16521 ± 757 | 16540 ± 685 | 53.4± 40.7 | 31.1 ± 17.3 | 112.7 ± 45.8 | 165.1 ± 36.8* | 22.7 ± 15.2 | 17.1 ± 10.8 |
| Total n-3 PUFAs | 13561 ± 279 | 13778± 657 | 14189 ± 541 | 14481 ± 502 | 2.9± 2.3 | 1.1 ± 0.5 | 35.6 ± 7.5 | 36.7 ± 4.8 | 2.8 ± 0.7 | 2.4 ± 0.5 |
| Total fatty acids | 119145 ± 5107 | 121819± 3894 | 109531 ± 4912 | 110521 ± 3879 | 200.9± 92.7 | 156.6 ± 51.4 | 615.5 ± 141.6 | 724.8 ± 120.3 | 122.4 ± 31.1 | 150.2 ± 104.6 |
| Ratio of n-6/n-3 | 1.1 ± 0.03 | 1.1± 0.04 | 1.2 ± 0.01 | 1.1 ± 0.04 | 20.1± 6.2 | 27.6 ± 4.3* | 3.1 ± 0.9 | 4.5 ± 0.9* | 8.3 ± 5.6 | 7.1 ± 4.2 |
| Ratio of AA/DHA | 0.9 ± 0.02 | 0.9± 0.03 | 1.0 ± 0.02 | 1.0 ± 0.03 | 10.4± 5.9 | 7.3 ± 2.6 | 0.9 ± 0.2 | 1.0 ± 0.2 | 1.2 ± 0.2 | 1.3 ± 0.3 |

Values are mean ± SD of n=7 per group.

SFAs, saturated fatty acids; MUFAs, monounsaturated fatty acids; PUFAs, polyunsaturated fatty acids; ND, not detected. P<0.05,

** P< 0.01,

*** P<0.001 by unpaired t-test.

**Table 5-B**

Fatty acid concentrations (nmol/g) in brain glycerophospholipids of control and HIV-1 Tg rats

| | EtnGpl | | ChoGpl | | PtdIns | | PtdSer | |
|---|---|---|---|---|---|---|---|---|
| | **Control** | **HIV** | **Control** | **HIV** | **Control** | **HIV** | **Control** | **HIV** |
| 14:0 | | | 79 ± 25 | 72 ± 2 | | | 15 ± 12 | 11 ± 7 |
| 16:0 | 2147 ± 533 | 2551 ± 106 | 18365 ± 715 | 18615 ± 812 | 513 ± 56 | 541 ± 42 | 439 ± 53 | 477 ± 58 |
| 18:0 | 6786 ± 319 | 6788 ± 310 | 6161 ± 271 | 6176 ± 175 | 1611 ± 124 | 1653 ± 64 | 6074 ± 399 | 6161 ± 403 |
| 20:0 | 62 ± 12 | 70 ± 13 | | | 12 ± 2 | 14 ± 1* | 71 ± 18 | 69 ± 11 |
| 22:0 | | | | | 15 ± 4 | 15 ± 4 | 100 ± 16 | 102 ± 12 |
| 24:0 | | | | | 11 ± 2 | 19 ± 5* | 43 ± 7 | 42 ± 8 |
| 16:1n-7 | 174 ± 10 | 174 ± 14 | 221 ± 21 | 213 ± 9 | 11 ± 3 | 10 ± 1 | 22 ± 17 | 14 ± 2 |
| 18:1n-9 | 6652 ± 612 | 6936 ± 696 | 8869 ± 414 | 8888 ± 337 | 628 ± 76 | 643 ± 51 | 2843 ± 227 | 2915 ± 281 |
| 18:1n-7 | 1743 ± 245 | 1946 ± 220 | 3609 ± 175 | 3768 ± 154 | 548 ± 792 | 230 ± 31 | 517 ± 148 | 542 ± 79 |
| 20:1n-9 | 342 ± 86 | 407 ± 97 | 284 ± 33 | 348 ± 100 | 28 ± 5 | 26 ± 10 | 77 ± 25 | 95 ± 25 |
| 22:1n-9 | | | | | 51 ± 15 | 40 ± 25 | 108 ± 14 | 133 ± 19* |
| 24:1n-9 | | | | | | | 35 ± 1 | 36 ± 7 |
| 18:2n-6 | 286 ± 26 | 340 ± 40* | 334 ± 31 | 468 ± 68*** | 35 ± 3 | 49 ± 7** | 34 ± 11 | 44 ± 7 |
| 18:3n-6 | 29 ± 7 | 31 ± 8 | | | | | 22 ± 9 | 19 ± 4 |
| 20:2n-6 | 53 ± 5 | 64 ± 17 | | | | | 21 ± 11 | 20 ± 6 |
| 20:4n-6 | 4881 ± 268 | 4856 ± 224 | 2314 ± 157 | 2230 ± 209 | 1353 ± 90 | 1385 ± 68 | 498 ± 41 | 496 ± 39 |
| 22:4n-6 | 1912 ± 139 | 1857 ± 93 | 316 ± 22 | 308 ± 11 | 56 ± 8 | 58 ± 3 | 472 ± 42 | 452 ± 24 |
| 22:5n-6 | 161 ± 16 | 157 ± 19 | | | | | 109 ± 14 | 104 ± 11 |
| 18:3n-3 | 1260 ± 225 | 1476 ± 269 | 479 ± 64 | 539 ± 73 | 82 ± 17 | 88 ± 17 | 353 ± 70 | 416 ± 93 |
| 20:3n-3 | 132 ± 13 | 129 ± 13 | 101 ± 12 | 100 ± 17 | 11 ± 6 | 12 ± 2 | 40 ± 6 | 39 ± 4 |
| 20:5n-3 | | | | | | | 42 ± 12 | 43 ± 8 |
| 22:5n-3 | 64 ± 21 | 82 ± 24 | | | | | 23 ± 7 | 30 ± 4 |
| 22:6n-3 | 5628 ± 252 | 5632 ± 255 | 1389 ± 32 | 1373 ± 61 | 120 ± 17 | 111 ± 17 | 2399 ± 166 | 2370 ± 191 |
| Total SFAs | 8996 ± 627 | 9411 ± 400 | 24605 ± 891 | 24863 ± 931 | 2159 ± 182 | 2234 ± 98 | 6740 ± 428 | 6860 ± 450 |
| Total MUFAs | 8911 ± 918 | 9464 ± 931 | 13039 ± 596 | 13285 ± 478 | 1213 ± 786 | 905 ± 89 | 3459 ± 386 | 3564 ± 305 |
| Total n-6 PUFAs | 7313 ± 404 | 7295 ± 304 | 2964 ± 184 | 3006 ± 230 | 1444 ± 97 | 1492 ± 68 | 1153 ± 91 | 1129 ± 72 |
| Total n-3 PUFAs | 7084 ± 371 | 7307 ± 305 | 1971 ± 81 | 2011 ± 107 | 213 ± 28 | 207 ± 37 | 2816 ± 171 | 2847 ± 166 |

| | EtnGpl | | ChoGpl | | PtdIns | | PtdSer | |
|---|---|---|---|---|---|---|---|---|
| | **Control** | **HIV** | **Control** | **HIV** | **Control** | **HIV** | **Control** | **HIV** |
| Total fatty acids | 32303 ± 1975 | 33477 ± 1513 | 42606 ± 1514 | 43179 ± 1354 | 5086 ± 843 | 4880 ± 258 | 14343 ± 1013 | 14606 ± 915 |
| Ratio of n-6/n-3 | 1.0 ± 0.02 | 1.0 ± 0.05 | 1.5 ± 0.1 | 1.5 ± 0.2 | 6.8 ± 0.5 | 7.4 ± 1.2 | 0.4 ± 0.03 | 0.4 ± 0.01 |
| Ratio of AA/DHA | 0.9 ± 0.03 | 0.9 ± 0.03 | 1.7 ± 0.1 | 1.6 ± 0.2 | 11.4 ± 1.4 | 12.7 ± 1.9 | 0.2 ± 0.02 | 0.2 ± 0.01 |

Values are mean ± SD of n=7 per group.

SFAs, saturated fatty acids; MUFAs, monounsaturated fatty acids; PUFAs, polyunsaturated fatty acids; ND, not detected. P<0.05,

** P< 0.01,

*** P<0.001 by unpaired t-test.



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