Review

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Application of fatty acid and lipid measurements in neuropsychiatry

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Abstract: The importance of lipids in the understanding of disease states is constantly increasing. Whilst the link between metabolic disorders and lipids seems to be clear, interpreting lipid regulation in the context of neuropsychiatric disorders is a new approach. Mental disorders account for almost 15% of the total global disease burden with Alzheimer’s disease, depression or schizophrenia being amongst the most widespread mental disorders in the general population. For this reason rapid and early diagnosis is crucial and finding the right biomarkers is of great importance. Lipids appear to be essential in learning the aetiopathology of neuropsychiatric diseases as well as in biomarker research as they are most abundantly present in the brain. This study discusses recent findings in neuropsychiatry in the context of lipid analysis.

Keywords: Alzheimer’s disease; attention deficit hyperactivity disorder; depression; lipids; schizophrenia.

Introduction

Lipids play many roles in a properly functioning organism including energy storage, signal transmission, cell membrane building blocks, etc. The main component of cell membranes are lipids called phospholipids with a phosphate group within their structure. Due to their structure, lipids are both hydrophobic (hydrocarbon chains) and hydrophilic (polar functional groups).

In aqueous environments, such as cells, phospholipids turn their polar heads to water molecules, whereas the hydrophobic tails cluster together, creating a lipid bilayer. The lipid bilayer is fluid and within the structure there are embedded proteins which can change their position [1]. Fluidity of the cell membrane can be influenced by, e.g. lipid composition [2, 3], temperature [4, 5] and the type of fatty acids within the phospholipid [6, 7]. Fatty acid chains interact with each other and that interaction is responsible for the membrane’s properties [3]. For instance, fluidity of the cell membrane increases if there are more unsaturated fatty acids in its structure, as they are more bulky as a result of the bend in the carbon chain from the double bond. Similarly, if there are more saturated fatty acids within the cell membrane, it becomes more compact and, therefore, its fluidity decreases. The length of the fatty acid chain also plays a role in the fluidity of the membrane [8]: shorter chains increase fluidity as there are less hydrophobic interactions between the tails.

Lipids and lipid metabolism have been linked to many disorders, both somatic [9–14] and neuropsychiatric [15–21]. McEwen and Stellar [22] proposed that exposure to frequent and chronic environmental stressors may produce insufficient or overreacting responses, resulting in cumulative damage that physiologic systems have endured in the process of adapting to stressors, increasing the risk of disease. Theoretical construction of allostatic load is associated with dysregulation of lipid metabolism and can lead to disease [23]. The biological relationship of mental disorders and the “stress response” involves a series of complex, interactive neurophysiological reactions in the brain, the autonomic nervous system, adrenocortical (HPA) axis, immune system and platelet adhesion [24]. The neurochemical system mediating the stress response becomes more “sensitive” to future stressors related to the original experience [25]. Dysregulated lipid
metabolism may be of particular importance for central nervous system (CNS) injuries and disorders as the CNS has the highest lipid concentration next to adipose tissue [26]. The exact pathophysiological mechanism linking lipids and mental disorders is still debatable. There are several hypotheses explaining the connection between lipids (fatty acids) and neuropsychiatric disorders [3]. These hypotheses include: 1) the fact that docosahexaenoic acid (DHA) is greatly abundant in neuronal cells and therefore its insufficiency may alter the properties of the neuronal cell membranes or even the nerve growth factors; and 2) the relationship and changes in signal transduction caused by phosphatidylinositol turnover and protein kinase C activity. Mirnikjoo and co-authors [27] show in experiments that in vitro eicosapentaenoic acid (EPA) and DHA reduced the activity of cAMP-dependent protein kinase A, protein kinase C (PKC) and mitogen-activated protein kinase (MAPK). Lipid and electrolyte abnormalities have an impact on neuronal disturbance.

Results of the Global Burden of Disease 2010 study [28] show that mental disorders belong to the most important group of health problems. Mental disorders are heterogeneous and diagnosed on the basis of a patient’s symptoms, not laboratory tests. Patients with mental disorders have polymorphisms in genetic factors and often experienced a stressful environmental event during early development which influenced brain functioning. Lipid biomarkers can be detected in various ways including testing body fluid or brain imaging. It would seem that to find biomarkers it is crucial to understand the mechanisms of a given disorder [29]. However, new analytical platforms, -omics techniques, such as proteomics [30–32], metabolomics [33–35] or genomics [36–39] are proving to be extremely helpful in this area as they do not require the knowledge of the disease’s pathoetiology [29, 40].

Neuropsychiatric disorders

Schizophrenia

It is believed that schizophrenia is caused by a prostaglandin deficiency state [41, 42] which leads to hyperactivity of phospholipase A₂. Whilst in such state the amount of arachidonic acid (AA) and EPA decreases to a level below the second-messenger function threshold as the cytosolic form of phospholipase A₂ favours C20 acyl chains [42]. Furthermore, phospholipase A₂ hyperactivity causes depletion of AA and EPA in the membrane cell, which in turn leads to the increased inflammation promoters, lipid peroxidation and free radical production [43]. Interestingly, it seems that schizophrenia patients with higher essential fatty acid concentrations in erythrocytes prior to antipsychotic therapy have a worse response in script tasks but have better results in positive symptoms [44]. Significant changes in lipids (Student’s t-test) were observed in the brain tissues of schizophrenia patients [45]. In grey matter, levels of phosphatidylcholines 38:6, 40:7, 36:4, 34:2, 38:5 and 30:0 were found to be most significantly altered, whereas in white matter phosphatidylcholines 35:1, 34:5, 38:2, ceramides 36:2, 36:1, 34:1 and free fatty acids 17:0 and 18:1 were mostly changed. Changes in phosphatidylcholines 36:1, 32:0 and free fatty acids 16:0, 18:0 were significant in both grey and white matter. However, it is noteworthy that the researchers found that the alterations in lipid composition (fatty acids and ceramides) were specific to the disease and not the drug treatment.

A study of twins, with one of the twins being schizophrenic, showed that the schizophrenic twin had elevated levels of ether lipids (such as phosphatidylethanolamines and phosphatidylcholines), abundant triglycerides as well as long-chain and PUFA (polyunsaturated fatty acids)-containing triglycerides [46]. However, their healthy twins had higher concentrations of PUFA-containing phosphatidylcholines and phosphatidylethanolamines, lysophosphatidylcholines and short-chain saturated fatty acids (SFA) and monounsaturated fatty acids (MUFA)-containing triglycerides. Those results were compared to results from healthy control twins (both twins had no schizophrenia). They had higher concentrations of lyso-phosphatidylcholines (like the healthy twin but even higher) and higher concentrations of abundant triglycerides (like the twin with schizophrenia but lower). The control twins also had elevated levels of sphingomyelins and major phospholipids.

Plasmalogens in plasma and platelets were also investigated in schizophrenia patients [47]. Levels of choline plasmalogens in plasma 34:1, 34:2, 34:3, 36:1, 36:2 and 36:5 are all higher in control groups compared to schizophrenia patients. However, platelets choline plasmalogens 34:2, 34:3 and 40:6 are lower in healthy volunteers compared to schizophrenia patients. The study investigated ethanolamine plasmalogens as well, and it was found plasma ethanolamine plasmalogens 34:2, 38:6, 40:6 and platelet ethanolamine plasmalogens 38:6, 40:6 are higher in controls than in the patient group.

Affective disorders

Biological markers for depression are of great interest to aid elucidating the cause of depression and the underlying
biological basis. Lipid biomarkers are considered for diagnostics and for evaluation of the effectiveness of antidepressant drug [25]. Recent evidence has suggested an important role of lipids in the aetiology and treatment of depression [48, 49]. Modern analytical platforms have also been applied in depression biomarker research [50–53].

The lipid that has been most commonly associated with depression is vitamin D. One of the first papers on the connection between vitamin D and depression was published in 1968 [54]; two cases of depressive patients with vitamin D intoxication are presented. In 1979 a paper presented further correlation between vitamin D and depression – patients with depression-like symptoms (asthenia) had vitamin D deficiencies and were compared to a control group (non-asthenia group) [55]. More recent publications confirm this relationship: lower vitamin D levels are found in patients with depression [56–58]. One of the studies shows that vitamin D supplementation in depressed adolescents increases their wellbeing [56]. McCue et al. reported that if vitamin D threshold was to be set at 30 ng/mL, as some suggest, the percentage of vitamin D deficient patients would increase from 52.3% (20 ng/mL) up to 85% [57].

Recent findings from a randomised trial suggest that high doses of supplemental vitamin D may improve mild depressive symptoms [59]. However, important questions persist concerning such issues as: 1) how does vitamin D affect monoamine function and hypothalamic-pituitary-adrenal axis response to stress; 2) does vitamin D supplementation improve mood in individuals with moderate-to-severe depression; and 3) is vitamin D sufficiency protective against incidents of depression and recurrence.

It has been reported that patients from a unit that predominantly treats patients with mood (unipolar and bipolar) adjustment, personality and substance use disorders within a private psychiatric facility had lower vitamin D levels (43 nmol/L) compared to the control group (65 nmol/L) [60]. Numerous cohort studies (on non-depressed subjects) have assessed the relationship between plasma cholesterol and mood disorders with contradictory results [49, 61–64]. Several possible explanations exist for these mixed findings. First of all, affective disorders are heterogeneous and psychopathology of affective symptoms vary in each patient, e.g. some subjects have a bigger appetite with a following weight gain, whereas other experience loss of appetite and weight. The fact that plasma fatty acids reflect dietary intake of the last few days could influence the results of those studies. Second, people with affective disorders on average have a higher body mass index (BMI) than the general population [63]. Nearly one in five patients with bipolar disorder have metabolic syndrome and from 16% up to 36% have components of it [65]. Lipid dysregulation can be associated with genetics, comorbidity, psychiatric psychopathology, lifestyle, diet, physical activity, alcohol abuse, smoking and pharmacotherapy [64, 66–71].

The results of studies of serum lipid parameters, often used in blood tests, i.e. total cholesterol (TC), triglycerides (TG), high-density (HDL), low-density (LDL) and very-low-density (VLDL) lipoproteins in the context of depression show that all those parameters were lower in the patient group, compared to the control group (TC: 144.97±30.98 mg/dL vs. 196.10±17.61 mg/dL; TG: 127.70±55.25 mg/dL vs. 162.13±48.67; HDL: 36.32±6.84 mg/dL vs. 44.43±7.69 mg/dL; LDL: 83.17±25.45 mg/dL vs. 117.16±19.77; VLDL: 25.47±11.08 mg/dL vs. 32.43±9.76 mg/dL) [72]. Dimopoulos found a correlation between low TC and depression in the elderly patients [73]. Shin in a meta-analysis [74] found that higher TC was associated with lower levels of depression. De Berardis and co. found that TC is low in all clinical groups with bipolar disorder [75]. The majority of the studies show that patients with major depression have low HDL concentration and higher ratios of total cholesterol/high-density lipoprotein cholesterol (TC/HDL) and low-density lipoprotein cholesterol (LDL/HDL) [76, 77]. Maes et al. [76] suggested that lower serum HDL levels are probably induced by immune/inflammatory response in depression. Depression and suicide are associated with low TC and HDL, adiposity and high waist to hip ratio [78–82]. Some studies suggest a relationship between lipid metabolism, serotonin function and poor control of aggressive impulses [78, 79, 83]. Papakostas et al. [84] suggest that low lipid levels are associated with decreased serotonergic function leading to depression and increased risk of suicide. Engelberg [85] hypothesised that decreased cholesterol levels can alter viscosity and functions of serotonin receptors and transporters. Some researchers have reported a positive correlation between total cholesterol levels and the level of cerebrospinal fluid (CSF) 5-Hydroxyindolacetic acid (5-HIAA) in suicide attempters [86, 87]. Jokinen et al. [86] suggested that the level of serum HDL correlates with CSF 5-HIAA levels in suicide attempters compared to healthy volunteers. Vilibić et al. found that higher serum TC is associated with lower presence of depressive symptoms, aggressiveness and suicide attempts in patients with chronic post-traumatic stress disorder (PTSD) [88]. Some studies also suggest that pharmacological treatment of depression results in an increase of serum cholesterol levels, whereas decrease of triglyceride alleviates the symptoms of depression.
A lipidomic study on a Dutch population was performed [89] and two lipids were found to be highly correlated with depressive symptoms (assessed by the Hospital Anxiety and Depression Scales): 1) PC O 36:4 (1-O-hexadecyl-2-arachidonoyl-sn-glycero-3-phosphocholine; an ether phospholipid that contains a bound AA (C20:4, n-3) in the sn-2 position; 2) SPM 23:1 (N-valeroylsphingosylphosphorylcholine; a plasma sphingomyelin species with dihydroxy 18:1 sphingosine as the main base). Table 1 presents lipid species that are significantly correlated with given depression tests. The study also gave mean concentrations of total cholesterol, both high and low density lipoprotein cholesterol, as well as triglycerides: 5.66±1.08, 3.78±0.98, 1.28±0.35 and 1.42±0.86 mmol/L, respectively [89].

Fatty acids were also investigated in relation to affective disorders and affective disorders treatment (in particular, omega-3 fatty acids) [90]. Omega-3 fatty acids appear to cross the blood brain barrier easily and are incorporated into neuronal membranes. Due to their highly folded chemical structure omega-3 FA increase the fluidity of the membranes lipid bilayer, thereby changing transmembrane protein function. It was reported that there is an inverse correlation between serum omega-3 ALA and depression, as well as between serum omega-6 LA and cholesterol omega-6 PUFA and depression [91]. However, no such correlation was found between other omega-3 fatty acids: EPA and DHA. This observation is in agreement with another study that reported no association between serum EPA and DHA levels and depression [92]. The reason for why only ALA levels seem to impact depressive symptoms is the fact that ALA is the precursor of omega-3 fatty acid synthesised in the human body, including EPA and DHA [93].

**Attention deficit hyperactivity disorder (ADHD)**

One of the earliest reports investigating lipids in ADHD shows that the concentrations of most omega-3 and omega-6 fatty acids, both in plasma and in red blood

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**Table 1**: Correlation between plasma phosphophingolipids (independent samples t-test) in patients with depression and anxiety issues (p-values <0.05) [89].

<table>
<thead>
<tr>
<th>Species</th>
<th>HASD-D</th>
<th>HASD-A</th>
<th>CES-D</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ceramides</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CER 20:0</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CER 18:0</td>
<td></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td><strong>Lysophosphatidylycholines</strong></td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>LPC 20:5</td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td><strong>Phosphatidylethanolamino—plasmogens</strong></td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>PLPE 16:0/22:6</td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>PLPE 18:1/18:1</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>PLPE 18:1/18:2</td>
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<td>✓</td>
<td></td>
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<tr>
<td>Total 16:0 PLPE</td>
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<td></td>
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</tr>
<tr>
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<td></td>
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</tr>
<tr>
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<tr>
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<tr>
<td>PE 40:6</td>
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<tr>
<td>PE 40:4</td>
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<td>✓</td>
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<tr>
<td>PE 42:6</td>
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</tr>
<tr>
<td><strong>Phosphatidylcholines</strong></td>
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<td>✓</td>
</tr>
<tr>
<td>PC O 34:3</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PC 34:2</td>
<td></td>
<td>✓</td>
<td></td>
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<tr>
<td>PC O 36:5</td>
<td>✓</td>
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<td></td>
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<tr>
<td>PC O 36:4</td>
<td>✓</td>
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<tr>
<td>PC O 36:3</td>
<td>✓</td>
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<tr>
<td>PC O 38:5</td>
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<tr>
<td>PC O 38:4</td>
<td>✓</td>
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<tr>
<td>PC O 38:1</td>
<td>✓</td>
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<tr>
<td>PC 38:6</td>
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<tr>
<td>PC O 40:6</td>
<td>✓</td>
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<tr>
<td>PC O 40:4</td>
<td>✓</td>
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<td></td>
</tr>
<tr>
<td>Ether PC</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Sphingomyelins</strong></td>
<td></td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>SPM 16:1-OH</td>
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<td>✓</td>
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<tr>
<td>SPM 22:2</td>
<td>✓</td>
<td></td>
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<tr>
<td>SPM 23:1</td>
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</table>
cells, in the patient group are significantly lower than in the control group [94]. In plasma, the levels of some of the omega-6 fatty acids were higher for the ADHD group (vaccenic acid, γ-linolenic acid, linoleic acid). Interestingly, the total concentration of omega-6 acid in plasma is comparable in both patient and control group (37.62±2.57, 37.88±1.82 [area %], respectively). Furthermore, omega-6 to omega-3 ratio, both in plasma and red blood cells, is increased in ADHD patients (Table 2). This can be interpreted as an indirect proof that high omega-6/omega-3 ratios are deleterious.

A study based in Italy showed that supplementing ADHD children with fish oil (rich in omega-3 fatty acids) is beneficial for their condition [95]. Both inattention and hyperactivity scores decreased after fish oil supplementation (13.90±2.01 and 15.50±4.41, respectively) compared to the scores before supplementation (19.00±4.20 and 20.00±4.18, respectively). The total concentration of omega-6 fatty acids decreased (before supplementation: 31.26±1.76; after supplementation: 29.53±2.68) and the total concentration of omega-3 fatty acids increased (before supplementation: 5.38±0.53; after supplementation: 7.24±0.88). Selected data from that study is presented in Table 3.

This finding is supported by a study where ADHD children were divided into two groups: one group was supplemented with active omega-3 fatty acids and the second was supplemented with sunflower oil (omega-6 fatty acids) and was counted as the placebo group [96]. It was shown that in the omega-3 group both inattention and hyperactivity decreased by 9.1% and 8.8% relative to the baseline values, respectively. Those factors also decrease in the placebo group, by 7.2% and 2.6% relative to baseline values, respectively. In their report, Sumich et al. [97] suggest that in patients with ADHD, adrenic acid (an omega-6 fatty acid) is correlated with neuroticism, agreeableness and conscientiousness, whereas oleic acid (omega-9 fatty acid) is correlated with extraversion and openness.

### Table 2: Fatty acid composition of plasma and red blood cells in patients with ADHD and control group [94].

<table>
<thead>
<tr>
<th></th>
<th>Plasma</th>
<th>Red blood cells</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Omega-3</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EPA</td>
<td>Decreased ↓</td>
<td>No data</td>
</tr>
<tr>
<td>DHA</td>
<td>Decreased ↓</td>
<td>Decreased ↓</td>
</tr>
<tr>
<td>ALA</td>
<td>Decreased ↓</td>
<td>No data</td>
</tr>
<tr>
<td>Total</td>
<td>Decreased ↓</td>
<td>Decreased ↓</td>
</tr>
<tr>
<td><strong>Omega-6</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AA</td>
<td>Decreased ↓</td>
<td>Decreased ↓</td>
</tr>
<tr>
<td>GLA</td>
<td>Increased ↑</td>
<td>No data</td>
</tr>
<tr>
<td>LA</td>
<td>Increased ↑</td>
<td>Decreased ↓</td>
</tr>
<tr>
<td>Total</td>
<td>Decreased ↓</td>
<td>Decreased ↓</td>
</tr>
<tr>
<td>OA</td>
<td>Increased ↑</td>
<td>Decreased ↓</td>
</tr>
<tr>
<td><strong>ω-6/ω-3 ratio</strong></td>
<td>Increased ↑</td>
<td>Increased ↑</td>
</tr>
</tbody>
</table>

Increased ↑, levels are higher in ADHD patients as compared to the control group; Decreased ↓, levels are lower in ADHD patients as compared to the control group.

### Table 3: Fatty acid composition of red blood cells in patients with ADHD before and after supplementation with omega-3 fatty acids.

<table>
<thead>
<tr>
<th></th>
<th>(Germano et al., 2007) [95]</th>
<th>(Bélanger and Vanasse, 2009) [96]</th>
</tr>
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<tbody>
<tr>
<td><strong>Omega-3</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EPA</td>
<td>Increased ↑</td>
<td>Decreased ↓</td>
</tr>
<tr>
<td>DHA</td>
<td>Increased ↑</td>
<td>Decreased ↓</td>
</tr>
<tr>
<td>ALA</td>
<td>Increased ↑</td>
<td>Decreased ↑</td>
</tr>
<tr>
<td>Total</td>
<td>Increased ↑</td>
<td>Decreased ↓</td>
</tr>
<tr>
<td><strong>Omega-6</strong></td>
<td></td>
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</tr>
<tr>
<td>AA</td>
<td>Decreased ↓</td>
<td>Increased ↑</td>
</tr>
<tr>
<td>LA</td>
<td>Decreased ↓</td>
<td>Increased ↑</td>
</tr>
<tr>
<td>GLA</td>
<td>No data</td>
<td>Increased ↑</td>
</tr>
<tr>
<td>Total</td>
<td>Decreased ↓</td>
<td>Increased ↑</td>
</tr>
<tr>
<td>OA</td>
<td>Increased ↑</td>
<td>Decreased ↓</td>
</tr>
<tr>
<td><strong>ω-6/ω-3 ratio</strong></td>
<td>Decreased ↓</td>
<td>Increased ↑</td>
</tr>
</tbody>
</table>

Increased ↑, higher levels after supplementation, as compared to baseline, before supplementation/placebo group; Decreased ↓, lower levels after supplementation, as compared to baseline, before supplementation/placebo group [95, 96].

Dementia

Atherosclerosis (a risk factor for ischemic stroke) results from accumulation of LDL-derived lipids in the arterial wall. Pro-inflammatory cytokins (TNF-α, IL-1), secretory phospholipase A2 IIA and lipoprotein-PLA2 are implicated in vascular inflammation. TNF-α and IL-1 alter lipid metabolism and stimulate production of eicosanoids, ceramide and reactive oxygen species leading to potential CNS injures and certain neurological disorders [26].

As with most neuropsychiatric disorders, the pathoetioloogy of Alzheimer’s disease (AD) is unclear. However, modern scientific approaches help in gathering as much information on the disorder as possible. Those methods are mainly proteomics methods [98–102] but also include metabolomics [103–106] and transcriptomics [107]. The ideal biomarker for AD should detect a fundamental feature of neuropathology and be validated in neuropathologically confirmed cases. It should have diagnostic sensitivity >80% for detecting AD and specificity of >80% percent for distinguishing from other dementias; it should be reliable, reproducible, non-invasive, simple to perform, and inexpensive [108]. It would be especially useful if the biomarker could also capture the beneficial effect of disease modifying therapy.
The correlation between AD occurrence and lipids lies with the protein apolipoproteinE (APOE) which is a lipid transporting protein [109]. Lipids that are transported by APOE are, among others, cholesterol and phospholipids. The latter are the building blocks of cell membranes and cholesterol plays a vital role in proper lipid raft functioning. Lipid rafts are responsible for signalling molecules on the cell surface [109]. Interestingly, the production of β-amyloid takes place on those lipid rafts and a cholesterol-rich diet can lead to great accumulation of β-amyloid in the brain [110, 111] which is one of the factors that cause AD [112]. Another group of lipids that was investigated in AD brains (post-mortem) were ceramides and it was found that saturated ceramides were increased in senile plaques, whereas unsaturated ceramides were decreased, even depleted [113]. Senile plaques are also one of the characteristics of AD and their main component is β-amyloid [112]. To counteract some of the AD symptoms, such as cognitive impairment, supplementing with omega-3 fatty acids showed a positive outcome both in mice models [114, 115] and AD patients [116].

A study on brain tissues from cognitively normal patients with and without AD showed that sulphatide levels were significantly lower in the AD group [117]. Furthermore, the authors detected that only three species of ethanolamine glycerophospholipids, including plasmalogens and diacyl ethanolamine glycerophospholipids, were reduced in pre-clinical AD patients (compared to the control group). The low levels of sulphatides in pre-clinical AD patients indicates brain cell membrane changes from early stages of AD, hence, the authors suggest sulphatides as biomarkers in early AD diagnosis and monitoring treatment progress [117]. A lipidomic profile of the brain revealed that the lipid profile of the cerebellum of the AD-patients and the control group marked no alterations [118]. However, there were differences in the lipidomic profiles of the prefrontal and entorhinal cortices between AD-patients and the control group. In the prefrontal cortex the most notable variation was that of diacylglycerol which increased almost two-fold in the AD-group (compared to the control group). Furthermore, levels of ceramides (including galactosylceramides and glucosylceramides) were also elevated. However, levels of lysophosphatidylcholines, lysoetherphosphatidylcholines and phosphatidylethanolamines were lower in AD-patients, compared to the control group. As far as the entorhinal cortex is concerned, AD-brains had higher concentrations of the lysosphatidic acid, ceramide-lactose-N-acetylenuraminic acid, sphingomyelins and cholesterol esters [118]. These differences in lipidomic profiles for each subregion suggest their different involvement in the pathogenesis of AD [118].

Conclusions

Lipids as biological markers of mental disorders might be vital not only as a diagnostic tool but also to understand the mechanisms that underlie mental disorders. It is clear that there is a link between lipids, such as polyunsaturated fatty acids, cholesterol or vitamin D and various neuropsychiatric diseases. For example, vitamin D deficiency can impact mental health in various ways: as relevant for depression, it can cause seasonal affective disorders (discomfort, depression, fatigue); is relevant to schizophrenia and autism, as the foetal brain develops vitamin D deficiency may cause permanent brain function impairment [119]; it leads to sleep disorders [120]. It is also hypothesised that vitamin D deficiency in adults may lead to parental germ cell degradation, causing autistic disorders. Vitamin D may have a neuroprotective action, as suggested for Alzheimer’s and Parkinson’s diseases as well [119]. Cholesterol is an important regulator of lipid organisation, required for functioning of neurotransmission in CNS. Cholesterol is substrate for all steroidal hormones, which productions is associated with manganese and it is increased in stress. The possible impact of fatty acids on mental disorders is based on their presence in neuronal cells; lipid imbalance in cell membranes should lead to changes in brain functioning and therefore might cause neuropsychiatric disorders.

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