

# **Polyunsaturated fatty acids and Psychiatric disorders**

*Essay*

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# الأحماض الدهنية المتعددة غير المشبعة والإضطرابات النفسية

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توطئة للحصول على درجة الماجستير في أمراض المخ  
والأعصاب والطب النفسي

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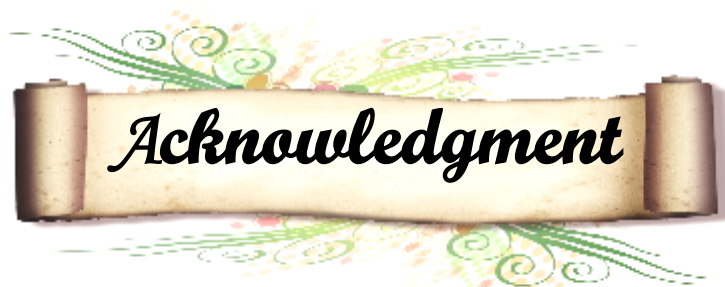
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## *List of Abbreviations*

<b>AA</b>	Arachidonic acid
<b>AD</b>	Alzheimer Disease
<b>ADHD</b>	Attention-deficit hyperactivity disorder
<b>ALA</b>	Alphalinolenic acid
<b>Apo-D</b>	Apo lipoprotein D
<b>APP</b>	Amyloid precursor protein
<b>A<math>\beta</math></b>	Amyloid $\beta$
<b>BDNF</b>	Brain-derived neurotrophic factor
<b>BPRS</b>	Brief psychiatric rating score
<b>CARS</b>	Childhood Autism Rating Scales
<b>CHQ</b>	Child Health Questionnaire
<b>COX</b>	Cyclooxygenase
<b>cPLA2</b>	Cytosolic phospholipase A2
<b>CPRS</b>	Comprehensive psychiatric rating scale
<b>CRS-P, T</b>	Conners' parent and teacher rating scales
<b>CSF</b>	Cerebrospinal fluid
<b>DAG</b>	Diacylglycerol
<b>DCD</b>	Developmental Coordination Disorder
<b>DGLA</b>	Dihomogammalinolenic acid
<b>DHA</b>	Docosaheptaenoic acid, 22:6 $\omega$ -3
<b>DPA</b>	Docosapentaenoic acid
<b>DSM</b>	Diagnostic and Statistical Manual for Mental Disorders
<b>DTI</b>	Diffusion tensor imaging
<b>EE</b>	Ethyl eicosapentaenoate
<b>E-EPA</b>	Ethyl eicosapentaenoic acid
<b>Efamol</b>	Evening primrose oil
<b>EFAs</b>	Essential fatty acids
<b>EFSA</b>	European Food Safety Authority

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<b>EPA</b>	Eicosapentaenoic acid
<b>EPUFAs</b>	Essential polyunsaturated fatty acids
<b>FAs</b>	Fatty acids
<b>FATP</b>	Fatty acid transport protein
<b>GLA</b>	Gammalinolenic acid
<b>GRAS</b>	Generally Regarded as Safe
<b>HDL</b>	High-density lipoprotein
<b>HDL</b>	High-density Lipoprotein
<b>HETE</b>	Hydroxyeicosatetraenoic acid
<b>HPETE</b>	Hydroperoxyeicosatetraenoic
<b>HUFAs</b>	Highly Unsaturated Fatty Acids
<b>IP3</b>	Inositotriphosphate
<b>iPLA2</b>	Independent phospholipase A2
<b>LA</b>	Linoleic acid, 18:2 $\omega$ -6
<b>LDL</b>	Low-density lipoprotein
<b>LOX</b>	Lipoxygenase
<b>LPL</b>	Lipoprotein lipase
<b>LT</b>	Leukotrienes
<b>LTP</b>	Long-term potentiation
<b>MDD</b>	Major depressive disorder
<b>MPC</b>	Membrane phospholipid composition
<b>N</b>	Number of human subjects in study
<b>NPD1</b>	Neuroprotection D1
<b>PANSS</b>	Positive and Negative Syndrome Scale
<b>PC</b>	Phosphatidylcholine
<b>PE</b>	Phosphatidylethanolamine
<b>PET</b>	Positron emission tomography
<b>PG</b>	Prostaglandins
<b>PI</b>	Phosphatidylinositol
<b>PI3-K</b>	Phosphatidylinositol-3kinase

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<b>PIP2</b>	Phosphatidylinositol biphosphate
<b>PIP3</b>	Phosphatidylinositol (3, 4, 5) Trisphosphate
<b>PLA2</b>	Phospholipase A2
<b>PPARs</b>	Peroxisome proliferator-activated receptors
<b>PPD</b>	Postpartum depression
<b>Ps</b>	Phosphatidylserine
<b>PTSD</b>	Post-traumatic stress disorder
<b>PUFAs</b>	Polyunsaturated fatty acids
<b>RAR</b>	Retinoic acid receptors
<b>RBCs</b>	Red blood cells
<b>RCT</b>	Randomized Controlled Trial
<b>RXR</b>	Retinoid X Receptors
<b>SAD</b>	Seasonal Affective Disorder
<b>SANS</b>	Scale Assessment of Negative symptoms
<b>SAPS</b>	Scale for the assessment of positive symptoms
<b>SDQ</b>	Strengths and Difficulties Questionnaire
<b>sPLA2</b>	Secretory phospholipase A2
<b>TAG</b>	Triacylglycerols
<b>TD</b>	Tardive dyskinesia
<b>TX</b>	Thromboxanes
<b>VLDL</b>	Very low-density lipoprotein
<b>ω</b>	Omega
<b>5-HIAA</b>	5-hydroxyindoleacetic acid
<b>5-HIAA</b>	5-hydroxyindoleacetic acid
<b>5-HT</b>	5-hydroxytryptamine

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## Introduction

The human brain is primarily composed of lipids (60–70% dry weight) comprised of a ratio of saturated fatty acids and unsaturated fatty acid (monounsaturated fatty acid and polyunsaturated fatty acids) (*McNamara and Carlson, 2006*).

Polyunsaturated fatty acids are important components of membrane cells and neurological tissue, Polyunsaturated fatty acids especially arachidonic acid and docosahexaenoic acid are particularly important for the central nervous system structure and function (*Sethom et al., 2010*).

Several biological mechanisms potentially explain the impact of omega-3 Eicosapentanoic acid in psychiatric disorders; these include (1) increased serotonergic neurotransmission, (2) alteration in dopaminergic function, (3) regulation of corticotrophin-releasing factor, (4) inhibition of protein kinase c, (5) suppression of phosphatidylinositol associated second messenger activity, (6) improved cerebral blood flow, (7) regulation of gene expression, (8) increased dendritic arborization and formation, (9) prevention of neuronal apoptosis, (10) competition of eicosapentanoic acid with arachidonic acid for enzymatic action and resultant reduction of the inflammation response (*Freeman et al., 2006*).

There is evidence to suggest that abnormal phospholipid and related fatty acid metabolism may play a role in the aetiology of several psychiatric illnesses, including schizophrenia, bipolar mood disorder, major depression, dementia and attention deficit hyperactivity disorder (*Parker et al., 2006*).

There is evidence that altered composition of membrane levels of fatty acids is correlated with severity of psychotic symptoms and also with impairment of distinct cognitive parameters in subjects with schizophrenia (*Sumiyoshi et al., 2010*).

Deficiencies in  $\omega$ -3 polyunsaturated fatty acids have been reported in a wide range of psychiatric disorders that have included (but are not limited to) depression, suicidal tendencies and aggressive disorders (*Young and Conquer, 2005*).

The “arachidonic acid cascade hypothesis” asserts that these agents commonly alleviate bipolar disorders symptoms, particularly bipolar mania, by downregulating brain arachidonic acid metabolism (*Rao et al., 2008*).

Several natural compounds, including omega-3 fatty acids, have been suggested as potential augmenters of antidepressant drug effects especially in treatment-resistant depression (*Liano et al., 2010*).

Also, decreased levels of the docosahexaenoic essential fatty acid have also been reported in autism (*Taylor and Benjamin, 2004*).

In patients with social phobia, the abundance of eicosapentaenoic acid and docosahexaenoic acid in erythrocyte membranes is decreased in those with the illness and the extent of the reduction is correlated with the severity of the illness (*Green et al., 2006*).

Besides, it has been recently reported the first clinical trial demonstrating omega-3 to be effective monotherapy in childhood depression (*Nemets et al., 2006*).

However, randomized controlled clinical trials have been slow to accrue. Most but not all trials with omega-3 indicate that these fatty acids are effective as an adjunctive treatment for unipolar depression and may be beneficial in other mood disorders (*Owen et al., 2008*).

There is no doubt that further research is needed in this field to clarify the efficacy of omega-3 as monotherapy for the treatment of unipolar, bipolar, perinatal and childhood depression as well as the optimal dose and type of omega-3 supplement for each case ( *Venna et al., 2009*).

## Rationale of the work

As over the past 10 years, numerous studies have investigated the role of polyunsaturated fatty acids in psychiatric disorders (pathogenesis, prevention and significant role in the management) on evidence that polyunsaturated fatty acids play roles in brain structure and function.

Therefore, this work seeks to throw light on polyunsaturated fatty acids and its relation to psychiatric disorders in different aspects and to increase awareness about the benefits of omega-3 fatty acids among psychiatrists as well as patients, which in turn may greatly improve the treatment outcomes in patients with these psychiatric disorders.

## Hypothesis

Polyunsaturated fatty acids have a valuable correlation to the pathogenesis and for the management of variable psychiatric disorders.

## Aim of the work

To highlight the role of polyunsaturated fatty acids in the pathogenesis, prevention and management of psychiatric disorders.