PLESKA, Kacper, WOJTANIA, Joanna, ŁEPIK, Michał, USZOK, Zofia, ROSIAK, Krzysztof, REGUŁA, Kacper, WALOCH, Kamil, PIASZCZYŃSKI, Szymon, CZAJKA, Andrzej and SZYMAŃSKI, Bartłomiej. Dyslipidemia among psychiatric patients with depression – common possible reasons and treatment implications – review. Quality in Sport. 2024;15:51715. eISSN 2450-3118.
https://dx.doi.org/10.12775/QS.2024.15.51715
https://apcz.umk.pl/QS/article/view/51715

The journal has had 20 points in Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 25.05.2024. Revised: 20.06.2024. Accepted: 01.07.2024. Published: 02.07.2024.

Dyslipidemia among psychiatric patients with depression – common possible reasons and treatment implications – review

Kacper Płeska, Medical University of Lodz, al. Tadeusza Kosciuszki 4, 90-419 Lodz, Poland
https://orcid.org/0000-0001-8495-8766
pleskakacper@gmail.com

Joanna Wojtania, Independent Public Health Care Facility of the Ministry of Internal Affairs and Administration, ul. Polnocna 42, 91-425 Lodz, Poland
https://orcid.org/0009-0006-3466-8860
joanna.wojtania@outlook.com

Michał Łepik, Military Medical Academy Memorial Teaching Hospital – Central Veterans' Hospital, ul. Zeromskiego 113, 90-549 Lodz, Poland
https://orcid.org/0009-0005-5441-2005
michal.lepik2@gmail.com

Zofia Uszok, Medical University of Lodz, al. Tadeusza Kosciuszki 4, 90-419 Lodz, Poland
https://orcid.org/0009-0002-2111-8094
zofia.uszok@stud.umed.lodz.pl

Krzysztof Rosiak, Military Medical Academy Memorial Teaching Hospital – Central Veterans' Hospital, ul. Zeromskiego 113, 90-549 Lodz, Poland
https://orcid.org/0009-0007-8536-9809
krzysztof.rosiak15@gmail.com

Kacper Reguła, County Hospital of Zawiercie, ul. Miodowa 14, 42-400 Zawiercie, Poland
https://orcid.org/0009-0001-5291-7043
kacfilreg@gmail.com

Kamil Waloch, Medical University of Lodz, al. Tadeusza Kosciuszki 4, 90-419 Lodz, Poland
https://orcid.org/0009-0003-0697-1393
kamilwaloch7@gmail.com

Szymon Piaszczyński, Medical University of Lodz, al. Tadeusza Kosciuszki 4, 90-419 Lodz, Poland
https://orcid.org/0009-0007-8600-2339
szpiaszczynski@gmail.com

Andrzej Czajka, Provincial Specialized Hospital in Zgierz Parzęczewska 35, 95-100 Zgierz, Poland
https://orcid.org/0009-0008-8888-3982
andrzej.czajka0509@gmail.com

Bartłomiej Szymański Norbert Barlicki Memorial Teaching Hospital no. 1 of the Medical University of Lodz, Dr. Stefana Kopcińskiego 22, 90-153 Lodz, Poland
https://orcid.org/0009-0006-8915-0364
szymanski.b458@gmail.com

Abstract

Dyslipidemia is a medical term used to describe an abnormal level of lipids (fats) in the blood. This can include elevated levels of total cholesterol, low-density lipoprotein (LDL) cholesterol, high density protein lipoprotein (HDL) cholesterol and serum triglicerides.

Depression, also known as depressive disorder, is a common mental illness. It is characterized by a persistent feeling of sadness, loss of pleasure, or lack of interest in activities that are present of at least two weeks and significantly impair patient everyday functioning. Dyslipidemia and depression can co-occur due to a complex interplay of shared risk factors, such as inflammation, metabolic syndrome, medication side effects, and lifestyle changes, suggesting a bidirectional relationship where each condition might contribute to the development or exacerbation of the other.

Given these considerations, a comprehensive approach to managing dyslipidemia in psychiatric patients with depression is essential. This should include regular monitoring of lipid profiles and monitoring of anticholesterol and antidepressant drugs. Interestingly, simple lifestyle changes, such as a healthy diet and exercise, have an impact on the treatment of depression and dyslipidemia.

Keywords: dyslipidemia, depression, physical exercises, diet, statins, inflammation

1. Introduction

Dyslipidemia is a medical term used to describe an abnormal level of lipids (fats) in the blood. This can include elevated levels of total cholesterol, low-density lipoprotein (LDL) cholesterol, high density protein lipoprotein (HDL) cholesterol and serum triglicerides (1). Lipid disorders presents a growing concern in numerous industrialized nations and stand as a significant risk factor for the development of many diseases, such as coronary heart disease (CHD) with further consequences. Moreover, these disorders extends beyond their impact on physical health to influence the overall well-being and management of psychiatric conditions (2).

Depression, commonly referred to as depressive disorder, is a common mental illness. It is characterized by a protracted period of sadness, loss of pleasure, or lack of interest in activities. A depressive state is not the same as normal mood swings or feelings related to daily living. It can have an impact on all facets of life, including ties to friends, family, and the community. An estimated 3.8% of people suffer from depression, including 5.7% of adults

over 60 and 5% of adults (4% of men and 6% of women). Depression affects about 280 million people worldwide (3).

Interisingly, the prevalence of lipid disorder in psychiatric patients is significantly higher compared to the general population (4). Psychiatric disorders, such as depression, bipolar disorder, shizophrenia, and anxiety disorders, commonly coincide with lifestyle factors that can disrupt lipid metabolism regulation. These factors include poor dietary habits, sedentary lifestyle, and medication side effects. Furthermore, although depression and dyslipidemia appear to be distinct disorders, they share some underlying processes that may explain their frequent co-occurrence (5).

High-density lipoprotein (HDL) cholesterol eliminates other types of cholesterol from the bloodstream and has an inverse relationship with the risk of coronary artery disease (CAD). On the contrarylow-density lipoprotein (LDL) cholesterol builds up in blood vessels and raises the risk of CAD (6). Moreover, there has been conflicting evidence in the past regarding the connection between depression and serum lipid profiles. Specific alterations in the serum lipid profiles, such as elevated (7) and lowered HDL (8) and elevated LDL (9) and triglyceride (8) levels, are seen in adults suffering from depression. Total cholesterol (TC) level among adults with depression have been studied; both elevated (10) and lowered (8) levels have been reported. Research conducted on adults diagnosed with major depressive disorder (MDD) has also revealed a significant correlation between the severity of depressive symptoms and the degree of dyslipidemia and hypertriglyceridemia (9).

Detecting dyslipidemia early allows for timely intervention, such as medication adjustments and lifestyle changes, which can help mitigate long-term health risks. . A multidisciplinary approach is crucial for managing dyslipidemia in psychiatric patients. This method involves collaboration among psychiatrists, cardiologists, endocrinologists, and primary care physicians to create integrated treatment plans that consider both the psychiatric needs and the physical health of the patient. (11).

The main aim of this article is to trace the complex relationship between psychiatric disorder, such as depression and dyslipidemia. It will focus on the common pathophisiology of dyslipidemia among psychiatric patients with depression, common risk factors and potential treatment strategies. Understanding these topics will help to acquire better treatment outcomes and inreased quality of life of psychiatric patients.

2. Possible mechanisms connecting dyslipidemia and depression

Depression and lipid disorders, like dyslipidemia, often co-occur due to shared biological, psychological and behavioural pathways, but he exact mechanisms of this relationship are not yet understood.

2.1Neuroendocrine dysreguation

2.1.1 Hypothalamic-Pituitry-Adrenal (HPA) axis dysfunction

An important part of the body's reaction to stress is controlled by the hypothalamic-pituitary-adrenal (HPA) axis. Corticotropin-releasin hormone (CRH), which is released by the hypothalamus in response to stress, causes the pituitary gland to release adrenocorticotropic hormone (ACTH). The main stress hormone, cortisol, is then released by the adrenal glands in response to ACTH (12). The HPA axis is frequently dysregulated in depression, which results in anomalies in cortisol secretion (13). Particulary in the early stages of the illness, some depressed people may have elevated cortisol levels, while others may show impaired cortisol response to stress (14). The immune system, mood regulation, metabolism, and other physiological processes can all be significantly impacted by dysregulation of the HPA axis (15). Increased inflammation, insulin resistance, and changes in lipid metabolism contributing to dyslipidemia are linked to persistent activation of the HPA axis (16).

2.1.2 Sympathetic Nervous System (SNS) Activtion

The body's "fight or flight" reaction in times of stress is brought on by the sympathetic nervous system. Catecholamines like norepinephrine and adrenaline are released when the SNS is activated. These chemicals raise blood pressure, heart rate and energy expenditure (17). Depression and chronic stress can cause the SNS to become dysregulated, which prolongs the activation of sympathetic pathways (18). Insulin resistance and dyslipidemia are two metabolic disorders that are also linked to excessive sympathetic activity (19).

2.1.3 Effect on lipids' metabolism

Lipid metabolism is impacted both directly and indirectly by the hallmark symptoms of depression, dysregulation of the HPA axis and SNS. The dyslipidemia that is a result of these neuroendocrine disruptions is caused by changes in hepatic triglycerife syntheis and adipose tissue lipolysis (20). Additionaly, through indirect mechanisms, dysregulated neuroendocrine signaling in depression affects insulin sensitivity, energy balance and appetite regulation, all of which exacerbate dyslipidemia (21).

2.2 Inflammation

2.2.1 Chronic Low-Grade Inflammatory State

Depression (22) and dyslipidemia (23) are both associated with elevated levels of inflammatiory markers, including C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α). These pro-inflammatiory cytokines have negative effects on lipid metabolism by influencing the metabolism of lipoproteins, hepatic lipogenesis, and adipose tissue lipolysis - all of which lead to dyslipidemia (24). Numerous studies have connected the adipose inflammatory process metabolic disease to the elevated production of inflammatory cytokines, including TNF-a, IL-17, IL-4, IL-6, and other cytokines (25,26). Interistingly, recently meta-analises in depressed individuals have been reported increased levels of TNFα, IL-6, IL-13, IL-18, IL-12, IL-1RA, and sTNFR2, as well as a drop in the proinflammatory cytokine IFNγ (27). Significant effects have also been shown for a wide range of chemokine levels, including elevated CCL2 (MCP-1), CXCL4, and CXCL7, with significantly lower levels of CCL4 in serum (28,29).

2.2.2 Pathways of Inflammatory Signaling and Lipid Metabolism

The pathophysiology of depression and dyslipidemia is probably linked to the activation of the nuclear factor-kappa B (NF-κB) signaling pathway, which is a central regulator of inflammation (30,31).

2.2.3 Insulin Resistance Induced by Inflammation

An important pathophysiological mechanism that connects depression and dyslipidemia is inflammation, which is a major factor in the development of insulin resistance (32–34). In insulin-sensitive tissues like a myocytes, elevated levels of pro-inflammatory cytokines can interfere with insulin signaling pathways. This can result in dysregulated lipid metabolism, increased lipolysis, and impaired glucose uptake, all of which can exacerbate dyslipidemia (35,36).

2.2.4 Neuropsychoimmunological Relationships

Psychoneuroimmunological pathways are linked to the pathophysiology of dyslipidemia and depression. These pathways explain the reciprocal communication between the immune system and the central nervous system (CNS). The persistence of dyslipidemia and depressive symptoms is linked to dysregulation of this complex communication network, which is typified by aberrant cytokine production, immune activation, and altered neurotransmitter metabolism, neuroendocrine function, and synaptic plasticity (37,38).

To sum up, persistent low-grade inflammation plays a crucial role as a mediator in the intricate relationship between depression and dyslipidemia by influencing insulin sensitivity, lipid metabolism, and central nervous system performance.

2.3 Hormonal dysregulation

2.3.1 Sex hormone dysregulation

Changes in the levels of sex hormones, including progesterone, testosterone, and estrogen, are essential in the shared pathophysiology of depression and dyslipidemia. Lower oestrogen levels, that are common in postmenopausal or perimenopausal conditions, are linked to dyslipidemia (39). Conversely, dyslipidemia and an increased risk of cardiovascular disease are linked to androgen excess synthesis, which is seen in conditions like polycystic ovary syndrome (PCOS) (40). In addition, changes in sex hormone levels affect energy metabolism, body composition, and mood regulation, which can also explain the co-occurrence of depression and dyslipidemia (41).

2.3.2 Dysregulation of thyroid hormones

Thyroid hormones, including T3 (triiodothyronine) and T4 (thyroxine), play a crucial role in regulating metabolism and energy production in the body (42). Depression has been linked to a number of thyroid abnormalities. However, in most cases the biochemical parameters are normal. (43,44). The main signs of thyroid abnormalities in patients diagnosed with depression are elevated T4 levels, low T3, elevated rT3, blunted TSH response to TRH, positive antithyroid antibodies, and elevated TRH concentrations in cerebrospinal fluid (CSF) (45–47). In addition, hypothyroidism negatively affects lipid synthesis, absorption, circulation, and metabolism, possibly leading to hyperlipidemia. Thyroid hormones are crutial for stimulating liver's HMG-CoA reductase expression, which in turn increases the synthesis of cholesterol. Decreased level of thyroid hormones seen in hypothyroidism leads toreduced hepatic cholesterol synthesis (48). Morover, hypothyroidism diminishes the excretion of cholesterol and the clearance of plasma triglycerides, the latter due to a reduction in lipoprotein lipase levels (49). To sum up, triglyceride accumulation in the liver, a minor increase in HDL and triglyceride levels, and an increase in total cholesterol and LDL levels are the combined effects of the aforementioned changes (50).

2.3.3 Neuropeptide dysregulation

Neurons release neuropeptides, which are small protein molecules containing from three to one hundred amino acids. Neuropeptides can affect both neuronal and non-neuronal cells. Neuropeptide Y (NPY), ghrelin, and leptin are among the neuropeptides whose dysregulation is linked to the pathophysiology of dyslipidemia and depression (51,52) Changes in neuropeptide levels affect energy balance, lipid metabolism, and appetite control, which can lead to dyslipidemia and metabolic problems. For example, increased NPY levels exacerbate dyslipidemia by inducing adipose tissue lipolysis and hepatic lipid accumulation (53). Moreover, in the prefrontal cortex and hippocampus regions of the postmortem brain of depressed suicide victims, researchers found a significant upregulation of NPY receptors, NPY1R and NPY2R mRNA, and a significant decrease in NPY mRNA relative to normal control subjects. Additionally, they reported a noteworthy reduction in the prefrontal cortex NPY protein expression in depressed suicide subjects (54).

2.4 Behavioral factors

2.4.1 Sedentary lifestyle and lack of exercise

To date, scientific reports investigating the link between sedentary lifestyle and depression remain inconsistent. According to a meta-analysis conducted by Huan et al., sedentary behaviors, particularly those that are mentally passive, have been linked to an increased risk of depression. The risk of depression may rise with each extra minute spent passively sitting in front of the television. When depression was diagnosed by a physician, subgroup analyses revealed a positive relationship between sedentary behavior and depression (55). Interestingly, study conducted by Crichton and Alkewri reported an inverse correlation between time spent in front of a computer screen and plasma HDL cholesterol levels. Furthermore, time spent in front of a computer screen was positively correlated with elevated plasma triglyceride concentration (56).

2.4.2 Unhealthy diet

The development of depression can be influenced by unhealthy dietary habits. A prime example is the Western diet, which is characterized by high consumption of processed and fast foods, red and processed meats, refined grains, sugary drinks, and high-fat dairy products. It is typically low in fruits, vegetables, whole grains, and legumes. (57). Following such dietary habits is linked to an increase in pro-inflammatory cytokines, as well as worse

symptoms of depression (58). Furthermore, there is a strong and positive correlation between the western dietary pattern and both total and LDL cholesterol (59).

2.4.3 Sleep disturbances

One of the main and most common symptom of depressive disorders is sleep disturbance. (60). These sleep dysregulation issues are not a side effect of the illness; rather, they frequently exist prior to depressive episodes and may continue even after the illness is under control. It has been discovered that better sleep quality improves outcomes in depressed patients (61,62). Furthermore, forced sleep deprivation can lessen depression symptoms in some people and trigger depressive episodes in others who are vulnerable (60).

Interistingly sleep disturbances are also associated with dyslipidemia. For example, in the primary care context of northeastern Greece, a population-based cross-sectional study revealed significant inverse correlationsbetween adults' sleep duration and dyslipidemia. Furthermore, it was discovered that the prevalence of dyslipidemia was strongly linked to insomnia, especifically in individuals with difficulty staying asleep and early morning awakening (63).

2.4.4 Alcohol abuse

Studies have indicated that there appears to be a reciprocal association between depressive disorder and alcohol use disorder (AUD). There are numerous and intricate pathways that may explain co-occurrance AUD and a depression. At first, alcohol may seem to offer temporary relief from depression symptoms like sadness, anxiety, or a sense of worthlessness. But the relief is usually short-term, and this can result in enhanced drinking with the potential for the development of an alcohol use disorder. Consequently, frequent or excessive drinking might alter brain chemistry and neurotransmitters that are involved in mood regulation, such as dopamine and serotonin. That can cause chemical imbalances over time which increase the risk of depression (64).

Importantly, regular drinkers are found to have lipid disorders in the form of elevated triglycerides, total cholesterol and LDL cholesterol, and reduced HDL cholesterol. Heavy and heavy drinkers have significantly elevated blood triliceride concentrations. Interestingly, elevated HDL cholesterol concentrations are observed among Europeans who consume large amounts of alcohol, especially red wine. The mechanisms of these processes remains unclear (65,66).

3. Treatment impications for patients with comorbid depression and dyslipidemia

3.1 Anticholesterol drugs

The first choice in treating patients with dyslipidaemia for primary and secondary prevention of cardiovascular disease are statins. They act by inhibiting 3-hydroksy-3-metyloglutarylokoenzymu A (HMG-CoA), thereby blocking the production of endogenous cholesterol in the liver (67). Statins, which work by inhibiting the synthesis of cholesterol, are useful in treating dyslipidemia and cardiovascular disease (CVD) and may also be helpful in reducing the negative neuropsychiatric symptoms associated with bipolar disorder and other mood disorders . Statins are clinically demonstrated to be dependent on serotonergic system modulation, so they can exert beneficisl clinical effect smultaniously with selective serotonin reuptake inhibitors (SSRIs) .Affinity can be used to categorize statins into hydrophilic and lipophilic groups. If it comes to menagement of depressive symptoms, studies show that lipophilic statins like atorvastatin, lovastatin, pitavastatin, simvastatin, and fluvastatin exert better results than hydrophilic statins like rosuvastatin and pravastatin (68). Researches have shown that atorvastatine have prevention of depressant by regulating neural synaptic plasticity. Other studies on animals have shown that atorvastatin prevents lipopolysaccharide-induced depressive behaviour. In patients with co-morbid coronary artery disease, diabetes, and hypertension, statins may serve as an effective adjuvant therapy to antidepressants because they protect against cardiovascular and cerebrovascular disease by reducing inflammation and affecting cholesterol synthesis, which in turn possitively affects the pathophysiology of depression (69). .

The second choice for the treatment of hypercholesterolaemia is ezetimibe. It works by inhibiting the absorption of cholesterol from the small intestine. Currently, there is no strong evidence of an effect of ezetimibe on the occurrence of depression, patients may report mood disorders or depressive symptoms (70).

Another drugs used in dyslipidaemia are Proprotein Convertase Subtilisin/Kexin type 9 (PCSK9) inhibitors. These drugs bind to the receptor for LDL (LDLR), leading to its degradation and reduction in its amount on the cell membrane of hepatocytes and in the circulatory system. The consequence of their action is a decrease in reuptake and an increase in serum LDL concentrations. Recent animal studies show that one of the PCSK9 inhibitors, by reducing pro-inflammatory cytokines and indoleamine 2,3-dioxygenase 1 (IDO-1) in the

hippocampus and rebalancing the tryptophan and kynurenine pools, has anti-inflammatory effects. Thus, it can alleviate depressive symptoms. However, further studies are needed to further explore the potential effects of PCKS9 inhibitors on depression among people population (71).

3.2 Antidepression drugs

One theory to explain the onset of depression is a disturbance in the amount of neurotransmitters in the central nervous system. Antidepressants function by regulating neurotransmitter levels in the brain to improve mood and reduce depressive symptoms. Antidepressants primarily target the neurotransmitters serotonin, norepinephrine, and dopamine. (72).

The main group of drugs used in depression are serotonin reuptake inhibitors (SSRIs), which prevent the transport of serotonin back into the nerve cell. As a result, its concentration in the brain increases (73). Studies do not find a clear effect of SSRI drugs on blood lipid concentrations. Some studies show that SSRIs lower total cholesterol and triglycerides (74). 3.3 Others report that SSRIs cause a decrease in LDL, HDL and total cholesterol, with no effect on triglycerides. (75).

Another group of drugs used for depression are drugs that inhibit the reuptake of serotonin and norepinephrine (SNRIs), neurotransmitters involved in mood regulation, thereby increasing their levels in the brain (76). The use of venlafaxine, which belongs to this group of drugs, has been shown to be associated with an increase in total blood cholesterol , LDL-C, triglycerides and lower HDL-C (77). The use of another SNRI drug, duloxetine, was also shown to increase total blood cholesterol level (78).

Tricyclic antidepressants, which include amitriptyline, clomipramine and doxepin, work by inhibiting the reuptake of serotonin and noradrenaline and blocking receptors for histamine and acetylcholine (79). Research indicates that this group of antidepressants may have negative effects on dyslipidemia, with tricyclic antidepressants being harmful in this regard (74).

Different kind of treatment can be mirtazapine. Its antidepressant effect is mainly attributed to enhanced noradrenergic and serotonergic (5-HT1-mediated) activity. Side effects of this drug include weight gain, as well as dyslipidaemia mainly manifested as an increase in triglycerides (80).

3.3 Physical exercises

Exercise is proposed as an effective therapeutic strategy for treating both depression and dyslipidemia, offering significant benefits for mental and cardiovascular health. A recent systematic review compared the effectiveness of exercise, antidepressants treatment and their effects on relieving depressive symptoms among adults. It found no clear differences in the therapeutic efficacy of either method. As exercise has similar efficacy in relieving depressive symptoms, it may serve as an alternative method in alleviating mild depression among adults, wtih no along side effects (81). Additionally, a network meta-analysis was carried out to evaluate the effects of various exercise modalities on mental health conditions, including depression. These modalities included aerobic, resistance workout, mind-body workout (yoga, tai chi, and dance), stretching, and multimodal exercise, which combines at least two exercise modalities. When compared to control conditions, aerobic exercise, mind-body exercise, and multimodal exercise were found to have significant effects on depressive symptoms, with moderate-to-large effect sizes. These results imply that different exercise modalities may be beneficial in a clinically meaningful way for depression management and, as such, should be proposed as an adjunct to medication (82). There are theories regarding the physiological and psychological processes by which physical activity may improve mental health. These mechanisms include modifications of sleep regulation and neurotransmitter availability and metabolism. According to some research, exercise may facilitate changes in neurogenesis, brain architecture, prefrontal cortex-related cognitive functions, and different inflammatory markers (83). Furthermore, the effects of exercise and sports on mental health are probably influenced by epigenetics. Exercising appears to have positive epigenetic effect that balances the negative effects of stress, potentially modulating changes in DNA methylation and gene expression brought on by stress (84).

Exercises are also important part of dyslipidemia treatment. According to epidemiological studies and prospective intervention studies, physical activity (in the sense of overall activity) and exercise training can lower cardiovascular morbidity and mortality by improving lipid profiles (85). The strongest correlation has been found between activity level and lower triglyceride and higher HDL levels. A meta-analysis which included 19 studies revealed that regular endurance training led to a significant increase in HDL2-C levels. It was noteworthy that this effect persisted even in the absence of variations in BMI and body weight (86). Data on how physical activity affects low-density lipoprotein (LDL) and its subfractions are inconsistant. Nonetheless, there are signs that physical training can lower the small LDL particles, which are thought to be especially atherogenic (87). The mechanisms by which

physical exercise affects dyslipidemia are complex. One of them is the metabolic effect of exercise. For instance, the upregulation of lipoprotein lipase (LPL) activity and quantity in skeletal muscle is the primary cause of the decrease in plasma triglyceride concentration. Depending on the duration, intramuscular triglycerides are the main energy source during moderate endurance exercise (88). Interestingly, exercise makes muscle and adipose tissue more active in terms of hormone-sensitive lipases (HSLs), which facilitates the more effective conversion of triglycerides into free fatty acids and the subsequent mobilization of the tissues. Regular activity also leads to an increase in the expression of plasma membrane fatty acid binding proteins (FABPPM), which facilitates the more efficient entry of fatty acids into muscle cells. Regular activity also improves the intramuscular capacity to bind free fatty acids in the cytosol and transport them to the mitochondria for β-oxidation (89).

Importantly, physical exercise reduces the concentration of inflammatory markers that underlie the pathophysiology of of depression and dyslipidemia. It has been demonstrated that the active skeletal muscle itself produces anti-inflammatory signals. As a result, more IL-6, also referred to as myokine, is released during muscle contraction while exercising. By inducing the production of immune regulatory mediators like IL-10 and the IL-1 receptor antagonist (90), as well as the downregulation of TNF-α by monocytes and macrophages, IL-6 exert an anti-inflammatory effect (91). Unlike endurance training, which has the potential to lower systemic levels of IL-6 and TNF-α (92), resistance training appears to have little to no impact on chronic inflammation (93). Even in the presence of inflammatory comorbidities, endurance and resistance training appear to influence basal levels of pro- or anti-inflammatory cytokines such as IL-6, -8, and -10 (94).

3.4 Antiinflammatory diet

Diet affects serum levels of inflammatory markers such as C-reactive protein (CRP), Il-1B, Il-6, Il-10 and TNF-α, increased levels of which may contribute to the development of depression (95,96). It was observed that the intake of whole grain products was associated with a reduction in CRP concentration values. Conversely, a lower dietary supply of these products led to increased concentration of the pro-inflammatory IL-6. Dietary patterns with a high pro-inflammatory potential (rich in saturated fat and trans fats), are associated with a significantly increased likelihood of depressive disorders (97). Interestingly, a randomized controlled trial by Parlett et al. assessed the effect of a Mediterranean dietary intervention combined with fish oil suplementation on the severity of depressive symptoms. This study reported that increasing the amount of nuts in the diet led to reduced levels of anxiety, stress,

and increased symptoms of depression. Legumes also had a positive effect by reducing the level of stress, anxiety and negative emotions (98). On this basis, it can be concluded that it is reasonable to promote a diet with anti-inflammatory properties, rich in fruit, vegetables, whole-grain products and olive oil (99).

One dietary pattern that has significant benefits on health is the Mediterranean Diet, mainly practised by populations living in the Mediterranean basin. It is characterised by a high intake of fruit and vegetables, legumes, unsaturated fats, moderately high fish consumption, low consumption of dairy products and low consumption of saturated fats, sweets and meat (100). Research has shown that increased adherence to the Mediterranean Diet (MD) correlates with improved cholesterol levels. Specifically, studies find that high-density lipoprotein (HDL) cholesterol tends to rise, while total cholesterol, triglycerides (TG), and low-density lipoprotein (LDL) cholesterol tend to fall with greater adherence to the Mediterranean Diet. This suggests that following the MD more closely is linked to a healthier lipid profile and reduced cardiovascular risk. (101–103). Research also indicates that certain dietary patterns are linked to a higher risk of dyslipidemia. Specifically, studies have found that consuming foods with a high dietary inflammation index (DII), diets high in protein and sugar or those with excessive caloric intake are corelated with elevated triglycerides (TG) and reduced high-density lipoprotein (HDL) cholesterol in the blod. (104,105). Furthermore, it has been noted that following a diet high in antioxidants and anti-inflammatory foods improves the lipid profile. There is evidence that the relationship between serum HDL and DII is inverse (106).

4. Discussion

The co-occurrence of depression and dyslipidaemia is common among psychiatric patients, which requires careful investigation and treatment. Our review explores several common causes underlying this clinical conditions. We focus on neuroendocrine disorders, hormonal imbalance, lifestyle factors and the effects of medications used in both diseases. Understanding these factors may allow developing of targeted interventions that can reduce the severity of depressive symptoms and improve the lipid profile.

An important aspect seems to be understanding the bidirectional relationship between these conditions. For example, patients with depression often exhibit unhealthy eating patterns, consume more alcohol, and engage in less physical activity. (107). These behaviours can lead to dyslipidaemia. Conversely, elevated plasma lipid concentrations may exacerbate depressive

symptoms. Importantly, both dyslipidaemia and depression can exacerbate the risk of cardiovascular disease (108).

Lifestyle modifications, including dietary changes or increased physical activity, have a key role in the treatment of depression and lipid disorders. Multidisciplinary collaboration is essential for effectively managing depression and dyslipidemia, especially given the complex interplay between mental health and metabolic disorders. A multidisciplinary approach involves the coordinated efforts of various healthcare professionals, each contributing their expertise to create optimise treatmentminimise the risk of cardiovascular events. Further research should focus on clarifying the common mechanisms linking the occurrence of depression and dyslipidaemia, enabling development of more effective strategies to concurrently treat both depression and dyslipidemia.

Disclosure

Author's contribution

Conceptualization: Kacper Płeska and Joanna Wojtania ; Methodology: Krzysztof Rosiak; Software: Michał Łepik ; Check: Kacper Reguła and Zofia Uszok; Formal analysis: Joanna Wojtania and Szymon Piaszczyński; Investigation: Andrzej Czajka and Bartłomej Szymański; Resources: Zofia Uszok; Data curation: Krzysztof Rosiak; Writing - rough preparation: Kacper Płeska and Kacper Reguła; Writing - review and editing: Michał Łepik and Kamil Waloch; Supervision: Joanna Wojtania; Project administration: Szymon Piaszczyński and Andrzej Czajka; Receiving funding - no specific funding.

All authors have read and agreed with the published version of the manuscript.

Financing statement

This research received no external funding.

Institutional Review Board Statement

Not applicable.

Informed Consent Statement

Not applicable.

Data Availability Statement

Not applicable.

Conflict of interest

The authors deny any conflict of interest.

References

1. Jacobsen AP, Whelton SP, Blumenthal RS, Mcevoy JW. Dyslipidemia. In: Hypertension: A Companion to Braunwald's Heart Disease. 2023.
2. Saravane D. Dyslipidemia and Mental Illness. In: Dyslipidemia - From Prevention to Treatment. 2012.
3. WHO. https://www.who.int/news-room/fact-sheets/detail/depression. Int Immunopharmacol. 2019;67(August 2018).
4. Fentie D, Yibabie S. Magnitude and associated factors of dyslipidemia among patients with severe mental illness in dire Dawa, Ethiopia: neglected public health concern. BMC Cardiovasc Disord. 2023;23(1).
5. Penninx BWJH, Lange SMM. Metabolic syndrome in psychiatric patients: Overview, mechanisms, and implications. Dialogues Clin Neurosci. 2018;20(1).
6. Wilson PWF. High-density lipoprotein, low-density lipoprotein and coronary artery disease. Am J Cardiol. 1990;66(6).
7. Shin JY, Suls J, Martin R. Are cholesterol and depression inversely related? A meta-analysis of the association between two cardiac risk factors. Ann Behav Med. 2008;36(1).
8. Bharti V, Bhardwaj A, Hood K, Elias DA, Metcalfe AWS, Kim JS. A systematic review and meta-analysis of lipid metabolomic signatures of Major Depressive Disorder. J Psychiatr Res. 2021;139.
9. Enko D, Brandmayr W, Halwachs-Baumann G, Schnedl WJ, Meinitzer A, Kriegshäuser G. Prospective plasma lipid profiling in individuals with and without depression. Lipids Health Dis. 2018;17(1).
10. Cepeda MS, Kern DM, Blacketer C, Drevets WC. Low levels of cholesterol and the cholesterol type are not associated with depression: Results of a cross-sectional NHANES study. J Clin Lipidol. 2020;14(4).

11. Kirkpatrick CF, Sikand G, Petersen KS, Anderson CAM, Aspry KE, Bolick JP, et al. Nutrition interventions for adults with dyslipidemia: A Clinical Perspective from the National Lipid Association. Vol. 17, Journal of Clinical Lipidology. 2023.
12. Herman JP, McKlveen JM, Ghosal S, Kopp B, Wulsin A, Makinson R, et al. Regulation of the hypothalamic-pituitary- adrenocortical stress response. Compr Physiol. 2016;6(2).
13. Lopez-Duran NL, Kovacs M, George CJ. Hypothalamic-pituitary-adrenal axis dysregulation in depressed children and adolescents: A meta-analysis. Vol. 34, Psychoneuroendocrinology. 2009.
14. Nandam LS, Brazel M, Zhou M, Jhaveri DJ. Cortisol and Major Depressive Disorder—Translating Findings From Humans to Animal Models and Back. Vol. 10, Frontiers in Psychiatry. 2020.
15. Stephens MAC, Wand G. Stress and the HPA axis: Role of glucocorticoids in alcohol dependence. Vol. 34, Alcohol Research: Current Reviews. 2012.
16. Yaribeygi H, Maleki M, Butler AE, Jamialahmadi T, Sahebkar A. MOLECULAR MECHANISMS LINKING STRESS AND INSULIN RESISTANCE. EXCLI J. 2022;21.
17. Alshak MN, M Das J. Neuroanatomy, Sympathetic Nervous System. StatPearls. 2019.
18. Won E, Kim Y-K. Stress, the Autonomic Nervous System, and the Immune-kynurenine Pathway in the Etiology of Depression. Curr Neuropharmacol. 2016;14(7).
19. Stanciu S, Rusu E, Miricescu D, Radu AC, Axinia B, Vrabie AM, et al. Links between Metabolic Syndrome and Hypertension: The Relationship with the Current Antidiabetic Drugs. Vol. 13, Metabolites. 2023.
20. Shao Q, Wu Y, Ji J, Xu T, Yu Q, Ma C, et al. Interaction Mechanisms Between Major Depressive Disorder and Non-alcoholic Fatty Liver Disease. Front Psychiatry. 2021;12.
21. Qiu W, Cai X, Zheng C, Qiu S, Ke H, Huang Y. Update on the Relationship Between Depression and Neuroendocrine Metabolism. Vol. 15, Frontiers in Neuroscience. 2021.
22. Lee CH, Giuliani F. The Role of Inflammation in Depression and Fatigue. Vol. 10, Frontiers in immunology. 2019.
23. Tangvarasittichai S, Pongthaisong S, Tangvarasittichai O. Tumor Necrosis Factor-A, Interleukin-6, C-Reactive Protein Levels and Insulin Resistance Associated with Type 2 Diabetes in Abdominal Obesity Women. Indian J Clin Biochem. 2016;31(1).
24. Chen Y, Yu CY, Deng WM. The role of pro-inflammatory cytokines in lipid

metabolism of metabolic diseases. Vol. 38, International Reviews of Immunology. 2019.

25. Maury E, Brichard SM. Adipokine dysregulation, adipose tissue inflammation and metabolic syndrome. Vol. 314, Molecular and Cellular Endocrinology. 2010.
26. Andersson CX, Gustafson B, Hammarstedt A, Hedjazifar S, Smith U. Inflamed adipose tissue, insulin resistance and vascular injury. Vol. 24, Diabetes/Metabolism Research and Reviews. 2008.
27. Köhler CA, Freitas TH, Maes M, de Andrade NQ, Liu CS, Fernandes BS, et al. Peripheral cytokine and chemokine alterations in depression: a meta-analysis of 82 studies. Acta Psychiatr Scand. 2017;135(5).
28. Eyre HA, Air T, Pradhan A, Johnston J, Lavretsky H, Stuart MJ, et al. A meta-analysis of chemokines in major depression. Prog Neuro-Psychopharmacology Biol Psychiatry. 2016;68.
29. Leighton SP, Nerurkar L, Krishnadas R, Johnman C, Graham GJ, Cavanagh J. Chemokines in depression in health and in inflammatory illness: A systematic review and meta-Analysis. Vol. 23, Molecular Psychiatry. 2018.
30. Koo JW, Russo SJ, Ferguson D, Nestler EJ, Duman RS. Nuclear factor-κB is a critical mediator of stress-impaired neurogenesis and depressive behavior. Proc Natl Acad Sci U S A. 2010;107(6).
31. Chatterjee T, De D, Chowdhury S, Bhattacharyya M. Nuclear factor NF-κB1 functional promoter polymorphism and its expression conferring the risk of Type 2 diabetes-associated dyslipidemia. Mamm Genome. 2020;31(7–8).
32. Chen L, Chen R, Wang H, Liang F. Mechanisms Linking Inflammation to Insulin Resistance. Vol. 2015, International Journal of Endocrinology. 2015.
33. Colasanto M, Madigan S, Korczak DJ. Depression and inflammation among children and adolescents: A meta-analysis. Vol. 277, Journal of Affective Disorders. 2020.
34. Hong N, Lin Y, Ye Z, Yang C, Huang Y, Duan Q, et al. The relationship between dyslipidemia and inflammation among adults in east coast China: A cross-sectional study. Front Immunol. 2022;13.
35. Shi J, Fan J, Su Q, Yang Z. Cytokines and Abnormal Glucose and Lipid Metabolism. Vol. 10, Frontiers in Endocrinology. 2019.
36. da Silva Rosa SC, Nayak N, Caymo AM, Gordon JW. Mechanisms of muscle insulin resistance and the cross-talk with liver and adipose tissue. Vol. 8, Physiological

Reports. 2020.
37. Sarno E, Moeser AJ, Robison AJ. Neuroimmunology of depression. In: Advances in Pharmacology. 2021.
38. Kim D, Chung H, Lee JE, Kim J, Hwang J, Chung Y. Immunologic aspects of dyslipidemia: A critical regulator of adaptive immunity and immune disorders. Vol. 10, Journal of Lipid and Atherosclerosis. 2021.
39. Ko SH, Kim HS. Menopause-associated lipid metabolic disorders and foods beneficial for postmenopausal women. Vol. 12, Nutrients. 2020.
40. Bizoń A, Franik G, Niepsuj J, Czwojdzińska M, Leśniewski M, Nowak A, et al. The associations between sex hormones and lipid profiles in serum of women with different phenotypes of polycystic ovary syndrome. J Clin Med. 2021;10(17).
41. Kundakovic M, Rocks D. Sex hormone fluctuation and increased female risk for depression and anxiety disorders: From clinical evidence to molecular mechanisms. Vol. 66, Frontiers in Neuroendocrinology. 2022.
42. Klop B, Elte JWF, Cabezas MC. Dyslipidemia in Obesity: Mechanisms and Potential Targets. Vol. 5, Nutrients. 2013.
43. Loosen PT. Hormones of the hypothalamic-pituitary-thyroid axis: A psychoneuroendocrine perspective. Pharmacopsychiatry. 1986;19(6).
44. Vandoolaeghe E, Maes M, Vandevyvere J, Neels H. Hypothalamic-pituitary-thyroid-axis function in treatment resistant depression. J Affect Disord. 1997;43(2).
45. Bauer MS, Whybrow PC, Winokur A. Rapid Cycling Bipolar Affective Disorder: I. Association with Grade I Hypothyroidism. Arch Gen Psychiatry. 1990;47(5).
46. Jackson IMD. The thyroid axis and depression. In: Thyroid. 1998.
47. Sullivan GM, Hatterer JA, Herbert J, Chen X, Roose SP, Attia E, et al. Low levels of transthyretin in the CSF of depressed patients. Am J Psychiatry. 1999;156(5).
48. Choi JW, Choi HS. The regulatory effects of thyroid hormone on the activity of 3-hydroxy- 3-methylglutaryl coenzyme a reductase. Endocr Res. 2000;26(1).
49. Lam KSL, Chan MK, Yeung RTT. High-density lipoprotein cholesterol, hepatic lipase and lipoprotein lipase activities in thyroid dysfunction – effects of treatment. QJM. 1986;59(2).
50. Mavromati M, Jornayvaz FR. Review hypothyroidism-associated dyslipidemia: Potential molecular mechanisms leading to NAFLD. Vol. 22, International Journal of Molecular Sciences. 2021.

51. Gajewska A, Strzelecki D, Gawlik-Kotelnicka O. Ghrelin as a Biomarker of "Immunometabolic Depression" and Its Connection with Dysbiosis. Vol. 15, Nutrients. 2023.
52. Zou X, Zhong L, Zhu C, Zhao H, Zhao F, Cui R, et al. Role of leptin in mood disorder and neurodegenerative disease. Vol. 13, Frontiers in Neuroscience. 2019.
53. Rojas JM, Bruinstroop E, Printz RL, Alijagic-Boers A, Foppen E, Turney MK, et al. Central nervous system neuropeptide Y regulates mediators of hepatic phospholipid remodeling and very low-density lipoprotein triglyceride secretion via sympathetic innervation. Mol Metab. 2015;4(3).
54. Sharma A, Ren X, Zhang H, Pandey GN. Effect of depression and suicidal behavior on neuropeptide Y (NPY) and its receptors in the adult human brain: A postmortem study. Prog Neuro-Psychopharmacology Biol Psychiatry. 2022;112.
55. Huang Y, Li L, Gan Y, Wang C, Jiang H, Cao S, et al. Sedentary behaviors and risk of depression: a meta-analysis of prospective studies. Vol. 10, Translational Psychiatry. 2020.
56. Crichton GE, Alkerwi A. Physical activity, sedentary behavior time and lipid levels in the Observation of Cardiovascular Risk Factors in Luxembourg study. Lipids Health Dis. 2015;14(1).
57. Guilleminault L, Williams EJ, Scott HA, Berthon BS, Jensen M, Wood LG. Diet and asthma: Is it time to adapt our message? Vol. 9, Nutrients. 2017.
58. Firth J, Marx W, Dash S, Carney R, Teasdale SB, Solmi M, et al. The Effects of Dietary Improvement on Symptoms of Depression and Anxiety: A Meta-Analysis of Randomized Controlled Trials. Psychosom Med. 2019;81(3).
59. Na W, Chung B, Sohn C. A Relationship between Dietary Patterns and Dyslipidemia in Urban-dwelling Middle-Aged Korean Men: Using Korean Genome and Epidemiology Study (KoGES). Clin Nutr Res. 2019;8(3).
60. Asarnow LD, Mirchandaney R. Sleep and Mood Disorders Among Youth. Vol. 30, Child and Adolescent Psychiatric Clinics of North America. 2021.
61. McCall WV, Blocker JN, D'Agostino R, Kimball J, Boggs N, Lasater B, et al. Treatment of insomnia in depressed insomniacs: Effects on health-related quality of life, objective and self-reported sleep, and depression. J Clin Sleep Med. 2010;6(4).
62. Manber R, Edinger JD, Gress JL, San Pedro-Salcedo MG, Kuo TF, Kalista T. Cognitive behavioral therapy for insomnia enhances depression outcome in patients

with comorbid major depressive disorder and insomnia. Sleep. 2008;31(4).

63. Tsiptsios D, Leontidou E, Fountoulakis PN, Ouranidis A, Matziridis A, Manolis A, et al. Association between sleep insufficiency and dyslipidemia: a cross-sectional study among Greek adults in the primary care setting. Sleep Sci. 2022;15.
64. Kathryn Mchugh R, Weiss RD. Alcohol use disorder and depressive disorders. Alcohol Res Curr Rev. 2019;40(1).
65. Huang S, Li J, Shearer GC, Lichtenstein AH, Zheng X, Wu Y, et al. Longitudinal study of alcohol consumption and HDL concentrations: A community-based study. Am J Clin Nutr. 2017;105(4).
66. Park H, Kim K. Relationship between alcohol consumption and serum lipid levels in elderly Korean men. Arch Gerontol Geriatr. 2012;55(2).
67. Walker AJ, Kim Y, Borissiouk I, Rehder R, Dodd S, Morris G, et al. Statins: Neurobiological underpinnings and mechanisms in mood disorders. Vol. 128, Neuroscience and Biobehavioral Reviews. 2021.
68. Giorgi R De, Crescenzo F De, Pesci NR, Martens M, Howard W, Cowen PJ, et al. Statins for major depressive disorder: A systematic review and meta-analysis of randomized controlled trials. Vol. 16, PLoS ONE. 2021.
69. Singh D, Lippmann S. Can statins diminish depression? Prim Care Companion J Clin Psychiatry. 2018;20(1).
70. Tatley M, Savage R. Psychiatric adverse reactions with statins, fibrates and ezetimibe: Implications for the use of lipid-lowering agents. Vol. 30, Drug Safety. 2007.
71. Bao X, Liang Y, Chang H, Cai T, Feng B, Gordon K, et al. Targeting proprotein convertase subtilisin/kexin type 9 (PCSK9): from bench to bedside. Vol. 9, Signal Transduction and Targeted Therapy. 2024.
72. Hasler G. Pathophysiology of depression: Do we have any solid evidence of interest to clinicians? Vol. 9, World Psychiatry. 2010.
73. Edinoff AN, Raveendran K, Colon MA, Thomas BH, Trettin KA, Hunt GW, et al. Selective Serotonin Reuptake Inhibitors and Associated Bleeding Risks: A Narrative and Clinical Review. Heal Psychol Res. 2022;10(4).
74. McIntyre RS, Park KY, Law CWY, Sultan F, Adams A, Lourenco MT, et al. The Association between Conventional Antidepressants and the Metabolic Syndrome. CNS Drugs. 2010;24(9).
75. Stuchtey FC, Block A, Osei F, Wippert PM. Lipid Biomarkers in Depression: Does

Antidepressant Therapy Have an Impact? Healthc. 2022;10(2).

76. Fanelli D, Weller G, Liu H. New serotonin-norepinephrine reuptake inhibitors and their anesthetic and analgesic considerations. Vol. 13, Neurology International. 2021.
77. Richards-Belle A, Austin-Zimmerman I, Wang B, Zartaloudi E, Cotic M, Gracie C, et al. Associations of antidepressants and antipsychotics with lipid parameters: Do CYP2C19/CYP2D6 genes play a role? A UK population-based study. J Psychopharmacol. 2023;37(4).
78. Oakes TM, Katona C, Liu P, Robinson M, Raskin J, Greist JH. Safety and tolerability of duloxetine in elderly patients with major depressive disorder: A pooled analysis of two placebo-controlled studies. Int Clin Psychopharmacol. 2013;28(1).
79. Vos CF, Aarnoutse RE, Op de Coul MJM, Spijker J, Groothedde-Kuyvenhoven MM, Mihaescu R, et al. Tricyclic antidepressants for major depressive disorder: a comprehensive evaluation of current practice in the Netherlands. BMC Psychiatry. 2021;21(1).
80. Lechner K, Heel S, Uhr M, Dose T, Holsboer F, Lucae S, et al. Weight-gain independent effect of mirtazapine on fasting plasma lipids in healthy men. Naunyn Schmiedebergs Arch Pharmacol. 2023;396(9).
81. Recchia F, Leung CK, Chin EC, Fong DY, Montero D, Cheng CP, et al. Comparative effectiveness of exercise, antidepressants and their combination in treating non-severe depression: A systematic review and network meta-analysis of randomised controlled trials. Vol. 56, British Journal of Sports Medicine. 2022.
82. Yu Q, Wong KK, Lei OK, Nie J, Shi Q, Zou L, et al. Comparative Effectiveness of Multiple Exercise Interventions in the Treatment of Mental Health Disorders: A Systematic Review and Network Meta-Analysis. Vol. 8, Sports Medicine - Open. 2022.
83. Schuch FB, Deslandes AC, Stubbs B, Gosmann NP, Silva CTB da, Fleck MP de A. Neurobiological effects of exercise on major depressive disorder: A systematic review. Vol. 61, Neuroscience and Biobehavioral Reviews. 2016.
84. Archer T. Physical Exercise as an Epigenetic Factor Determining Behavioral Outcomes. Clin Exp Psychol. 2015;01(01).
85. Rhee EJ, Kim HC, Kim JH, Lee EY, Kim BJ, Kim EM, et al. 2018 guidelines for the management of dyslipidemia. Korean J Intern Med. 2019;34(4).
86. Kelley GA, Kelley KS. Aerobic exercise and HDL2-C: A meta-analysis of randomized controlled trials. Atherosclerosis. 2006;184(1).

87. Varady KA, St-Pierre AC, Lamarche B, Jones PJH. Effect of plant sterols and endurance training on LDL particle size and distribution in previously sedentary hypercholesterolemic adults. Eur J Clin Nutr. 2005;59(4).
88. Watt MJ, Heigenhauser GJF, Dyck DJ, Spriet LL. Intramuscular triacyglycerol, glycogen and acetyl group metabolism during 4 h of moderate exercise in man. J Physiol. 2002;541(3).
89. Ringseis R, Mooren FC, Keller J, Couturier A, Wen G, Hirche F, et al. Regular endurance exercise improves the diminished hepatic carnitine status in mice fed a high-fat diet. Mol Nutr Food Res. 2011;55(SUPPL. 2).
90. Steensberg A, Fischer CP, Keller C, Møller K, Pedersen BK. IL-6 enhances plasma IL-1ra, IL-10, and cortisol in humans. Am J Physiol - Endocrinol Metab. 2003;285(2 48-2).
91. Starkie R, Ostrowski SR, Jauffred S, Febbraio M, Pedersen BK. Exercise and IL-6 infusion inhibit endotoxin-induced TNF-α production in humans. FASEB J. 2003;17(8).
92. Zheng G, Qiu P, Xia R, Lin H, Ye B, Tao J, et al. Effect of aerobic exercise on inflammatory markers in healthy middle-aged and older adults: A systematic review and meta-analysis of randomized controlled trials. Vol. 11, Frontiers in Aging Neuroscience. 2019.
93. Rose GL, Mielke GI, Durr M, Schaumberg MA. Effect of resistance training on chronic inflammation: A systematic review and meta-analysis. Vol. 4, Translational Sports Medicine. 2021.
94. Despeghel M, Reichel T, Zander J, Krüger K, Weyh C. Effects of a 6 week low-dose combined resistance and endurance training on t cells and systemic inflammation in the elderly. Cells. 2021;10(4).
95. Dowlati Y, Herrmann N, Swardfager W, Liu H, Sham L, Reim EK, et al. A Meta-Analysis of Cytokines in Major Depression. Biol Psychiatry. 2010;67(5).
96. Goldsmith DR, Rapaport MH, Miller BJ. A meta-analysis of blood cytokine network alterations in psychiatric patients: Comparisons between schizophrenia, bipolar disorder and depression. In: Molecular Psychiatry. 2016.
97. Oddy WH, Allen KL, Trapp GSA, Ambrosini GL, Black LJ, Huang RC, et al. Dietary patterns, body mass index and inflammation: Pathways to depression and mental health problems in adolescents. Brain Behav Immun. 2018;69.
98. Parletta N, Zarnowiecki D, Cho J, Wilson A, Bogomolova S, Villani A, et al. A

Mediterranean-style dietary intervention supplemented with fish oil improves diet quality and mental health in people with depression: A randomized controlled trial (HELFIMED). Nutr Neurosci. 2019;22(7).

99. Li X, Chen M, Yao Z, Zhang T, Li Z. Dietary inflammatory potential and the incidence of depression and anxiety: a meta-analysis. Vol. 41, Journal of Health, Population and Nutrition. 2022.
100. Ostan R, Lanzarini C, Pini E, Scurti M, Vianello D, Bertarelli C, et al. Inflammaging and Cancer: A challenge for the mediterranean diet. Vol. 7, Nutrients. 2015.
101. Platania A, Zappala G, Mirabella MU, Gullo C, Mellini G, Beneventano G, et al. Association between Mediterranean diet adherence and dyslipidaemia in a cohort of adults living in the Mediterranean area. Int J Food Sci Nutr. 2018;69(5).
102. Mertens E, Mullie P, Deforche B, Lefevre J, Charlier R, Huybrechts I, et al. Cross-sectional study on the relationship between the Mediterranean Diet Score and blood lipids. Nutr J. 2014;13(1).
103. Magriplis E, Panagiotakos D, Mitsopoulou AV, Karageorgou D, Bakogianni I, Dimakopoulos I, et al. Prevalence of hyperlipidaemia in adults and its relation to the Mediterranean diet: the Hellenic National Nutrition and Health Survey (HNNHS). Eur J Prev Cardiol. 2019;26(18).
104. Giannini C, Diesse L, D'Adamo E, Chiavaroli V, de Giorgis T, Di Iorio C, et al. Influence of the Mediterranean diet on carotid intima-media thickness in hypercholesterolaemic children: A 12-month intervention study. Nutr Metab Cardiovasc Dis. 2014;24(1).
105. Vitale M, Masulli M, Calabrese I, Rivellese AA, Bonora E, Signorini S, et al. Impact of a mediterranean dietary pattern and its components on cardiovascular risk factors, glucose control, and body weight in people with type 2 diabetes: A real-life study. Nutrients. 2018;10(8).
106. Neufcourt L, Assmann KE, Fezeu LK, Touvier M, Graffouillère L, Shivappa N, et al. Prospective association between the dietary inflammatory index and metabolic syndrome: Findings from the SU.VI.MAX study. Nutr Metab Cardiovasc Dis. 2015;25(11).
107. Briguglio M, Vitale JA, Galentino R, Banfi G, Dina CZ, Bona A, et al. Healthy eating, physical activity, and sleep hygiene (HEPAS) as the winning triad for sustaining physical and mental health in patients at risk for or with neuropsychiatric disorders:

Considerations for clinical practice. Neuropsychiatr Dis Treat. 2020;16.

108. Huffman JC, Celano CM, Beach SR, Motiwala SR, Januzzi JL. Depression and cardiac disease: Epidemiology, mechanisms, and diagnosis. Vol. 2013, Cardiovascular Psychiatry and Neurology. 2013.