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Nutrition and late-life depression: etiological considerations

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Abstract

Depression is a debilitating mental disorder that frequently occurs in older adults, especially in those with vascular diseases. Nutritional factors have the potential to decrease the occurrence of late-life depression but have not been adequately studied. Low folate levels, disturbed omega-3 fatty acid metabolism and obesity have been associated with depression, and may be causal factors. Longitudinal studies are urgently needed in order to examine the potential of dietary factors to prevent late-life depression.

Keywords

brain lesion; depression; folate; omega-3; serotonin; vascular

Depression: a significant problem for older adults

Depression is a common and debilitating mental disorder. It is the fourth leading cause of disease burden and the leading cause of years lived with disability, according to the WHO [1]. Depression is accountable for a majority of the almost 900,000 annual suicides worldwide [2]. Prevalence estimates range from 2.7 to 10.1% in the older adult community [3,4] but are higher among unhealthy individuals and those in nursing homes [1]. Healthcare costs are increased by half in those with late-life depression, and this discrepancy is not accounted for by mental healthcare expenses [5]. This relationship may be partially explained by the adverse effects of depression on medical health and mortality. Depression increases one's risk of vascular diseases [6,7] and may also promote hip fractures [8]. Depression also causes impaired psychosocial and cognitive functioning [1]. Taken together, these sequelae can have an enormous impact on the emotional and socio-economic wellbeing of caregivers, relatives and the community. Lost productivity, financial costs and a diminished quality of life for family members may follow [1]. The stigma of mental illness may lead to humiliation, isolation and unemployment [1].

Late-life depression, or depression in individuals aged 60 years and older, has a more malignant course than depression in early or middle adulthood, as characterized by the increased risk of relapse, decreased remission and the increased likelihood of progression to dementia or death [9–11]. The proper assessment of late-life depression may be hindered by comorbid medical

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conditions, effects of polypharmacy, concurrent grieving and the mistaken tendency for clinicians to view depression as a normal occurrence in old age.

Characteristic symptoms of depression are sadness, feeling down or blue and being less interested in usual activities. Low mood occurs persistently, unlike the daily mood fluctuations that most individuals experience. This dysphoria may or may not be associated with a negative situation or event. In addition to mood changes, depressed individuals have vegetative and ideational symptoms. Vegetative symptoms encompass energy and appetite disturbances. Ideational symptoms include feelings of guilt and hopelessness, as well as suicidal thoughts. Diagnostic criteria are listed in Box 1 [12].

Depression may be diagnosed by a primary care practitioner, psychologist, psychiatrist or other healthcare professional. Unfortunately, approximately half of depression cases are undetected and untreated [13].

Box 1

Diagnosis of major depression

Five of the following symptoms are required for at least 2 weeks:

- Feeling depressed, sad or blue*
- Loss of interest or pleasure*
- Increased or decreased sleep
- Increased or decreased appetite with weight change
- Feeling agitated, restless or slowed down
- Feelings of worthlessness or excessive guilt
- Low energy
- Difficulty concentrating
- Feeling that life is not worth living or suicidal behaviors

*One of these is required.

Etiology of late-life depression

Etiological factors need to be elucidated in order to provide the opportunity to prevent late-life depression. Prevention is obviously preferable to treatment-based approaches, particularly given depression's recurring nature and the fact that treatment is not successful in many cases, characterized by a lack of remission and continued symptomatology [14]. Factors that affect one's risk of depression include gender, socio-economic status, social support, stress, genes, medical illnesses and vascular brain changes (hyperintense regions seen on MRI that are caused by ischemia [15]). Nutrition is another critical factor in the etiology of depression and is particularly important given that neurological and other biological factors (including medical comorbidity and hypothalamic–pituitary–adrenal dysregulation) may figure more prominently in late-life than in early-life depression [9,16]. This review will focus on only a few nutritional factors, namely ones that have been examined in multiple late-life depression studies and that relate to vascular health. These factors are folate, vitamin B_{12}, omega-3 fatty acids and obesity. Nutrients that are associated with depression in very few studies, those only examined in early-

*One of these is required.

life depression and those that are less related to vascular health (such as tryptophan) are not addressed in this review.

Numerous vascular risk factors and diseases, including hypertension, atherosclerosis, heart disease, cerebrovascular disease, stroke, diabetes mellitus and ischemic brain lesions, are more common in older depressed subjects than in younger depressed subjects [9,17,18]. Depressed individuals are at a greater risk of heart disease and diabetes, and, conversely, these medical conditions increase the risk of depression [19–21]. Importantly, individuals with both depression and comorbid vascular disease are at a greater risk for poor outcomes; for example, myocardial infarction patients with comorbid depression are four times more likely to die within 18 months compared with patients without depression [22]. The role of vascular risk factors and, in particular, ischemic brain lesions has led to the development of the vascular depression hypothesis, which states that cerebrovascular disease may precipitate, predispose or perpetuate late-life depression [16,23]. In this situation, damage occurs to the cerebral vasculature, particularly to the small cerebral vessels, causing ischemia and brain lesions, which may promote depression if they impact the mood regulation pathways.

In order to influence depression risk, dietary factors must alter the brain biochemistry or structure, or both. Diet may influence depression risk by directly affecting brain health, such as by changing neurotransmitter levels or membrane fluidity, or by promoting vascular illnesses that lead to brain changes [24–26]. Some diet-related factors such as elevated homocysteine levels may influence brain health both directly and indirectly via vascular pathways [24].

In the nervous system, neurotransmitter metabolism, myelin production and membrane fluidity are critical [27]. Serotonin and other neurotransmitter systems are dysregulated in depression, and the regulation of serotonin metabolism has become a major target for pharmacotherapy [27]. Nutrient intake and energy balance can greatly impact all of these brain factors as well as vascular health. Folate, omega-3 fatty acids and obesity have been studied more than other dietary factors in depression and are believed to influence both brain and vascular health.

Candidate nutritional factors

B vitamins

Of all the micronutrients, B vitamins may be the most important to the etiology and progression of late-life depression. They are certainly the most studied, especially folate and vitamin B_{12}. Both vitamins affect brain health through their roles in neurotransmitter synthesis, myelin formation and energy metabolism [28].

Folate

Folate, or vitamin B_9, occurs naturally in orange juice, strawberries, green vegetables, beans, eggs and whole grains among other foods [28]. The synthetic oxidized form of folic acid is found in dietary supplements and fortified refined grain products (in the USA) [28]. The US Government mandated folic acid fortification of refined grain products in 1998 in an effort to reduce the occurrence of neural tube defects. Other countries have instituted similar fortification programs. A steady dietary supply of folate is required since there are few body stores [28]. Folate may influence depression through its many functions in the brain and throughout the body. These functions include methylation reactions that are necessary for the production of neurotransmitters, phospholipids, *S*-adenosyl methionine (the sole methyl donor of the nervous system) and for the conversion of homocysteine to methionine [24]. Folate is required for the synthesis and release of serotonin and other neurotransmitters, and folate deficiency has been demonstrated to cause decreased serotonin synthesis in humans and rats [29].

A folate–depression relationship was reported as early as the 1960s when a study of psychiatric inpatients found that half had low folate levels [30]. Causality is unclear, not only because the study was cross-sectional but because many of the low-folate subjects were alcoholics or had used folate-diminishing medications [30]. Another hospital study found that depressed subjects had lower folate levels than either nondepressed psychiatric patients or nonpsychiatric patients [31]. Folate levels were inversely related to depression scores. Other clinical studies have consistently associated low folate status with depression and depression severity [32–36]. Unfortunately, studies have not examined causality and many have failed to adequately control for other depression risk factors. Researchers have speculated that folate deficiency is secondary to depression [32,37], perhaps owing to its increased utilization during a depressive episode [34].

Cross-sectional studies of older adult populations have examined the relationship between folate status (levels) and late-life depression. Three studies found an association between depression symptoms and low serum folate levels [38–40], while five found no significant association between folate status and depression [41–45]. Studies varied significantly in size (n = 66–5984), location (Europe, Australia and North America), depression assessment and age, although no specific factors appear to differentiate the significant and nonsignificant findings. The only longitudinal study of folate status found that Korean elders (aged > 65 years) with low folate levels had an increased risk of incident depression over a 2–3 year follow-up, after controlling for age, sex, education, Mini-Mental State Examination (MMSE), smoking, alcohol, physical activity, vascular risk, serum creatinine levels, vitamin supplementation, vitamin B_{12} and homocysteine [46].

Studies examining dietary the intake of folate, rather than folate levels, have generally supported a role for folate in depression. One cross-sectional examination of older adults (aged > 60 years) found that folate intake was significantly lower in individuals with a depression diagnosis than in comparison subjects, after controlling for age, sex, race, education and total energy intake [47]. Interestingly, this finding was specific to naturally-occurring folate and was not explained by the presence of vascular disease. There were no significant differences between groups in fortified folic acid, supplemental folic acid or total folate intake. Natural folate may be more advantageous than folic acid, perhaps because folic acid must undergo an additional reduction reaction before it can cross the blood–brain barrier. Another possibility is that natural folate consumption may be associated with other beneficial elements in the diet, including fruits and vegetables. Two other cross-sectional studies examined dietary folate and depressive symptoms in adults, one exclusively in older men and the other in only a minority of elders. Low folate intake was not associated with depression symptoms in the Zutphen Elderly Study of men [48]. This study excluded subjects with comorbid cardiovascular disease at the time of depression symptom assessment, which may have lessened the likelihood of detecting a folate-moderated vascular effect on depression. A study of adults in Japan (aged 21–67 years) found that dietary folate was only related to a lower prevalence of depression in men, which may be related to the fact that most women in the study consumed adequate folate [49]. These findings were due to differences in naturally-occurring folate, since fortification did not occur and dietary supplements were not included in the analyses owing to the small number of consumers. Only one longitudinal dietary study has been conducted, which found that lower dietary folate was associated with incident depression in middle-aged men [50]. In effect, this Finnish study again demonstrated a relationship with natural folate since its participants did not consume folic acid from either fortified foods or dietary supplements.

Issues to consider when interpreting the literature on folate include homocysteine, vitamin B_{12} and genetic polymorphisms. Homocysteine is believed to be both cardiotoxic and neurotoxic, and may become elevated in the absence of adequate folate [24]. Studies have shown both cross-sectional and longitudinal relationships between elevated homocysteine

levels and late-life depression [40,46,51]. One study of older adults found a positive association between homocysteine levels and Beck depression scores, after controlling for folate levels and other covariates [52]. Low folate levels in previous studies may have been a marker for, or confounded with, elevated homocysteine. Vitamin B_{12}, as discussed in next section, interacts metabolically with both folate and homocysteine, and may also be related to depression.

One additional factor to consider when interpreting folate–depression studies is that genes for folate metabolism have been associated with depression. In particular, polymorphisms in methylenetetrahydrofolate reductase (*MTHFR*) have been implicated. MTHFR catalyzes an irreversible reaction that is the rate-limiting step in folate metabolism. Decreased MTHFR activity is related to poor folate status. The *MTHFR* 677C>T polymorphism (cytosine replaced by thymine at nucleotide 677) has been associated with low folate levels. Some studies have found that TT homozygotes are more likely to have current or prior depression [44,53–55]. A second *MTHFR* polymorphism (1298A>C) has also been linked to depression [56]. Conflicting results from epidemiological studies of folate and depression may have resulted from genetic variability in the population samples.

Vitamin B_{12}

Vitamin B_{12}, also termed cobalamin, is found in foods of animal origin and dietary supplements. Food intakes tend to be adequate, except among vegans, and the liver typically stores a 5–7-year supply [57]. However, older adults often have impaired utilization of dietary cobalamin owing to changes in their gastric environment and loss of intrinsic factor that is necessary for absorption [57]. For this reason, studies seeking to examine associations between vitamin B_{12} and depression always assess vitamin status (levels) rather than intake. Vitamin B_{12} functions in folate metabolism, serotonin synthesis, myelin sheath formation and as a coenzyme for fatty acid and amino acid oxidation [43]. Vitamin B_{12} deficiency can lead to permanent neurological damage, even in the absence of macrocytic anemia, the classic sign of vitamin B_{12} deficiency [58]. Owing to the known neurological effects of vitamin B_{12} deficiency-induced pernicious anemia, cobalamin has been investigated for its role in mental disorders including depression and dementia [59].

Epidemiological investigations have reported conflicting results with regard to vitamin B_{12} and depression. A study of older women with physical disabilities living in Baltimore (MD, USA; n = 700) showed that those with a vitamin B_{12} deficiency were more likely to be severely depressed than the nondeficient participants (odds ratio: 2), after controlling for health status and sociodemographics [43]. The prevalence of depression was high (32%) as expected owing to the presence of functional disabilities. A Rotterdam (The Netherlands) study of vitamin status among older individuals (n = 806) also found that vitamin B_{12} deficiency was associated with depression, after controlling for cardiovascular disease and functional disability [45]. By contrast, three epidemiological studies failed to find a significant association between cobalamin levels and depression (the Survey in Europe on Nutrition and the Elderly, a Concerted Action [SENECA] project population study, the Hordaland Health Study and an Australian community study) [38,41,44]. The distinction between cobalamin deficiency (using cut-off points) and cobalamin status (modeled as a continuous variable) may be of crucial importance. The two studies measuring vitamin B_{12} deficiency found an association with depression, while those examining vitamin B_{12} levels did not find an association with depression. In addition to the deficiency/status question, conflicting results may be due to differences in vitamin B_{12} assessment methodology and diagnostic criteria used to define vitamin B_{12} deficiency.

Only one longitudinal study has evaluated vitamin B_{12} and depression – the same project that examined folate status in Korean elders. As with folate, this study found that those with low

levels at baseline had an increased risk of incident depression over a 2–3-year follow-up, after controlling for numerous covariates including homocysteine and folate [46].

Dietary fat

The amount and types of fats consumed may be important factors for depression. Fats are separated into four categories: saturated, transunsaturated, monounsaturated and polyunsaturated, with the latter being subdivided into omega-6 and omega-3 fatty acids (based upon the location of their double bonds). Intake of saturated fat, a known promoter of vascular disease, has been found to be associated with depression [60–62]. Omega-3 polyunsaturated fatty acids have been studied extensively in depression. Omega-3 fatty acid intakes as well as the ratio of omega-3:omega-6 fats are believed to be important determinants of brain and cardiovascular health. A dietary decline in both omega-3 fatty acids and the omega-6:omega-3 fatty acid ratio over the past century has been blamed for the increase in many illnesses, including depression [63].

Omega-3 fatty acids

Omega-3 fatty acids are found in salmon, mackerel and other cold water fish, as well as flaxseed, walnuts and canola oil. Docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) are long-chain omega-3 fatty acids that are present in fish oils, seafood, algae and fortified foods, while α-linolenic acid (ALA) is derived from plant sources. ALA is converted to DHA and EPA, but because this process is inefficient in humans, some nutritionists recommend consumption of DHA and/or EPA. DHA is the omega-3 fatty acid that has been studied most extensively in relation to brain health. A total of 3% of dry brain weight is DHA, and levels are higher in gray matter than white matter [26]. There are many potential mechanisms, including brain and vascular effects, that could explain a protective relationship between omega-3 fatty acids and late-life depression. Omega-3 fatty acids are important for serotonin metabolism, membrane fluidity, cellular regulation and protection from oxidative stress, and they serve to decrease triglycerides, blood pressure, inflammation and platelet aggregation [26]. Omega-3 fatty acid deficiency is characterized by many of the same traits as depression, including altered neurotransmission, decreased cerebral blood flood, increased proinflammatory cytokines and neuronal atrophy [26]. Rats that were provided with an omega-3 fatty acid-deficient diet had lowered brain levels of DHA and increased depressive behaviors [64]. Rats and pigs who were given omega-3 fatty acid supplements during early life exhibited higher levels of serotonin, one of the neurotransmitters that is dysregulated in depression [65,66].

Studies of fish consumption were the first to implicate omega-3 fatty acids as being potentially protective for depression. An ecological study compared nations in terms of depression and fish consumption and found that the two were significantly negatively correlated [67]. The prevalence of depression varied by 60-fold across the countries that were included in the study. This variation was similar to the differences seen in coronary disease mortality, which may indicate that heart disease and depression are influenced by the same dietary factors. Two cross-sectional population studies in Finland measured depression and fish intake, but few older adult subjects were included. The first study found that frequent fish consumption (two or more servings per week) was correlated with a reduced risk of depressive symptoms (odds ratio: 0.6) compared with infrequent consumption, after controlling for age, sex, marital status, education, employment status, disability, region, income, general health, smoking, alcohol and coffee consumption, and physical activity [68]. The other study examined the Northern Finland 1966 Birth Cohort and determined that rare fish consumers (one or fewer servings per month) were at an increased risk of depression (odds ratio: 2.6) compared with more frequent consumers, after controlling for BMI, serum cholesterol and socio-economic status [69]. This relationship

was only significant among women. A second logistic regression model controlled for smoking, ethanol intake, physical inactivity and marital status and yielded similar results.

The assumption has been made that omega-3 fatty acids are responsible for the relationships found between seafood intake and depression. Therefore, dietary omega-3 fatty acids have been examined for their role in depression; several of these studies have included, or focused exclusively on, older adults. Unexpectedly, most of these studies failed to find a significant association between depression and omega-3 fatty acid intake in multivariable models. Only a small population study performed in The Netherlands (n = 332) found that older adults who consumed more omega-3 fatty acids were less likely to have depressive symptoms [70]. Cross-sectional studies in Australia, Finland and the UK demonstrated no significant relationship between the dietary intake of omega-3 fatty acids and either depression or depressive symptoms (n = 29, 133, 2982 and 755, respectively) [71–73].

Omega-3 fatty acid levels from plasma and adipose tissue rather than dietary intake have also been investigated for their association with depression. Unfortunately, most of these studies did not also include dietary-intake measures, making it difficult to distinguish dietary deficiencies from metabolic disturbances. In addition, few of these studies included older adult subjects. A small clinical study found lower omega-3 levels in the phospholipids and cholesterol esters of those with depression than in control subjects [63]. Along with other measures, this result was considered indicative of activation of the inflammatory response system, which might lead to increases in lipid peroxidation, neuronal membrane damage and disturbed serotonin metabolism. In Crete (Greece), a study of older adults (aged 80–96 years) demonstrated an inverse relationship between adipose tissue omega-3 fatty acids, an indicator of long-term intake, and depression [74]. The omega-6:omega-3 fatty acid ratio has also been found to be associated with depression, including in a study of older postmyocardial infarction patients [63,75].

Depression severity and biomarkers have also been examined in relation to omega-3 fatty acid levels. The Bordeaux (France) portion of the Three-City Study found that higher plasma levels of EPA were associated with lower depressive symptomatology, especially among individuals taking an antidepressant [76]. Low plasma DHA levels have been demonstrated to predict low levels of 5-hydroxyindoleacetic acid (5-HIAA), a metabolite of serotonin [77]. Both depression and suicidal behavior have been linked to low levels of 5-HIAA [78,79]. Major depression patients have shown a negative relationship between omega-3 fatty acid levels and Hamilton Depression Scale scores [80]. The omega-6:omega3 fatty acid ratio was positively associated with depression scores. Interestingly, these correlations were not explained by dietary intake [63,80].

In conclusion, omega-3 fatty acid metabolism may be altered in individuals with depression, but the origin of this dysregulation is uncertain. Longitudinal research is required in order to ascertain whether altered fatty acid metabolism leads to depression, is the result of depression or is caused by a third factor. Dietary omega-3 fatty acids may or may not be fundamental to lowered physiological levels of omega-3 fatty acids in depressed individuals. However, it is likely that omega-3 fatty acid supplementation may be used to correct such imbalances. Fish consumption may be protective but, given the negative findings for dietary omega-3 fatty acids, other nutrients in fish may help to explain this relationship. To date, studies of omega-3 fatty acids, fish consumption and late-life depression have been cross-sectional.

Energy balance & weight

Weight loss and weight gain are known symptoms of depression; however, it is uncertain whether these factors are etiologically related to depression. Unfortunately, most of the studies that have examined weight loss and depression have been cross-sectional and, therefore, it is

not possible to determine which came first. The assumption made in many studies is that these weight changes are actually the result of depression, but this cannot be temporality confirmed without longitudinal investigation. Given the heterogeneity of depression subtypes, both weight loss and weight gain may affect the development of depression. There is also a possibility that a third factor may be promoting both depression and weight change.

Depression is considered to be the primary explanation for weight loss in the elderly and weight loss is common among depressed individuals [81]. Decline in weight is of special concern for older adults since they are already at a higher risk of nutritional inadequacy. Underweight individuals are more likely to report depressive symptoms [82]. However, recent studies have implicated weight gain and obesity for their roles in late-life depression.

Obesity

Obesity has been correlated with depression and may be etiologically important via a variety of mechanisms. Obesity is a condition characterized by weight-loss dieting behaviors, low physical activity, vascular risk and physical impairment, all of which have been independently associated with depression risk [83–86]. Dieting itself was first proposed by Ross in 1994 as an explanatory factor to link obesity and depression [85] and recent research has supported this notion. Animal studies have shown that chronic food restriction may lead to depressive behaviors via dysregulation of the serotonin system [87] and that a history of caloric restriction and weight loss is associated with neurochemical changes that hinder mood regulation [88]. The use of some appetite suppressants has also been associated with depression in humans [89].

Epidemiological studies of depression and obesity have measured obesity indirectly using BMI instead of assessing true adiposity. Cross-sectional studies have yielded conflicting results, generally along Eastern–Western societal lines. Two studies in Asia found that BMI was negatively associated with depression. Obese older adults in China (n = 56,167) were found to be 20% less likely to suffer from depression [90]. A higher BMI was also found to be associated with fewer depressive symptoms in the Singapore Longitudinal Aging Study (n = 2604) [91]. By contrast, studies performed in Western countries have found a positive association between obesity and depression, including two US studies, a Canadian study and an Australian study. A US health plan study of women aged 40–65 years (n = 4641) found that moderate and severe depression increases with BMI, and that obesity increases with depression [92]. Almost 60% of women with moderate or severe depression were obese, while 26% of moderately obese (BMI > 35) women had moderate or severe depression. The National Health and Nutrition Examination Survey (NHANES) for 2005–2006 assessed 1857 women, 19% of whom were 65 years or older, and determined that both the presence and severity of obesity were associated with depression [93]. In Germany, depressed adults in the Munich Antidepressant Response Signature Study had significantly higher BMI scores than healthy controls [94]. The Stirling County Study, a community study in Canada, found no significant association between obesity and depression, although it did show that depression among obese subjects was more severe than in nonobese subjects [95]. Depression severity was characterized by longer episodes, a larger number of episodes and greater preoccupation with death.

A number of factors may explain the conflicting findings of cross-sectional studies, including differences in age and sex across the studies, genetic differences, cultural factors and differential effects of elevated BMI. Societal pressures to be thin and the stigma of obesity predominates in Western societies and may lead to poor body image, underemployment and other problems, especially among women. Eastern cultures tend to be less critical, if not admiring, of excess adiposity. This cultural difference may explain support of the ‘Jolly Fat’ hypothesis [96] in some Asian populations, while Western countries often show the opposite effect.

Two prospective studies help to resolve the question of the role of obesity in late-life depression. The Alameda County Study (CA, USA), which included 1886 adults over the age of 50 years, found that baseline obesity, defined as BMI levels greater than or equal to 30, increased depression risk by twofold during the 5-year follow-up, after controlling for age, sex, education, marital status, social support, life events, medical illnesses and functional limitations [97]. Baseline depression did not increase the risk of developing obesity. The Health in Men Study (HIMS) in Perth, Australia, followed 12,066 older adult men for up to 10 years and determined that baseline obesity (BMI $\geq$ 30) increased the risk of depression by 31% compared with nonobese men [98].

In addition to obesity, intra-abdominal fat (I-AF) in particular has been linked with depression. This central adiposity is considered to be an especially powerful vascular risk factor [99]. I-AF was measured with a computed tomography (CT) scan in two small studies of depressed subjects. Depressed women demonstrated a greater amount of I-AF than controls in one clinical study [100]. Surprisingly, most of the depressed subjects were close to the ideal body weight, indicating that depression may be associated with I-AF abnormalities, as well as being associated with obesity. The second study followed older adults for up to 2 years and showed that depressed subjects accumulated more I-AF than nondepressed individuals [101].

A preponderance of evidence suggests that obesity is etiologically related to late-life depression, particularly in non-Asian countries. This is particularly concerning given the obesity epidemic, the aging of the population and the overlap between vascular disease and late-life depression [102]. Some investigators consider depression to be a component or consequence of the metabolic syndrome, of which abdominal adiposity is one diagnostic trait. The HIMS found that metabolic syndrome at baseline increased the risk of depression by 137% [98]. Perhaps common factors such as poor diet and inflammation, which are both associated with obesity, promote both metabolic syndrome and depression.

Conclusion & future perspective

As with physical disorders, mental disorders are likely to be influenced by nutrition; however, much less research has been carried out on the impact of nutrition on mental disorders, particularly longitudinal work. Given that diet is more amenable to modifications than some other risk factors for depression, this oversight should be corrected. In addition to the paucity of studies, the quality of research has been sub-optimal in the area of nutrition and depression. Many studies inadequately assess either diet or depression, with the latter often being identified by the presence of one or two symptoms rather than by a diagnostic interview or a more lengthy questionnaire. Accurate dietary assessment is difficult in the best of circumstances, but studies of late-life depression are additionally hindered by the cognitive impairment of subjects, dietary changes that occur during a depressive episode, use of medications that alter eating behaviors and concerns regarding subject burden (owing to the time and strain involved with additional assessments).

Late-life depression is a serious and debilitating condition. Nutritional modification may be one path toward depression prevention. In particular, folate, omega-3 fatty acids and obesity may be etiologically related to late-life depression through their effects on vascular and brain health. Dietary changes in the past century, including a reduction in omega-3 fatty acid intake and an excess consumption of energy, may have skewed human populations towards late-life depression and poor mental health. Longitudinal studies are needed in order to examine these relationships. Future studies must involve interdisciplinary collaborations and incorporate quality measures of diet, nutrient metabolism, depression and vascular illnesses.

With adequate research funding and attention, a clearer picture will hopefully emerge that causally links diet with late-life depression. In the next 10–20 years, it may be possible to reduce the prevalence of late-life depression through prudent dietary recommendations. Given the current trends in obesity, population aging and astronomical increases in healthcare costs, preventive approaches will be critical for promoting mental health in seniors.

Executive summary

Depression: a significant problem for older adults

- Depression is a serious and debilitating problem for older adults.
- Dietary factors that affect brain health, either directly or indirectly (via vascular mechanisms), may be related to depression etiology.

Candidate nutritional factors

- Obesity may lead to depression.
- Omega-3 fatty acid metabolism may be disturbed in depression.
- Folate may be protective for late-life depression through its beneficial effects on vascular and nervous system health.

Future perspective

- Nutritional factors are critical elements of a prevention-based approach to late-life depression.
- The aging of the population combined with the current obesity epidemic and poor dietary habits predict a disastrous increase in the occurrence of late-life depression, with resultant broad societal costs.
- Longitudinal studies are urgently needed in order to identify causal nutritional factors of depression, the mechanisms by which these factors influence depression, and to confirm the success of dietary modifications in preventing late-life depression.

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