Clinical overview

Lifestyle management of unipolar depression

Berk M, Sarris J, Coulson CE, Jacka FN. Lifestyle management of unipolar depression.


Method: A search of pertinent literature was conducted up to August 2012 in the area of lifestyle factors and depression. A narrative review was then conducted.

Results: There is evidence that level of physical activity plays a role in the risk of depression, and there is a large and validated evidence base for exercise as a therapeutic modality. Smoking and alcohol and substance misuse appear to be independent risk factors for depression, while the new epidemiological evidence supports the contention that diet is a risk factor for depression; good quality diets appear protective and poor diets increase risk.

Conclusion: Lifestyle modification, with a focus on exercise, diet, smoking and alcohol, may be of substantial value in reducing the burden of depression in individuals and the community.

Clinical recommendations

- Lifestyle factors, such as poor diet, sedentary lifestyle, smoking and substance abuse, contribute to depression risk, and these factors are interactive and mutually reinforcing.
- Exercise has a validated evidence base as a therapeutic modality.
- While there is yet little trial evidence to support smoking cessation or dietary advice in depression management, the precautionary principle would support both.

Additional comments

- Attention to lifestyle factors additionally addresses common medical comorbidities.
- The contemporary clinical management of depression has a binary focus on medication and psychotherapy.
- Quality trials are required regarding both the efficacy of lifestyle interventions and their implementation at a health systems level.

Introduction

The clinical management of depression has had a binocular focus on medication (1) and psychotherapy (2) and tends to largely neglect the role of potentially reversible lifestyle factors in the genesis and management of depression. In practice, biopsychosocial models frequently distil to selective serotonin reuptake inhibitors (SSRIs) and cognitive behaviour therapy (CBT). This is despite the existence of a large and robust evidence base for insufficient physical activity (PA) and alcohol and substance misuse as key risk factors for depression, and a rapidly growing one for factors such as diet, smoking, and exposure to green space (nature). Indeed, this binocular focus may be associated with the poor response to treatment that is extensively documented (3, 4) and is concordant...
with these relevant operative and active lifestyle factors not being addressed.

While there are many theories regarding the aetiology of depression, the disorder is known to be influenced by social, environmental, psychological, behavioural, genetic, hormonal, immunological, biochemical and neurodegenerative factors (5–7). While many of these factors are immutable, some are open to modification and could provide the basis of practical interventions for the management of depression. Specifically, many of these variables are influenced by lifestyle factors, which play a role in the aetiology of depression (8–11). In this study, we will assess the literature on diet, exercise, smoking, alcohol misuse and green space. While clearly playing a role, other lifestyle and social factors such as social networks, peer support, economic and health systems and substance use are beyond the scope of this study (12–15).

Aims of the study

This paper aims to address key lifestyle factors that are linked with depression risk and tie the evidence base into clinical recommendations for a broader and more individualised management plan.

Material and methods

A range of databases (PubMed, Scopus, Web of Science and The Cochrane Library) were searched up to August 2012. Each author contributed to an area of their respective expertise (MB and CC: smoking and alcohol; JS: PA and exercise; FJ: nutrition and diet). The database search focused on key literature for lifestyle modification involving PA, exercise, diet and restriction of alcohol, and smoking. As a narrative inclusive review was conducted, the studies included a range of evidence (from epidemiological to human clinical studies, and meta-analyses and systematic reviews). The literature reviewed was restricted to papers written in English. The term ‘significant’ was applied to results with a P value of <0.05.

Results

Physical activity and exercise

Industrialisation, urbanisation and globalisation have shaped society in the previous century and have dramatically reduced the amount of PA that the average person undertakes. Our lifestyles are increasingly sedentary, with a lack of PA, particularly for those living in urban centres currently recognised as a major health problem worldwide (16). Epidemiological studies consistently suggest that adequate PA is associated with fewer depressive symptoms, while physical inactivity may be a risk factor for the development of depressive symptoms (17–22). This may be true at both ends of the lifespan. Jacka et al. (23) have shown that regular PA in childhood is associated with reduced risk of developing depression in adulthood, even after adjusting for adult PA. Pasco et al. (24), in counterpoint, has shown that higher levels of habitual PA reduce the subsequent risk of developing de novo depression in elderly people. However, not all evidence supports a direct causal relationship between PA and lower depressive symptoms. De Moor et al. (25) performed genetic modelling in a large population-based longitudinal twin study to assess the relationship between PA level and depressive symptoms in physically active and inactive twins. They reported, in both group and within-individuals analyses, that a greater level of PA did not predict a reduction in depressive symptoms, suggesting that genetic factors may influence both a tendency to exercise and a reduced risk of depression. The relationship between PA and depression may also be context specific; studies have noted that an inverse relationship exists only between leisure-time exercise and depression, with no relationship observed between workplace PA and depression (26).

While evidence regarding a direct causal relationship between increased PA and prevention of depression is equivocal to date, exercise appears to be an effective mood elevator (27–29). Exercise is also a relatively cheap and safe intervention that has been shown to provide a range of physical and mental health benefits (30). Aside from providing marked beneficial neuroendocrine effects, exercise also increases self-esteem and self-efficacy (via activity scheduling and attainment of goals), which are important psychological effects for people who are depressed (31). Furthermore, engaging in exercise may have supplementary beneficial effects of increased social engagement and enhanced body image from weight management (31).

Inflammatory cytokines, oxidative stress, neurotrophins and neurogenesis are thought to be key pathways in the evolution of mood disorders (32, 33). In this context, exercise provides various biological effects via multiple mechanisms seen in animal models, including increased levels of brain-derived neurotrophic factor (BDNF) (8, 34) and enhanced neurogenesis (35). Modulation of monoamine systems has also been observed, with increased expression of serotonin in animal models as a result of increased PA (36), and this is theorised to explain much of the antidepressant effect of exercise (29). A reduction in oxidative stress and

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inflammatory cytokines has also been found to occur as a result of exercise (10), and this immunological effect may reduce depressed mood via effects on the psychoneuroimmunological nexus (37). While exercise can produce an acute increase in cortisol if the overload is excessive and/or appropriate nutritional intake does not accompany the exercise session, long-term effects of regular exercise may assist in regulating the neuroendocrine axis and produce a normalisation of cortisol levels (10). Human studies have also documented that acute exercise increases circulating endorphins, promoting mood elevation and increasing the pain threshold (38).

Clinical evidence

A recent Cochrane review (updated from 2009) included 32 studies (n = 1858) involving exercise for the treatment of researcher-defined depression (39). From these studies, 28 RCTs (n = 1101) were included in a meta-analysis revealing an effect size of −0.67 (95% CI: −0.90, −0.43) in favour of exercise over standard treatment or control. However, only four trials (n = 326) with adequate allocation concealment, blinding and ITT analysis were located, resulting in a more modest effect size in favour of exercise of −0.31 (95% CI: −0.63, 0.01). Pooled data from seven trials (n = 373) with long-term follow-up data also found a small clinical effect in favour of exercise of −0.39 (95% CI: −0.69 to −0.09). Further to this finding, Krogh et al. (40) found no significant long-term effect in a meta-analysis of five pooled studies. However, they did find an association between exercise intensity and duration, and improved clinical effect, thus it is possible that participants in longer-term studies may lack the motivation of shorter-term interventions.

Not all individual studies are in favour of exercise. A recent methodologically rigorous three-arm trial (DEMO study) by Krogh et al. (41) examining differences between a 4-month intervention of either strength training, aerobic exercise or relaxation on 165 participants with unipolar depression, reported no beneficial impact on depression symptoms for strength training or aerobic exercise compared with the relaxation condition. Results did, however, reveal that the strength training group had significantly fewer days off sick than relaxation group, thereby suggesting that regular exercise may be useful in maintaining work capacity. The use of relaxation as an ‘inert control’ can be questioned as this has been shown to be an effective intervention. A Cochrane review and meta-analysis by Jorm et al. (42) of 11 trials using relaxation techniques vs. control (wait list, no or minimal treatment) found that self-rated depressive symptoms were significantly reduced with an effect size of −0.59 (95% CI: −0.94, −0.24), although clinician-rated outcomes were non-significant.

Alternative forms of exercise

Non-mainstream forms of exercise, such as yoga and Tai Chi, also comprise a developing evidence base. A review documenting five RCTs using several types of yoga to treat depression found that, compared with various controls (relaxation, no treatment), and positive controls (electroconvulsive therapy and imipramine), yoga significantly reduced symptoms of depression in each of the five studies (43). However, while the studies reviewed all reported positive results, the methodologies used and the reporting were poor, thereby no firm conclusion can be reached. Tai Chi has also been documented to have beneficial physical and mental effects and often has an application in older persons as it is a gentle exercise (44, 45). A recent review and meta-analysis by Wang et al. (46) of nine RCTs (n = 479) reported that Tai Chi significantly reduced depressive symptoms over control (Hedge’s g = 0.48, 95% CI: 0.17, 0.78). Marked heterogeneity was found due to inclusion of one study with an effect size of 2.32; however, when this study was removed, results maintained statistical significance.

Specific populations

Aside from beneficial effects of PA and exercise in clinical populations (47), several studies have observed benefit in specific populations. A recent meta-analysis of exercise for sedentary patients with a chronic illness, involving 90 RCTs (n = 10 534), reported a modest effect size for reducing depressed mood, d = 0.30 (95% CI: 0.25, 0.36) (48). A Cochrane review (49) of exercise in an adolescent and child population (up to age 20) found five studies that showed a statistically significant difference in favour of the exercise group on depression outcomes, with a moderate effect size of −0.66 (95% CI: −1.25, −0.08). However, the authors noted that trials were generally of low methodological quality, and in an analysis of three studies involving children, no significant effect was found. Systematic reviews of clinical trials in an older population found four trials in people with clinical depression or dysthymia (50, 51). Three of these studies had a non-exercise control group, and all found significant benefits from exercise, with the fourth finding equivalent effects to the antidepressant sertraline.
Exercise in postnatal depression is an intriguing therapeutic option, as breastfeeding mothers should avoid medication where possible. A review and meta-analysis by Daley et al. (52) of five studies comparing exercise to control revealed a large effect size in favour of exercise of $-0.81$ (95% CI: 1.53, 0.10), corresponding to a pooled reduction of 4.00 points over controls on the Edinburgh Postnatal Depression Scale (EPDS). Interestingly, the largest clinical effect was found for the Australian Armstrong and Edwards’ study (53), which used pram walking and social support as the intervention (10.10 point reduction on EPDS over control). This highlights the clinical strength of integrating biophysical and psychosocial treatments for depression. Exercise during pregnancy does not, however, appear to be a preventative for postnatal depression. A recent large RCT involved 855 pregnant women who were randomised to a 12-week exercise programme vs. regular antenatal care as the control (54). Three months after birth, no significant difference was found in postnatal depression and EPDS scores amongst women randomised to regular exercise or control during pregnancy.

Green space

Exposure to green space (nature) may also provide benefits for mental health, and exercising in nature may synergistically increase wellbeing beyond PA in an urban setting (55). PA in the presence of nature has been coined ‘green exercise’ (56). An initial study by Pretty et al. (56) exposed participants to pleasant images of nature (video-projected wall images) while they exercised and found increased mood and self-esteem over exercise control with either no images or negative images of nature (e.g. destroyed natural habitat). A later multi-study meta-analytic analysis of 10 UK studies involving 1252 participants found that the overall effect size for green exercise in improving self-esteem was $d = 0.46$ (95% CI: 0.34, 0.59) and for mood $d = 0.54$ (95% CI: 0.38, 0.69) (55). Dose-dependent responses for both intensity and duration showed large benefits from short engagements in green exercise which, while diminishing over time, still maintained positive effects. Every green environment was found to enhance both mood and self-esteem, and the presence of water generated greater effects. Men and women had similar improvements in self-esteem after green exercise, while men and younger-aged people had a greater effect for mood. Pertinently, studies of green exercise in mentally ill populations reported the greatest improvements in self-esteem.

In respect to dosage and type of exercise, research supports a dose-dependent effect, with regular moderate-to-strong-intensity exercise eliciting more positive results. Examples to support this include a study of people with mild-to-moderate depression, who were randomised into one of four aerobic exercise groups of different intensity (supervised indoor treadmill and cycling) vs. a control group who undertook 15–20 min of stretching (57). These groups had energy expenditures of either 7 kcal/kg/week or 17.5 kcal/kg/week and exercised for either three or 5 days/week. A statistically significant reduction in depression compared with controls was only found for the groups engaging in high-energy expenditure. A high-quality Australian study also demonstrated an exercise intensity effect in 60 older adults with depression (58). High-intensity anabolic exercise (80% of maximum strength) was discovered to be substantially more effective in reducing depressive symptoms than low-intensity training. A significant reduction of >50% in depressive symptoms was achieved in 61% of the higher-intensity group, compared with 29% low-intensity group and 21% of routine GP care group. Interestingly, strength gain was directly associated with a reduction in depressive symptoms. On the other hand, a review of 27 observational studies and 40 intervention studies by Teychenne et al. (59) concluded that even low doses of PA may be protective against depression. Regardless, it appears that offering general advice and follow monitoring for increasing PA in a clinical setting provide little benefit over usual care for reducing depression. The TREATing Depression with physical activity (TREAD) study investigated over a 12-month period the efficacy and cost-effectiveness of personalised PA (in addition to usual general practitioner care) as a treatment for 361 people with depression (60). While the PA intervention group had a slightly lower Beck Depression Inventory score than usual medical care at 5 months, the authors noted that the intervention was not cost-effective. Potentially, only more vigorous activity might be of benefit, while previous positive studies may have recruited individuals with pre-existing motivation to PA.

Clinical guidelines for exercise recommend physician and/or exercise physiologist assessment before commencing a new regime, which should consist of moderate-to-vigorous aerobic exercise (30–60 min) in addition to anaerobic weight-bearing exercises approximately four to 6 days per
week (61, 62). Exposure to social interaction and nature when exercising is also advised.

Clinical application

It is paradoxical that exercise is seldom applied as an intervention for depression in clinical populations, despite the respectable evidence base. This may be partly a result of reductionist models of care that focus on antidepressant treatment and psychotherapy. It is noteworthy that in surveys asking people with mood disorders what self-management strategies are the most helpful, exercise frequently appears towards the top of the list (63). However, it is recognised that more recent methodologically robust studies indicate that the clinical effect of exercise is more modest than previously believed. Regardless, adequate PA and exercise are of even greater relevance, given the increased burden of obesity and the metabolic syndrome in individuals with psychiatric disorders and the well-established benefits of PA in those comorbid conditions. In summary, the balance of evidence supports the use of exercise of adequate intensity and duration to improve mood and reduce depressive symptoms, with stronger effects being seen in clinical depression. This effect is comparable with conventional antidepressants (64).

Diet

The previous century has seen major changes to dietary intakes across the globe (65). In the West, common dietary patterns are high in saturated fats and refined sugar, with nutrient-poor and energy-dense foods now contributing approximately 30% of the daily intakes of American adults (66). A comprehensive review of data from the recurrent National Health and Nutrition Examination Surveys in the United States concluded that only one in 10 Americans has a ‘good’ diet (67). Concurrently, new data suggest an increase in the prevalence of psychological distress, particularly amongst young people (68, 69) where the changes in diet may be most notable (70, 71). The last decade has seen an increasing interest in the impact of dietary factors on mental health. However, until very recently, individual nutrients and lipids had received the most attention, with a particular research focus on the role of long-chain omega-3 fatty acids in depression. Here we offer a brief narrative review of the most commonly studied nutrients in mental health, followed by an overview of the more recent research on overall dietary quality and the common mental disorders.

Fish oils

In several population studies, low levels of fish and/or n-3 PUFA consumption are associated with increased depression (72–77), although a linear relationship has not always been observed (78–82). However, trials of n-3 PUFA supplementation in depression have yielded equivocal results. A very recent meta-analysis determined that there was a small beneficial effect of treatment with n-3 compared with placebo, but that the benefit of supplementation was restricted to those with more severe clinical depression (83). This may reflect an increased need for the long-chain omega-three fatty acids for those suffering major depression, wherein increased oxidative stress (84) results in increased lipid peroxidation (85) and a reduction in lipid levels in neuronal membranes.

Folate

The other nutrient receiving particular attention in psychiatry is folate, with some observational studies showing a relationship between low folate intake or status and the risk of depression. The first study to examine the dietary intake of folate in relation to depression was undertaken in 2443 middle-aged Finnish men (86), wherein the odds of self-reported depression for those in the lowest tertile of folate intake were increased by nearly 50% after all adjustments. Another cross-sectional, population-based study examined 517 Japanese adults and reported a significant, linear association of folate intake with depressive symptoms in men, but not women (80), while yet another cross-sectional study in Australian women reported an inverse relationship between folate intake and major depressive disorder (87). However, a cross-sectional study of more than 27 000 Finnish male smokers reported no differences in folate consumption between those experiencing chronic symptoms of depression, anxiety and/or insomnia and those with no such symptoms, over a 12-month period (88), although mean folate intakes in this sample were at or above the recommended level. In contrast, a large prospective population study of 2313 middle-aged Finnish men reported that intakes of folate below the median were associated with a threefold increased risk of MDD over more than 10 years of follow-up (89). Similarly, a study of 732 elderly Korean men reported that lower serum levels of folate and B12 and higher levels of homocysteine were all associated with an increased risk of clinically significant depression over the follow-up period (90), while another recent Japanese study reported that serum folate levels predicted
depression risk over 3 years of follow-up in office workers (91). A Cochrane review, based on three intervention trials, concluded that folate may be useful as an adjunctive treatment for depression, although it is still unclear as to whether supplementation will benefit both those with low and normal levels of folate (92).

**Magnesium**

Magnesium is another micronutrient that may influence depression risk. In animal models, a magnesium-deficient diet increases depression and anxiety-related behaviour (93), while magnesium treatment appears to improve such behaviours (94, 95). Jacka et al. (96) reported an inverse relationship between dietary magnesium intake and depression in a large sample of community-dwelling men and women in Norway, while another study in Australian women reported a similar inverse relationship between magnesium intake and clinical depressive disorders (87). The data are not unequivocal, however. Derom et al. reported no predictive effect of magnesium intake and depression risk in the large, ongoing SUN cohort study (97), although average magnesium intake was relatively high in this cohort. There have been few studies of magnesium supplementation as a treatment strategy in depression. Barragan-Rodriguez et al. (98) reported that magnesium supplementation was as effective as pharmacotherapy in treating depression in elderly diabetic patients with hypomagnesemia; however, supplementation was not found to alleviate symptoms of depression or anxiety in premenstrual women (99).

**Zinc**

Zinc may also be related to depressive illness. There have now been cross-sectional studies showing inverse relationships between the dietary intake of zinc and self-reported depression in pregnant women (100), female students (101) and a large representative sample of Australian women (87). In support of this finding, a recent study has also reported that women habitually consuming less than the recommended intake of red meat, a food rich in zinc, were more likely to be diagnosed with clinical depressive and/or anxiety disorders (102). In a clinical context, zinc deficiency is commonly observed in patients with major depression (e.g. (103–105), while zinc supplementation has been shown to be efficacious in enhancing antidepressant therapy (106). There are also supportive data from animal studies suggesting that zinc may exert antidepressant effects [e.g. (107)]. Further studies of zinc as a both a mono- and adjunctive therapy in depression may thus be warranted.

**Diet quality**

It is important to recognise that magnesium, folate, zinc and long-chain fatty acids are all components of a healthy diet, found primarily in foods such as leafy green vegetables, legumes, whole-grains, lean red meat and fish. As such, it is possible that the apparent relationship between the consumption of these individual components of food and mental health is explained by the overall quality of an individual’s habitual diet. As a response to this understanding, the new field of nutritional psychiatry has now, in concert with the wider field of nutrition research, moved away from examining individual nutrients towards an examination of the importance of whole diet in mental health. In this context, there have been a number of observational studies published in the last 3 years demonstrating both cross-sectional and prospective relationships between diet quality and the common mental disorders in adults, adolescents and children.

**Cross-sectional studies**

In an Australian study, conducted in a randomly selected, population-based sample of 1046 adult women, a dietary pattern comprising vegetables, fruit, beef, lamb, fish, and wholegrain foods was associated with a reduced likelihood of clinically diagnosed depressive and anxiety disorders, whereas a ‘Western’ dietary pattern comprising processed and ‘unhealthy’ foods was associated with a reduced likelihood of clinically diagnosed depressive and anxiety disorders, whereas a ‘Western’ dietary pattern comprising processed and ‘unhealthy’ foods was associated with an increased likelihood of psychological symptoms, as well as major depressive disorder and dysthymia. Increased a priori diet quality scores were also associated with reduced psychological symptoms (108). In this same cohort of women, increased scores on the same healthy dietary pattern were also associated with a halving in the odds for bipolar disorder, while those with higher scores on both the Western dietary pattern and glycaemic load measures were more likely to have bipolar disorder (109).

Further research in disparate countries has yielded largely concordant results. Associations between diet quality and mental health outcomes have also been reported in the large HUSK study of more than 7000 adults in western Norway (110). A healthier diet, measured with an a priori diet quality score, was associated with a reduction in the odds ratios for both depression and anxiety in women and with reduced odds for depression, but
Berk et al. not anxiety, in men. Nanri et al. (111) have also reported that middle-aged municipal employees who were in the highest tertile of healthy Japanese dietary pattern scores, characterised by higher intakes of vegetables, fruit, soy products and mushrooms, were significantly less likely to be depressed than those in the lowest tertile, although there was no discernible relationship between unhealthy food intake and depression. Similarly, an American study of more than 1000 adults aged 30–64 years examined the association of diet quality, measured with the validated Healthy Eating Index (HEI-2005), and depressive symptoms cross-sectionally. They reported an inverse association between the two, even after adjustment for confounders including race, gender, age, education and income (112). Conversely, an increased consumption of high-calorie sweet foods was associated with increased depressive symptoms in more than 4500 middle-aged American women (113). In the same study, an increased intake of low-calorie foods (such as green salads, roast chicken, baked fish, low-fat milk and cold cereals) was associated with reduced depressive symptoms, independent of age, race, BMI and education.

Such relationships have also been shown in older adults: in a study of older French women and men, higher scores on a healthy dietary pattern, characterised by higher intakes of fruits and vegetables, was associated with a reduced likelihood of depression in women, but not in men (114), although unhealthy food intake was not associated with mental health in either men or women. In another study of 887 community-dwelling elderly people in Japan, those reporting the daily intake of ‘well-balanced meals’ were less likely to report depressive symptoms (115). Similarly, a study of more than 1000 elderly Greeks reported that those with low scores on the Geriatric Depression Scale were more likely to consume fish, vegetables and cereals, although there was no direct relationship between Mediterranean diet scores and depressive symptoms (116).

At the other end of the age spectrum, diet quality is also associated with better mental health in adolescents and children. In an Australian study, both a lower adherence to the consumption of foods comprising a healthy diet and an increased consumption of unhealthy and processed foods were associated with increased odds for self-reported symptomatic depression in more than 7000 young adolescents (117). For those adolescents in the highest category of ‘healthy’ diet scores, the likelihood of depression was nearly halved compared with those in the lowest category, while for those in the highest quintile of ‘unhealthy’ diet score, the likelihood of depression was increased by nearly 80% compared with the lowest quintile. These relationships demonstrated dose–response patterns and are reported after adjustment for a wide range of potential confounding factors, including sociodemographic factors, health and dieting behaviours and familial environment (117). Oddy et al. (118) reported that adolescents with a ‘Western’ dietary pattern, higher in take-away foods, red meat and sweets, exhibited higher levels of internalising and externalising behaviours, which are markers of mental health status. However, there was no relationship observed between a healthy dietary pattern and such behaviours. A more recent study in Chinese adolescents showed inverse relationships between higher scores on a ‘traditional’ dietary pattern, comprising wholegrains, vegetables, fruit, rice and soya products, and depression and anxiety and positive relationships between both an unhealthy ‘snacking’ dietary pattern and a high-meat dietary pattern and depression and anxiety (119). In Norway, a high consumption of unhealthy sugary and snack foods was associated with increased odds for behavioural problems in adolescents, while both fruit and fish consumption were associated with fewer behavioural problems (120), although there was no relationship between vegetable consumption and behaviour. Finally, a recent German study reported similar findings in children, wherein an increased intake of confectionery was associated with increased emotional symptoms compared with low intake and a higher diet quality score was associated with lower odds for emotional symptoms, after adjustment for variables such as sociodemographic characteristics, BMI, PA, television viewing and computer use (121).

Prospective studies

However, without prospective studies, the direction of the relationship between diet quality and mental health cannot be established. Depression itself may cause poor dietary choices, which may in turn worsen an existing condition. Recent prospective data from the SUN cohort study in Spain have shed light on this question. Sanchez-Villagas et al. (122) demonstrated an inverse association between the level of adherence to a Mediterranean dietary pattern (MDP) and the risk of incident depression over approximately 4 years in more than 10 000 middle-aged professionals. This association existed before and after controlling for a comprehensive range of potentially confounding factors including sociodemographic, anthropometric and lifestyle factors, other health behaviours
and medical history. Importantly, this study attempted to exclude reverse causality as an explanatory factor by repeating analyses after excluding participants who reported depression in the first 2 years of follow-up, as well as examining depression at or before the baseline assessment as an exposure, with adherence to the MDP as the outcome variable. Results of these analyses did not support the reverse causality hypothesis (that depression causes poor diet choices): the relationship of diet to MDP adherence was strengthened rather than diminished after removing participants with incipient depression, while there was no observable relationship between earlier depression and adherence to the MDP.

A similar study was undertaken in the ongoing Whitehall II cohort study, which found an increased risk of incident depression over 5 years in people consuming a ‘Western’ style diet pattern and a reduced risk of those eating a ‘whole-foods’ diet pattern (123). These authors also conducted sensitivity analyses to examine the reverse causality hypothesis, excluding those identified with depression at baseline and reanalysing the data and examining depression at an early time point as a predictor of diet quality at the next follow-up. Once again, results of these analyses did not support depression as a predictor of poor dietary behaviour. Interestingly, a recent Australian study of depression in primary care settings indicated that nearly 30% of individuals with depressive symptoms voluntarily improved their dietary quality in an attempt to improve symptoms (personal communication). Such data suggest that the relationship between depressive symptoms and dietary changes may not be straightforward, making an explicit examination of this issue an imperative.

Finally, a new prospective study in Australia has provided comparable data on the relationship between diet quality and mental health in adolescents. Jacka et al. (124) examined approximately 3000 Australian adolescents and found that diet quality was associated with adolescent mental health both cross-sectionally and prospectively. Moreover, improvements in diet quality were mirrored by improvements in mental health, while reductions in diet quality were associated with declining psychological functioning. Finally, the reverse causality hypothesis, that the reported associations reflect poorer eating habits as a consequence of mental health problems, was not supported by the data. Given that the majority of mental health problems develop by age 25 and that diet is a modifiable environmental factor for the entire population, these data may have important public health implications. Indeed, there are now concerning new data from Australia (125), Britain (68) and the United States (69), indicating that the prevalence of depression may actually be increasing. These reports offer an intriguing epidemiological insight into the changing landscape of population mental health and tentatively offer the possibility that these increases are linked to lifestyle changes, including the marked changes in dietary intakes that have occurred in these countries over the past few decades. If this is the case, this insight opens the door to both primary prevention approaches at a public health level, as well as treatments focussed on identified risk factors.

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This new body of observational data are notable for the relative consistency of both the reported relationships and the observed effect sizes. Inverse relationships between diet quality and mental health have now been reported across a multitude of countries, from children through to the elderly, in men and women, and utilising a wide range of mental health and dietary measures. However, there have been no studies to date that have specifically sought to answer the question ‘if I improve my diet will I feel less depressed?’ This is an increasingly common question, both in clinical practice and the general community, and it remains unanswered to date. This is a serious gap in our knowledge base. As above, we know that exercise is a highly effective treatment strategy for depression. While the recent epidemiological data are compelling, there are no equivalent data regarding the therapeutic impact of dietary changes on existing mental illness. Recent dietary intervention studies in individuals with mental illness, conducted with the intention of mitigating the detrimental impacts of both illness and pharmacological treatments on physical parameters, have almost exclusively focused on anthropometric and metabolic outcomes. There are tantalising hints in a new pilot study in which McMillan et al. (126) conducted a randomised controlled trial into the effects of dietary change on mood and cognition in healthy individuals. They examined the effects of 10 days of adherence to a nutrient-rich diet, compared with no dietary change, on mood and cognitive performance in 25 young female adults. Compared with the control group, the dietary change group showed significant improvements in self-rated vigour, alertness and contentment. These results suggest that trials of dietary change in those with depression may yield positive results; however, such trials are yet to be conducted.
Impact path

There are many pathways by which an insufficiency of nutrient-rich foods and/or an excess of poor-quality foods may impact on mental health. As with exercise, diet modulates biological processes that underpin mood disorders, including inflammation, brain plasticity and function, the stress response system and oxidative processes (33). Diet may therefore operate on factors influencing the development and course of depression (127). In people with major depression, systemic immune activation, characterised by increased levels of pro-inflammatory cytokines (128, 129) and changes in the acute-phase protein response (130), has been documented. An aetiological role for inflammation in the pathophysiology of depression is suggested by recent data showing that higher levels of serum high-sensitivity C-reactive protein (CRP), a marker of systemic inflammation, are an independent risk factor for de novo major depression (131).

Diet has a profound impact on systemic inflammation and immune system functioning, with healthy dietary patterns associated with reduced markers of inflammation (132, 133) and unhealthy ('Western') patterns associated with increased markers (132). These observational data are supported by intervention studies, wherein men randomised to a diet high in fruits and vegetables (eight serves per day) for 8 weeks demonstrated a significant decrease in CRP compared with those consuming only two serves per day (134). Nutritional factors also exert a direct and potent effect on neural physiology (135). For example, laboratory experiments have demonstrated that a high-fat, refined sugar diet, as a model of a Western-style diet, has a pronounced detrimental effect on brain structure and function via regulation of BDNF over both a short and long time frame (136). It also impairs cognitive functioning (137) and promotes anxiety-like behaviour (138). BDNF is known to be important in the pathophysiology of mood disorders (139, 140) and protects neurons from oxidative stress. These data suggest that a Western diet may affect the growth and functioning of neural circuits particularly germane to depression.

Clinical applications

This new literature provides face validity for the role of nutritional factors in the genesis and management of depression. It needs to be acknowledged that there is minimal evidence to date that dietary modulation can treat depression and equally that adherence to dietary modulation is a complex issue. However, diet has a major impact on comorbid physical disorders that are disproportionately more common in people with depression, such as cardiovascular disorders and diabetes. While the nascent evidence base consists primarily of reports from observational studies, the data are consistent and compelling. As such, attention paid to the diets of patients and those in the community with depressive symptoms is likely to yield important benefits to both physical and mental health (141).

Smoking

There is a consistently documented association between tobacco smoking and mental illness (142). Smoking increases the risk of the development of mood disorders (143–146) and seems to be a risk factor for the development of de novo depression (147). Cigarette smoking in adolescence appears to significantly increase the risk of the later development of clinically significant depression (148). Smoking appears to transmit a transgenerational risk; smoking in pregnancy is linked to a greater risk of attention deficit disorder and oppositional disorders in offspring (149). There is a risk of escalation of smoking with depression (145), and there is evidence for a shared genetic vulnerability to smoking and depression (150). In mood disorders such as depression and bipolar disorder, but perhaps not psychosis, smoking has a deleterious effect on symptom severity (151), response to treatment and clinical outcome (152–154). This appears true of even subthreshold depression, which is associated with a greater risk of continued smoking and lower abstinence rates (155).

The pathways whereby smoking impacts on mood disorders are complex and multidimensional and encompass environmental, psychological, biological and genetic factors. Smoking may be a form of self-medication for dysphoric symptom reduction (145, 156), evidenced by data that smoking reduces anxiety and provides relaxation for patients. It is necessary to emphasise that, as a result of homoeostatic adaptation, the acute effects of any dependence-producing agent are the opposite of its long-term effects; acute euphoria is the mirror of chronic dysphoria. Smoking can be seen as a persistent and rather dysphoric withdrawal state, punctuated by brief intoxications.

A key mechanism linking smoking and mood is the dopaminergic system. Dopamine has a crucial role in the reward pathways that both underlie the substrate of addiction, as well as the regulation of mood (157). Nicotine is a nicotinic cholinergic
agonist, which causes the release of neurotransmitters such as dopamine, noradrenaline, serotonin, 3-aminobutyric acid (GABA) and glutamate, via the diffuse cholinergic innervations in the brain (158). Smoking is associated with downregulation and hence low availability of dorsal striatal D2 and D3 receptors, similar to other addictions (159). This dysregulation of the dopaminergic system impacts on mood regulation and may contribute face validity to the link between smoking and psychopathology. Depression is an inflammatory condition; smoking aggravates inflammation, and a similar relationship is evident for oxidative stress (160). Tobacco dysregulates the stress response systems, which are part of the pathophysiology of depression (161).

The evidence for smoking as a risk factor for depression, as an aggravator of existing depression and as a factor potentially worsening treatment outcomes suggests that the management of smoking in individuals with mood disorders needs to be a core and routine part of treatment. This is resonant with smoking being a risk factor for other medical disorders that are more prevalent in people with depression, such as cardiovascular disorder (162) and osteoporosis (163). What is often neglected in cessation decisions is personal valence; people stop smoking when there is clear evidence that it impacts them, such as after an acute cardiac event. It is necessary to communicate the message that a person’s smoking is a risk factor for their depression, as this is concordant with the principles of motivational interviewing, an effective psychological strategy for substance misuse. Smoking cessation messages need to be routinely communicated as part of clinical care and individuals offered evidence-based smoking cessation interventions (164). Curiously, PA concurrent with smoking cessation seems to be protective against relapse in quitters, dovetailing with and reinforcing recommendations regarding exercise in this study (165).

A caveat is required, inasmuch as the act of cessation is associated with withdrawal symptoms including transient dysphoria, irritability and a risk of aggravation of depression (166). Once the set point of mood and anxiety has re-adapted, via homoeostasis, to the absence of nicotine, this will normalise. The assumption is that the new set point will be associated with a subsequent reduction in risk of mood disorders; however, it needs to be noted that trials of smoking cessation that examine long-term change in risk have not been conducted. Nevertheless, new data suggest that quitting smoking is associated with better social functioning and self-perceived health status (167).

**Alcohol**

Community surveys and epidemiological studies indicate that alcohol abuse and dependence commonly co-occur with both depressive and anxiety disorders, although the specific mechanisms of the associations are still unclear (168). There is evidence from prospective community studies that heavy alcohol use in adolescence and young adulthood predicts later onset of major depression (169) and that hazardous or harmful alcohol use, according to ICD-10 criteria, in early adulthood predicts greater depressive symptomatology when compared with light alcohol drinkers, even after controlling for potential confounders (170).

A meta-analysis of four large-scale epidemiological studies demonstrated a two- to threefold increased lifetime risk of both anxiety and depressive disorders in those with alcohol abuse or dependence, as well as an increased number of illness symptoms in those with comorbid alcohol problems (168). This has been supported by a more recent meta-analysis which found that the presence of either an alcohol use disorder or a major depression doubles the risk of the other disorder (171). In the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study of 2541 out-patients with MDD, those with a comorbid substance use disorder (66% alcohol use disorders) experienced greater depressive symptomatology, more previous suicide attempts, more frequent concurrent anxiety disorders and greater functional impairment than those without a dual diagnosis (172). Additionally, in a study women participating in the Epidemiologic Catchment Area project, the risk of incident cases of heavy drinking within the 12-month follow-up period in those with a history of depressive disorder was 2.6 times greater than the risk in women with no history of depressive disorder (173).

Despite the well-accepted association between affective and substance use disorders, no consistent evidence exists that moderate alcohol intake is associated with worse outcomes for those with depression. In fact, many studies have reported that amongst moderate drinkers, rates of depressive illness and symptomatology are lower than amongst abstainers or those with alcohol dependence (174–176). This ‘J-’ or ‘U’-shaped relationship has been widely reported, and although it is not universally accepted (177, 178), it suggests that moderate alcohol consumption may be permissible amongst depressed individuals. As such, in a clinical setting, the focus should be on differentiating and managing problem drinking, where it is identified, and on educating patients...
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regarding maintaining moderate alcohol consumption and avoiding heavy episodic drinking. Further education may be required regarding potential interactions between alcohol use and medications.

Despite the potential impact of alcohol use upon the efficacy of treatment for depression (179, 180), routine questioning regarding alcohol use may not occur as frequently as appropriate. Within Australia, the National Health and Medical Research Council (NHMRC) recommends that people who are depressed discuss their alcohol intake with a healthcare professional and that temporary or permanent abstinence may be necessary (181). Several studies have demonstrated that depressive syndromes are substantially improved within a very short time of abstaining from alcohol [e.g. (182–184)]. A recent study of women with postpartum depression found a brief alcohol intervention to be effective compared with no intervention at reducing depressive symptomatology at 6 months following intervention (185). However, while abstinence has been shown to positively impact upon depressive symptoms, antidepressant treatment alone has not been shown to result in sustained abstinence, even when effectively alleviating mood symptoms (186). As such, the need has been identified for therapies directly targeting the alcohol use disorder while treating depression in dually diagnosed individuals (187).

For patients whose goal may not be abstinence from alcohol, other treatment approaches, such as motivational interviewing, may support a reduction in hazardous alcohol consumption. Indeed, a recent systematic review of interventions targeting depressed patients with concurrent alcohol misuse reported improvement in both depressive symptoms and measures of alcohol intake following an intervention combining motivational interviewing and cognitive behavioural therapy (188). This systematic review supports the notion of being able to effectively intervene with depressed patients whose alcohol use does not meet dependence criteria, but has, nevertheless, been identified as problematic to achieve improvements in drinking and depression symptoms. For these patients, incorporating advice about how to reduce alcohol consumption, and the targeted use of motivational interviewing into routine care, may be beneficial (187, 189). Finally, for patients consuming alcohol moderately and not experiencing any difficulties with their drinking, the provision of psycho-education around the link between heavy alcohol intake and changes in depression severity and suicide risk, and the ongoing routine assessment of alcohol consumption may suffice.

Discussion

Many factors, including genetics, personality, stress and lifestyle, contribute to the aetiology of depression, and these factors are interactive and mutually reinforcing. In this context, the contemporary clinical management of depression has had a narrow focus on medication and psychotherapy and has to date not incorporated the evidence regarding potentially reversible lifestyle factors into management. Indeed, there has been a tendency for many clinicians to regard unhealthy lifestyle practices by psychiatric patients as innocuous self-comfort strategies, with little clinical relevance. However, there is now a comprehensive evidence base for lifestyle as a key aetiological factor in depression, suggesting that these behaviours may be of particular importance to the genesis and progression of common psychiatric illnesses and of key relevance to practitioners. Exercise is perhaps the best validated lifestyle factor, both in terms of aetiology and as an evidence-based therapeutic avenue. It is a paradox that exercise remains infrequently utilised in practice, particularly given the evidence that exercise programmes designed to encourage compliance with recommended levels of PA are feasible and well received in psychiatric populations (47). Smoking appears to be an independent risk factor for depression, although the evidence suggesting that cessation has direct effects on improving mood remains to be gathered. Smoking cessation is, however, infrequently incorporated into routine treatment packages, despite the inordinately high prevalence of smoking in psychiatric cohorts and the attendant medical and psychiatric risks. Similarly, poor diet is now emerging as a risk factor for depression, although the evidence suggesting that dietary modification may be of therapeutic value. The data to date have focussed on individual nutrient supplementation, but the first studies of the therapeutic benefits of modification of whole-diet patterns are underway. Lifestyle modification, with a focus on exercise, enhancing social networks, exposure to green space, diet and smoking, is of substantial potential value, not only to the high prevalence psychiatric disorders, but to those medical disorders that are over-represented in these individuals. Lastly, recognition of lifestyle risk factors open the door to novel primary and secondary preventative strategies based on lifestyle modification (190).

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