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Complementary and alternative medicine use for treatment and prevention of late-life mood and cognitive disorders

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Abstract

Late-life mood disorders and cognitive aging are the most common reasons for using complementary and alternative therapies. The amount of rigorous scientific data to support the efficacy of complementary therapies in the treatment of depression or cognitive impairment is extremely limited. The areas with the most evidence for beneficial effects are exercise, herbal therapy (*Hypericum perforatum*), the use of fish oil, and, to a lesser extent, acupuncture and relaxation therapies. There is a need for further research involving randomized, controlled trials to investigate the efficacy of complementary and alternative therapies in the treatment of depression and cognitive impairment in late-life. This research may lead to the development of effective treatment and preventive approaches for these serious conditions.

Keywords

acupuncture; art therapy; ayurveda; cognition; complementary medicine; dementia; exercise; gingko; hypericum; late-life depression; omega-3 fatty acids; SAMe; spirituality; yoga

Trends in use of complementary & alternative medicine in the USA

The use of complementary and alternative medicine (CAM) in the USA is increasing rapidly, exceeding a prevalence of 60% in a nationally representative survey conducted by the National Center for Health Statistics in 2002 [1,2]. CAM therapies are defined by the National Center for Complementary and Alternative Medicine as a group of diverse medical and health systems, practices, and products that are not currently considered to be part of conventional medicine [201]. An alternative approach to mental healthcare is one that emphasizes the interrelationship between mind, body and spirit. A national US survey noted a 47% increase in total visits to CAM practitioners, from 427 million in 1990 to 629 million in 1997. These figures surpass the total number of visits to primary care physicians [3,4]. Estimated expenditures for CAM professional services were conservatively estimated at US$21.2 billion in 1997, with at least US$12.2 billion of out-of-pocket expenditures, exceeding out-of-pocket expenditures for all US hospitalizations [201]. In a more recent nationwide survey, 36% of US adults aged 18 years

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and over use some form of CAM, and aging baby-boomers are expected to accelerate the use of CAM in the coming years [5].

Despite the increasing use of CAM by individuals, the scientific support for its efficacy is limited. The treatments with the best evidence of effectiveness are St John's wort (SJW), exercise, cognitive behavior therapy and light therapy (for seasonal depression). There is only some degree of evidence to support the effectiveness of acupuncture, light therapy (for nonseasonal depression), massage therapy, negative air ionization (for winter depression), relaxation therapy, *S*-adenosyl-L-methionine (SAMe), folate and yoga breathing exercises [6]. The use of CAM therapies is typically associated with higher levels of education, poorer health status, environmentalism, feminism and interest in spirituality and personal growth psychology [7]. CAM users tended to be female, younger, better educated and employed [8]; however, older adults are also using CAM at increasingly higher rates. Barnes and colleagues noted that nearly 33% of older adults used CAM in the preceding year (2004) [5]. In a survey, 42% of the patients in a managed care organization reported using at least one CAM therapy, most commonly relaxation techniques (18%), massage (12%), herbal medicine (10%) or megavitamin therapy (9%) [8]. Perceived efficacy of CAM was very high, ranging from 98% (energy healing) to 76% (hypnosis). The most commonly used CAM approaches include prayer and megavitamin supplements.

Although some alternative approaches have a long history, many remain controversial owing to less than comprehensive research and poor integration of the Western and Eastern methods of diagnosis and treatment that are often mutually misunderstood and criticized. These practices encompass a diverse range of therapies and techniques but have in common a general lack of acceptance or use in traditional medical settings. However, with the increasing public use of CAM for preventive and therapeutic purposes, including a very active 'antiaging' movement, a significant effort is now devoted to the integration of alternative methods of treatment into mainstream healthcare practice and research. The principal uses in older adults include stress reduction, antiaging effects of CAM for prevention of diseases of aging, memory enhancement and treatment of various neuropsychiatric disorders, such as depression, anxiety, insomnia, pain and many other specific indications. Our review is devoted to the description of the existing CAM treatments applied to the care of older adults with neuropsychiatric illnesses that include late-life mood and cognitive disorders.

To identify articles related to this subject, we conducted a systematic search of the MEDLINE database and of Cochrane Database of Systematic Reviews for English articles published in the past 10 years using the following keywords: late life, depression, dementia, memory, cognition, sleep, complementary medicine, omega-3 fatty acids, hypericum, SAMe, acupuncture, ayurveda, massage, energy therapies, therapeutic massage, yoga and herbal remedies, diet, art (music and dance) therapy and spirituality/prayer.

Complementary & alternative medicine use in late-life mood & cognitive disorders

Mood and cognitive impairment are the most frequently occurring psychiatric syndromes in older adults. Depressive symptoms occur in approximately 10–15% of patients in primary care settings. Cognitive disorders are on the rise owing to the 'graying' of the population around the world. Mood disturbances are commonly observed in patients with neurodegenerative disorders including probable Alzheimer's disease (AD), Parkinson's disease (PD), and post-stroke depression. Depression in later life is a treatable condition. Improvement with treatment occurs in mood symptoms and activities of daily living (ADLs), and in the quality of life of the patients and their caregivers, but not necessarily in memory and other cognitive functions. Clinically, preference is given to therapy with antidepressants that do not have a significant

anticholinergic effect. Other treatment strategies include treatment of pain and infection, environmental and behavioral management and professional caregiver training. Despite rigorous research, the response to these therapies remains only modest and partial for most patients [9]. While CAM treatments are widely used by consumers, very little research is available to guide patients and their caregivers, or even practitioners in the field. A 2001 US survey of a nationally representative sample of patients diagnosed with a mood or anxiety disorder reported that 57% of those with anxiety attacks and 54% of those with severe depression were using CAM therapies to treat these conditions (either as primary or as adjunctive medication) [10]. These proportions increased to 66 and 67%, respectively, among those who were seeing a conventional healthcare professional for these conditions [10]. The perceived helpfulness of CAM therapies was similar to that of conventional therapies [10].

In this article, the literature that pertains to the use of diet and the use of nutritional and herbal supplements, expressive therapies (e.g., art, dance and music), stress reduction, culturally based therapies (e.g., Ayurveda and acupuncture) and spiritual practices is reviewed. Whenever possible, the review of the efficacy provided by positive meta-analyses, followed by one large or several smaller double-blind, placebo-controlled trials, and open trials is also included. This hierarchy of evidence is not available in each of the area of CAM. Although some animal studies are referred to, these are not a reliable indication of efficacy in humans (Table 1).

Diet & the use of nutritional & herbal supplements

Adjusting both diet and nutrition may help some people with mental illnesses manage their symptoms and promote recovery. For example, research suggests that eliminating milk and wheat products can reduce the severity of symptoms for some people who have schizophrenia and some children with autism [11]. Similarly, some holistic/natural physicians use herbal treatments, B-complex vitamins, riboflavin, magnesium and thiamine to treat anxiety, depression, drug-induced psychoses and memory loss.

A number of herbs and dietary supplements have demonstrable effects on mood, memory and insomnia [12]. There is a significant amount of evidence supporting the use of *Hypericum perforatum* (SJW) for depression, and omega-3 fatty acids and gingko biloba for dementia as reviewed below.

St John's Wort (*Hypericum perforatum*)

St John's wort has been extensively studied in Europe, particularly in Germany. A recent meta-analysis of 23 randomized trials (20 were double-blinded) in a total of 1757 outpatients with mild-to-moderate depression found improvement in depressive symptoms in all groups. In 15 placebo-controlled studies, medication was more effective than placebo. In eight treatment-controlled trials, SJW was as effective as tricyclic antidepressants. However, a recent large NIH-sponsored US multisite randomized trial of SJW compared with sertraline and placebo for the treatment of major depression failed to find drug–placebo differences [13]. A recent Cochran database review provided the analyses for a total of 37 trials, including 26 comparisons with placebo and 14 comparisons with synthetic standard antidepressants [14]. The results of placebo-controlled trials demonstrated a marked heterogeneity. In trials restricted to patients with major depression, the combined response rate ratio (RR) for hypericum extracts compared with placebo from six larger trials was 1.15 (95% CI: 1.02–1.29) and from six smaller trials was 2.06 (95% CI: 1.65–2.59). In trials not restricted to patients with major depression, the RR from six larger trials was 1.71 (95% CI: 1.40–2.09) and from five smaller trials was 6.13 (95% CI: 3.63–10.38). Trials comparing hypericum extracts and standard antidepressants were statistically homogeneous. Compared with selective serotonin-reuptake inhibitors (SSRIs) and tri- or tetra-cyclic antidepressants, respectively, RRs were 0.98 (95% CI: 0.85–1.12; six trials) and 1.03 (95% CI: 0.93–1.14; seven trials). Patients given hypericum extracts dropped out of

trials owing to adverse effects less frequently than those given older antidepressants (odds ratio [OR]: 0.25; 95% CI: 0.14–0.45); such comparisons were in the same direction, but not statistically significantly different, between hypericum extracts and SSRIs (OR: 0.60; 95% CI: 0.31–1.15). Therefore, current evidence regarding hypericum extracts is inconsistent and confusing. In patients who meet criteria for major depression, several recent placebo-controlled trials suggest that the tested hypericum extracts have minimal beneficial effects while other trials suggest that hypericum and standard antidepressants have similar beneficial effects. The recommended doses include 300 mg three-times daily or 450 mg twice daily. As the preparations available on the market might vary considerably in their pharmaceutical quality, the results of this review apply only to the products tested in the included studies.

Interestingly, hyperforinm, an acylphloroglucinol compound isolated from *Hypericum perforatum* (SJW), has been used in animal models of AD and has been found to: decrease amyloid deposit formation in rats injected with amyloid fibrils in the hippocampus; decrease the neuro-pathological changes and behavioral impairments in a rat model of amyloidosis; and prevent Aβ-induced neurotoxicity in hippocampal neurons both from amyloid fibrils and Aβ oligomers, avoiding the increase in reactive oxidative species associated with amyloid toxicity. Both effects could be explained by the capacity of hyperforin to disaggregate amyloid deposits in a dose and time-dependent manner and to decrease Aβ aggregation and amyloid formation. Altogether, this evidence suggests that hyperforin may be useful to decrease amyloid burden and toxicity in AD patients, and may be a putative therapeutic agent to fight the disease [15].

Although it is commonly believed that herbal preparations are safer than the synthetic ones, many of them have limiting side effects. SJW is useful for the treatment of mild-to-moderate depression, but has multiple potentially dangerous and lethal drug interactions owing to its monoamine oxidase inhibition demonstrated *in vitro* [12,16,17]. In addition, concurrent use of drugs metabolized by the cytochrome CYP450 liver enzyme system may result in altered therapeutic levels due to induction or inhibition of enzymes by SJW that might preclude its use in elderly patients who are taking multiple medications owing to potential drug interactions. Human pharmacokinetic studies have reported induction of CYP 3A/3A4 by reductions of drug concentrations. The drug levels of such medications as carbamazepine, cyclosporine, estrogens and oral contraceptives, as well as statins, may be altered causing potentially dangerous and life-threatening side effects. A significant decrease in cyclosporin levels in transplant recipients (e.g., kidney and heart) taking SJW may result in acute transplant rejection and death [18].

Other herbal products

Many users of CAM may take a variety of herbal products other than SJW [19]. In primary care settings, 11% of patients with symptoms of anxiety or depression reported using herbal products. Their use was predicted by a diagnosis of major depression, higher education and a lower burden of medical illness [20]. Various herbal products (e.g., *Corni fructus*, *Lycii fructus*, *Pinelliae rhizome* or *Rehmanniae radix preparat*) are used in the treatment of depression in different parts of the world even though most of them have not been scientifically evaluated [21]. One product has been evaluated in persons with bipolar disorder [22] and three in rodent models of depression [21,23,24].

Gingko biloba

Ginkgo biloba leaf extract is among the most widely sold herbal dietary supplements in the USA. Its purported biological effects include: scavenging free radicals; lowering oxidative stress; reducing neural damages, reducing platelets aggregation; anti-inflammation; antitumor activities; and antiaging. Clinically, it has been prescribed to treat CNS disorders such as AD and cognitive deficits. It exerts allergy and changes in bleeding time. While its mutagenicity or carcinogenic activity has not been reported, its components, quercetin, kaempferol and rutin

have been shown to be genotoxic. There are no standards or guidelines regulating the constituent components of ginkgo biloba leaf extract nor are exposure limits imposed. Safety evaluation of ginkgo biloba leaf extract is being conducted by the US National Toxicology Program.

Ginkgo biloba has been widely used for many years by people with symptoms attributed to 'cerebrovascular insufficiency', despite the lack of evidence of a causal role. Approximately 30 placebo-controlled trials in patients with various types of dementia have been published, with highly inconsistent results. If these studies demonstrated any effect on cognition, it was weak and did not last more than 6months. Cases of hemorrhage were reported, and this means that caution is needed, especially in patients at increased risk of hemorrhage, such as those on ongoing anticoagulant or antiplatelet treatment. In practice, ginkgo biloba extract appears to be little or no different from placebo in the treatment of AD. The recommended doses range widely, but in the recent trial of prevention of AD, gingko biloba at 120 mg twice a day was not effective in reducing either the overall incidence rate of dementia or AD incidence in elderly individuals with normal cognition or those with MCI [25]. Its short-term use is acceptable under some conditions, but the potential risk of bleeding must be seriously considered [26]. Gingko has been reported to reduce depression in dementia patients and counteract sexual side effects of antidepressants [27,28].

Use of nutritional supplements

In addition to herbal remedies, consumers use a variety of nutritional supplements (including vitamins, amino acids and fish oil) that may affect mood and functioning. Although evidence for the use of vitamins, antioxidants and amino acids as sole agents for treatment of psychiatric symptoms is not as strong, there is some preliminary evidence for the use of folate, tryptophan and phenylalanine as adjuncts to enhance the effectiveness of conventional antidepressants in the treatment of depression. SAMe seems to have antidepressant effects, and omega-3 polyunsaturated fatty acids, particularly docosahexaenoic acid, may have mood-stabilizing effects. More research should be conducted on the role of these and other natural products in the prevention and treatment of psychiatric symptoms.

Depression is associated with poor nutrition, with severely compromised cognition and functioning resulting from malnutrition. Early recognition and intervention may prevent poor nutrition in these disorders. For example, the role of L-tryptophan in neuropsychiatric disorders appears to be profound [29]. Tryptophan is an essential amino acid precursor for serotonin synthesis in the brain. Dietary tryptophan supplementation has been used with variable success in psychiatric patients. In a recent study, a 200 mg dose of L-5-hydroxytryptophan (L-5HTP) significantly augmented the prolactin and cortisol response AUC (0–3 h) to 20 mg oral citalopram. The results of this study suggest that an augmented neuroendocrine challenge may be a suitable marker to demonstrate increased 5-HT-mediated responses when exploring novel agents as improved SSRIs [30]. This suggests that it could be useful as an adjunct therapy in the treatment of depression and dementia, but this requires further systematic investigation.

Elevated plasma homocysteine concentrations have been implicated with risk of cognitive impairment and dementia, but it is unclear whether low vitamin B12 or folate status is responsible for cognitive decline or can prevent against it [31,32]. Most studies reporting associations between cognitive function and homocysteine or B-vitamins have used a cross-sectional or case–control design and have been unable to exclude the possibility that such associations are a result of the disease rather than being causal. The homocysteine hypothesis of dementia has attracted considerable interest, since homocysteine can be easily lowered by folic acid and vitamin B12, raising the prospect that B-vitamin supplementation could lower the risk of dementia. Incident dementia is more strongly associated with changes in folate,

vitamin B12 and homocysteine, than with previous concentrations. These changes may be linked to other somatic manifestations of early dementia, such as weight loss [33]. However, in a recent trial of high-dose vitamin B in patients with AD, it did not slow cognitive decline in individuals with mild-to-moderate AD [34]. Two other placebo-controlled trials of treatment with B12, folic acid, and B6 showed no advantage of vitamins over placebo at reducing the severity of depressive symptoms or the incidence of clinically significant depression over a period of 2 years in older men [35]. Similarly, a recent Cochrane review found no evidence for short-term benefit from vitamin B6 in improving mood (depression, fatigue and tension symptoms) or cognitive functions. For the older people included in one of the two trials included in the review, oral vitamin B6 supplements improved biochemical indices of vitamin B6 status, but potential effects on blood homocysteine levels were not assessed in either study. This review found evidence that there is scope for increasing some biochemical indices of vitamin B6 status among older people [36]. However, the limited available evidence suggests folate may have a potential role as a supplement to other treatments for depression. It is currently unclear if this is the case both for people with normal folate levels, and for those with folate deficiency [37]. More randomized, controlled trials are needed to explore possible benefits from vitamin B6 supplementation for healthy older people and those with cognitively impairment or dementia.

Omega-3 fatty acids

Other common dietary supplements are fish oil and omega-3 fatty acids. Reductions in cardiovascular risk, depression and rheumatoid arthritis symptoms have been correlated with omega-3 fatty acid intake, and there is increased interest in the use of omega-3 fatty acid supplementation for other psychiatric illnesses and prevention of AD. Omega-3 fatty acids are found principally in fish and seafood although some can be derived from green vegetables. By contrast, omega-6 fatty acids are found in soft margarine, most vegetable oils and animal fat. Omega-6 is plentiful in most modern Western diets while omega-3 is often relatively lacking. A high dietary ratio of omega-6 to omega-3 has been linked to vulnerability to many physical and mental disorders [38]. Reported health benefits include improvements in mood in unipolar and bipolar disorders, as well as dementia [39].

Following the well-publicized promising results from a placebo-controlled study [40], there has been a broad interest in the use of omega-3 fatty acids for the treatment of bipolar disorder and depression. There is mounting evidence that dietary supplementation with omega-3 fatty acids may be beneficial in treating a variety of conditions including several psychiatric disorders [39,41], although not all studies are in agreement [42]. Most studies recommend omega-3 essential fatty acids with an eicosapentaenoic acid (EPA):docosahexaenoic acid (DHA) ratio of 7:1.

In a prospective, naturalistic study of 5386 nondemented participants, fish consumption was inversely related to incident dementia. There is one case report of a patient with AD whose agitated behaviors improved after incorporation of fish in his diet. This suggests that omega-3 fatty acids may have a possible role in the prevention and treatment of dementia. To address potential mechanisms, a study documented the effect of DHA on inflammatory markers: AD patients treated with DHA-rich n-3 fatty acid supplementation increased their plasma concentrations of DHA (and EPA), which were associated with reduced release of IL-1β, IL-6 and granulocyte colony-stimulating factor from peripheral blood mononuclear cells [43]. However, in the recent well designed, placebo-controlled trial of the effect of EPA and DHA on mental wellbeing in a double-blind, placebo-controlled trial in the general older population, the study failed to find drug–placebo difference in improving cognition or wellbeing in older adults [44]. In a recent meta-analysis, omega-3 was suggested as an adjunctive treatment for depressive but not manic symptoms in bipolar disorder [45]. Another meta-analysis concluded

that available data are insufficient to draw strong conclusions about the effects of omega-3 fatty acids on cognitive function in normal aging or on the incidence or treatment of dementia. However, limited evidence suggests a possible association between omega-3 fatty acids and reduced risk of dementia [46].

In summary, omega-3 fatty acids may have a role in the treatment of late-life neuropsychiatric disorders. However, given the conflicting data on their efficacy, additional studies are needed before their use can be recommended confidently to patients. These studies should clarify the role and the optimal dose of omega-3 fatty acids or EPA in the treatment of the depression or cognitive decline and address lingering questions regarding the purity of marketed supplements.

S-adenosyl-L-methionine

S-adenosyl-L-methionine is one of the CAM products that has been studied under rigorous controlled conditions. SAMe is derived from the amino acid L-methionine through the one-carbon cycle and it is a methyl donor involved in the synthesis of the monoaminergic neurotransmitters. SAMe has been investigated for its antidepressant properties in both open [4,47] and randomized, controlled trials [48]. SAMe dosages of 200–1600 mg/day (orally or parenterally) have been shown to be superior to placebo and as effective as tricyclic antidepressants in alleviating depression, although some individuals may require higher doses [47,48]. SAMe may have a faster onset of action than conventional antidepressants and may potentiate the effect of tricyclic antidepressants [48] or of serotonin reuptake inhibitors [49]. At this time, the recommended doses vary but most commonly used include SAMe 200 mg twice daily, up to 800 mg twice daily. Oral dosages of SAMe up to 1600 mg/day appear to be significantly bioavailable and safe [50]. SAMe has been associated with minor adverse effects (e.g., gastrointestinal symptoms and headaches) [49]. However, as with any antidepressant compound, some cases of mania have been reported in bipolar patients taking SAMe [48,51].

Overall, SAMe appears to be safe and efficacious in the treatment of depression but further controlled studies are required since current evidence comes mostly from open trials or small controlled studies. It may have a role in the management of patients with bipolar disorder but more research is needed, in particular to determine its effective dose and to better assess the risk of switch to mania or hypomania [48].

Culturally based healing arts

Culturally based healing includes traditional Asian medicine (e.g., acupuncture, shiatsu, and reiki), Indian systems of healthcare (such as Ayurveda and yoga) and Native American healing practices (such as the Sweat Lodge and Talking Circles). All incorporate the beliefs that: wellness is a state of balance between the spiritual, physical, and mental/emotional ‘selves’; an imbalance of forces within the body is the cause of illness; and herbal/natural remedies, combined with sound nutrition, exercise and meditation/prayer, will correct this imbalance.

Acupuncture

The Chinese practice of inserting needles into the body at specific points manipulates the body’s flow of energy to balance the endocrine system. This manipulation regulates functions such as heart rate, body temperature and respiration, as well as sleep patterns and emotional changes. Acupuncture has been used in clinics to assist people with substance abuse disorders through detoxification; to relieve stress and anxiety; to treat attention deficit and hyperactivity disorder in children; to reduce symptoms of depression; and to help people with physical ailments. Compared with other empirically validated treatments, acupuncture designed specifically to treat major depression produced results that are comparable in terms of rates of

response and of relapse or recurrence. These results warrant a larger trial of acupuncture in the acute- and maintenance-phase treatment of depression [52]. In a recent small study of acupuncture, positive subjective and objective effect was found on mood and wellbeing [53]. However, in the recent Cochrane database review [54] of seven trials comprising 517 subjects who generally had mild-to-moderate depression, there was no evidence that medication was better than acupuncture in reducing the severity of depression, or in achieving remission.

There are fewer studies of acupuncture for dementia compared with depression or stress. Interestingly, in a recent Chinese study, Zhou and Jin reported acupuncture performed on corresponding scalp regions of the brain regions of AD [55]. A total of 26 patients with clinically diagnosed AD underwent functional MRI (fMRI) while undergoing acupuncture at the four acupoints. fMRI block design paradigm was chosen by electroacupuncture interval stimulation, and the data of fMRI were analyzed by Statistical Parametric Mapping (SPM 99). The results demonstrated that there were right main hemisphere activations (the temporal lobe, such as hippocampal gyrus, insula and some areas of the parietal lobe) and left-activated regions (the temporal lobe, parietal lobule and some regions of the cerebellum). The activated regions induced by these acupoints were consistent with impaired areas in brain for AD patients, which were closely correlated with the cognitive function (the memory, reason, language, executive and so on). The present study provided strong evidence that acupuncture had a potential effect on AD, and in partial revealed the mechanism. In summary, there is insufficient evidence to determine the efficacy of acupuncture compared with medication, or to wait list control or sham acupuncture, in the management of depression. Scientific study design is generally poor and the number of people studied was relatively small. One of the barriers to conducting appropriate studies of acupuncture is the difference in the diagnostic systems in the Western and Chinese medicine, precluding fair comparison.

Ayurveda

Ayurveda is a comprehensive natural health-care system that originated in India more than 5000 years ago and has been used for antiaging, memory enhancement, and as nerve tonic, anxiolytic, anti-inflammatory and immunopotentive remedies. It is still widely used in India as a system of primary healthcare, and interest in it is growing worldwide as well. Ayurveda means ‘the science of life’ (Ayur means ‘life’ and Veda means ‘knowledge or science). Ayurvedic medicine is described as ‘knowledge of how to live’. It incorporates an individualized regimen, such as diet, meditation, herbal preparations or other techniques to treat a variety of conditions, including depression, to facilitate lifestyle changes, and to teach people how to release stress and tension through yoga or transcendental meditation. There are some preliminary encouraging results for its effectiveness in treating various ailments, including chronic disorders associated with the aging process. Pilot studies of depression, anxiety, sleep disorders, hypertension, diabetes mellitus, PD and AD yielded positive results [56,57]. However, no extensive, controlled studies of Ayurveda in older adults are available to date.

There is an increasing number of publications on antioxidant, neuroprotective and memory-enhancing properties of various herbal Ayurvedic preparations in rat and mice models of AD [58,59]. The part of the Ayurvedic system that provides an approach to prevention and treatment of degenerative diseases is known as Rasayana, and plants used for this purpose are classed as rejuvenators. Traditional medicinal plants in various countries, particularly in India have been used for centuries for various ailments; however, there has been little scientific effort to validate these anecdotal uses mentioned in the literature.

A number of these traditionally used plant extracts and various Ayurvedic medicines that are highly valued in Ayurveda, have been screened using the National Institute of Mental Health (NIMH) Synthetic Screening Program for scientific validation and the development of new

leads of psychotherapeutic compounds using Radioligand Receptor Binding Assays (RRA) [58,59]. The focus was on plants showing the highest displacement of GABA, cholecystokinin (CCK), NMDA, monoamine oxidase and benzodiazopines. A bioactivity-guided fractionation of *Terminalia bellerica* fruit extract led to the isolation of several pure compounds that retained the original activity of the crude extract for CCK and GABA receptors, with the exception of compound B3EA-6, which exhibited high affinity for the neurokinin receptor.

In young and aging mice models, Anwala churna (50, 100 and 200 mg/kg, *per orem*) produced a dose-dependent improvement in memory scores. Furthermore, it reversed the amnesia induced by scopolamine (0.4 mg/kg, intraperitoneal) and diazepam (1 mg/kg, intraperitoneal). Interestingly, brain cholinesterase activity and total cholesterol levels were reduced by Anwala churna administered orally for 15 days. Anwala churna may prove to be a useful remedy for the management of AD on account of its multifarious beneficial effects such as its memory improving property, cholesterol-lowering property and anticholinesterase activity.

Ocimum sanctum (OS), a plant widely used in Ayurveda, has been shown to possess anti-inflammatory, antioxidant and cognition-enhancing properties [60]. In rats, the effect of methanolic extract of OS leaves was studied in cerebral reperfusion injury as well as long-term hypoperfusion. OS treatment (200 mg/kg/day for 15 days) significantly prevented long-term hypoperfusion-induced functional and structural disturbances. The results suggest that OS may be useful in treatment of cerebral reperfusion injury and cerebrovascular insufficiency states.

Trasina is a herbal formulation of some Indian medicinal plants classified in Ayurveda, the classic Indian system of medicine, as Medhyarasayanas, or drugs reputed to improve memory and intellect [61,62]. Earlier experimental and clinical investigations have indicated that the formulation has a memory-facilitating action. The effect of trasina was studied in the rodent model of AD simulating some biochemical features known to be associated with AD after subchronic administration for 21 days. Trasina (200 and 500 mg/kg) reversed deficits in acetylcholine after 14 and 21 days of treatment. The findings indicate that the herbal formulation exerts a significant nootropic effect after subchronic treatment that may be due to reversal of perturbed cholinergic function.

Conducting research that compares Ayurveda's comprehensive treatment approach, Western allopathic treatment, and an integrated approach combining the Ayurvedic and allopathic treatments would shed light on which treatment approach is the most effective for the benefit of the patient.

Yoga & meditation

Practitioners of yoga, the ancient Indian system of healthcare, use breathing exercises, posture, stretch and meditation to balance the body's energy centers. Mindful physical exercise is a special kind of physical exercise with an additional element that focuses on one's state of mind. It has recently emerged as a therapeutic intervention for improving the psychosocial wellbeing of individuals. According to IDEA Mind–body Fitness Committee (1997–2001), the mindful physical exercise is characterized by 'physical exercise executed with a profound inwardly directed contemplative focus'. A physical exercise is considered mindful if:

- It has a meditative/contemplative component that is noncompetitive and nonjudgmental;
- It has proprioceptive awareness that involves a low-to-moderate level of muscular activity with mental focus on muscular movement;
- It is breath centering;

- It focuses on anatomic alignment, such as spine, trunk and pelvis, or proper physical form;
- It concerns energy centric as awareness of individuals' flow of intrinsic energy, vital life force, qi and so on [63].

With the above framework, yoga and qigong are two major streams of mindful physical exercise based on the literature. Yoga is used in combination with other treatments for depression, anxiety and stress-related disorders.

The principle of yoga is to achieve integration of mind, body and spirit. There are 22 types of yoga and many more modifications. The most popular type in the USA is Hatha yoga, a branch of yoga that requires a vast repertoire of physical postures during sitting, standing or lying on the floor, along with specific breathing patterns. Other than physical movement, participants are required to maintain a 'homeostasis' of mind and body, which refers to the relaxation of body tension with quieting of thoughts. The qigong exercise is a system of self-practicing physical exercise, which includes healing posture, movement, self-massage, breath work and meditation. All forms of qigong are featured on balance, relaxation, breathing and good posture. The movements of qigong are executed at very low energy expenditure levels. A specific breathing pattern also applies to qigong. Similar to yoga, the breathing style of qigong is slow and deep in order to achieve body relaxation, clearing of mind, and, additionally, maintenance of health. Combining all of the above components, the mindful physical exercise has been shown to provide an immediate source of relaxation and mental quiescence [63]. Scientific evidence demonstrates that medical conditions, such as hypertension, cardiovascular disease, insulin resistance, depression and anxiety disorders, respond favorably to the mindful physical exercises [64].

Despite a growing body of evidence to show the effects of mindful physical exercises such as qigong, tai chi and yoga on depression [59,65–73], there is a dearth of reviews that have examined mindful physical exercise as to its effects on alleviating depression [74,75]. A recently published review on complementary and alternative treatments in older adults demonstrated that mind–body interventions were effective on treating depression, anxiety and insomnia in ten out of 12 studies reviewed [2].

The effects of yoga and Ayurveda on geriatric depression were evaluated in 69 patients older than 60 years who were living in a residential home [76]. Participants were stratified by age and gender and randomly allocated to three groups: yoga, Ayurveda or wait-list control. The 15-item Geriatric Depression Scale (GDS) was used to assess depressive symptoms prior to the intervention and after 3months and 6 months postinter-vention. Participation in one of the three groups lasted 24 weeks. The yoga program (7 h 30 min per week) included physical postures, relaxation techniques, regulated breathing, devotional songs and lectures. The Ayurveda group received an herbal preparation twice daily for the whole period. The depression symptom scores of the yoga group at both 3 and 6 months decreased significantly, from a group average baseline of 10.6–8.1 and 6.7, respectively ($p < 0.001$, paired t-test). The other groups showed no change. Hence, an integrated approach of yoga including the mental and philosophical aspects in addition to the physical practices was useful for institutionalized older persons.

Chen and Tseng reported the results of a pilot study on the health-promoting effects of a silver yoga exercise program for female seniors [77]. Using a one-group, prepost test design, a convenience sample of 16 community-dwelling female seniors was recruited. The silver yoga exercise intervention was administered three times a week, 70min per session, for 4 weeks. Data were collected at baseline and after completion of the 4-week intervention. Results indicated that participants' body fat percentage and systolic blood pressure decreased, balance

and range of motion on shoulder flexion and abduction improved, and sleep disturbance was minimized (all $p < 0.05$).

In a small randomized pilot study, Butler *etal.* investigated the effects of meditation with yoga (and psychoeducation) versus group therapy with hypnosis (and psychoeducation) versus psychoeducation alone on diagnostic status and symptom levels among 46individuals with long-term depressive disorders [78]. Results indicate that significantly more meditation group participants experienced a remission compared with controls at 9-month follow-up. Eight hypnosis group participants also experienced remission, but the difference from controls was not statistically significant. Three control participants, but no meditation or hypnosis participants, developed a new depressive episode during the study, although this difference did not reach statistical significance in any case. Although all groups reported some reduction in symptom levels, they did not differ significantly in that outcome. Overall, these results suggest that these two interventions show promise for treating mild-to-moderate depression.

Meditation, spirituality & pastoral care

Some people prefer to seek help for mental health problems from their pastor, rabbi or priest, rather than from therapists who are not affiliated with a religious community. Counselors working within traditional faith communities are increasingly recognizing the need to incorporate psychotherapy and/or medication, along with prayer and spirituality to effectively help some people with mental disorders. Both religiousness and social support have been shown to influence depression outcome, yet some researchers have theorized that religiousness largely reflects social support. In a recent study, religious coping was related to social support, but was independently related to depression outcome. The authors concluded that clinicians caring for older depressives should consider inquiring about spirituality and religious coping as a way of improving depressive outcomes [79]. The protective effects of religion against late-life depression may depend on the broader socio–cultural environment. Religious practice, church attendance or prayer, especially when it is embedded within a traditional value-orientation, may facilitate coping with adversity in later life and stress reduction [80–84].

Clinical effects of meditation impact a broad spectrum of physical and psychological symptoms and syndromes, including reduced anxiety, pain and depression, enhanced mood and self-esteem, and decreased stress. Meditation has been studied in populations with fibromyalgia, cancer, hypertension and psoriasis. While earlier studies were small and lacked experimental controls, the quality and quantity of valid research is growing. Meditation practice can positively influence the experience of chronic illness and can serve as a primary, secondary, and/or tertiary prevention strategy. Health professionals demonstrate commitment to holistic practice by asking patients about use of meditation, and can encourage this self-care activity. Simple techniques for mindfulness can be taught in the clinical setting. Living mindfully with chronic illness is a fruitful area for research, and it can be predicted that evidence will grow to support the role of consciousness in the human experience of disease [85]. Mindfulness-based cognitive therapy (MBCT) is a recently developed class-based program designed to prevent relapse or recurrence of major depression [86]. Although research in this area is in its infancy, MBCT is generally discussed as a promising therapy in terms of clinical effectiveness in treatment and relapse prevention in major depression [87]. No studies of MBCT are available in the elderly.

Relaxation & stress reduction techniques: biofeedback

Learning to control muscle tension and ‘involuntary’ body functioning, such as heart rate and skin temperature, can be a path to mastering one’s fears. It is used in combination with, or as an alternative to medication to treat disorders such as anxiety, panic and phobias. For example, a person can learn to ‘retrain’ his or her breathing habits in stressful situations in order to induce

relaxation and decrease hyperventilation. Some preliminary research indicates it may offer an additional tool for treating depression [88]. Although there are no data in geriatric depression, an increasing number of publications use biofeedback for memory training and cognitive enhancement using neurofeedback (NF). NF is an electroencephalographic (EEG) biofeedback technique for training individuals to alter their brain activity via operant conditioning. Research has demonstrated that NF helps to reduce the symptoms of several neurological and psychiatric disorders, with ongoing research currently investigating applications to other disorders and to the enhancement of nondisordered cognition.

Angelakis *et al.* used EEG peak alpha frequency (PAF) for NF because it has been shown to correlate positively with cognitive performance and to correlate negatively with age [89]. In a pilot double-blind study of NF, training older individuals to increase PAF resulted in improved cognitive performance. The results suggested that PAF NF improved cognitive processing speed and executive function, but that it had no clear effect on memory. Kotchoubey *etal.* reported the results of two groups of subject comparison, aged 20–28 and 50–64 years, respectively, matched for health status and verbal abilities [90]. Subjects learned to control their slow cortical potentials (SCP) in a feedback paradigm by producing, on command, SCP shifts in either a positive or negative direction. Both groups were able to differentiate significantly between the positivity task and the negativity task, with the differentiation score being only slightly (and not significantly) lower in older than in younger subjects. Older subjects had only explicit, but not implicit, learning deficits. The pattern of consistently more negative SCP shifts produced by elderly subjects may indicate their impaired cortical inhibition probably caused by brain aging. The question remains if biofeedback could be helpful in reducing cognitive deficits associated with aging or dementia.

Massage therapy

The underlying principle of this approach is that rubbing, kneading, brushing and tapping a person's muscles can help release tension and pent emotions. It has been used to treat trauma-related depression and stress. A highly unregulated industry, certification for massage therapy varies widely from state to state. Few studies have been carried out on the effects of massage therapy among older adults. Furthermore, existing studies of massage effects on anxiety, depression and stress have tended to focus on clinic population samples with relatively high levels of distress, rather than community-based samples of people who have not exhibited clinical levels of distress. The potential of massage therapy to promote older adults' perceptions of wellbeing and reduce perceived stress has not been studied, nor is it known if massage might be superior to guided relaxation in affecting these perceptions. Sharpe *et al.* reported significant improvements for the anxiety, depression, vitality, general health and positive wellbeing sub-scales of the General Wellbeing Schedule and for Perceived Stress among the massage participants compared with guided relaxation [91]. However, Hirakawa *et al.* in a study of home massage rehabilitation therapy, did not demonstrate a positive effect on the bed-ridden elderly, either mentally or physically [92]. Cambron *etal.* reported the side effects of massage therapy in 10% of the massage clients who experienced some minor discomfort after the massage session; however, 23% experienced unexpected, nonmusculoskeletal positive side effects [93]. The majority of negative symptoms started less than 12 h after the massage and lasted for 36 h or less. The majority of positive benefits began immediately after massage and lasted more than 48 h.

Exercise

Human and other animal studies demonstrate that exercise targets many aspects of brain function providing broad effects on overall brain health. The benefits of exercise have been best defined for learning and memory, protection from neurodegeneration and alleviation of depression, particularly in the elderly populations. Exercise increases synaptic plasticity by

directly affecting synaptic structure and potentiating synaptic strength, and by strengthening the underlying systems that support plasticity including neurogenesis, metabolism and vascular function. Such exercise-induced structural and functional change has been documented in various brain regions but has been best studied in the hippocampus [94].

Emerging evidence suggests that exercise has therapeutic and preventative effects on depression [94]. The prevention and treatment of depression are important areas to define: depression is linked to cognitive decline [95] and is considered to cause a worldwide health burden greater than that of ischemic heart disease, cerebrovascular disease or tuberculosis [96]. Therapeutic effects of exercise on depression have been most clearly established in human studies. Randomized and crossover clinical trials demonstrate the efficacy of aerobic or resistance-training exercise (2–4 months) as a treatment for depression in both young [97] and older individuals [98,99]. The benefits are similar to those achieved with anti-depressants [98]. They are also dose dependent: greater improvements are seen with higher levels of exercise [99].

Furthermore, the therapeutic effects of exercise on depressive symptoms have been demonstrated in conditions of neurodegeneration in humans. Specifically, in a randomized clinical trial, 3 months of exercise intervention improved depressive symptoms in individuals with AD, whereas nonexercising subjects showed worsening of depressive symptoms [97]. In addition to a therapeutic effect, evidence from human studies demonstrate that exercise can provide some protection from the development of depression [100]. A protective effect of sustained exercise (>2 weeks) has been clearly demonstrated in animal models of depression, including stress-induced learned helplessness [101,102]. In addition, a therapeutic effect of exercise on exiting depression has been recently established in an animal model [103]; this therapeutic effect parallels that observed in human studies. In a recent study of exercise in early AD, cardiorespiratory fitness was modestly reduced in subjects with AD compared with subjects without dementia and was associated with whole-brain volume and white matter volume reductions after controlling for age [104]. In participants with no dementia, there was no relationship between fitness and brain atrophy. Therefore, cardiovascular fitness may moderate AD-related brain atrophy; however, further studies are needed to resolve inconsistent findings.

Although exercise seems to have both preventative and therapeutic effects on the course of depression, the underlying mechanisms are poorly understood. Protective effects of exercise from stress have focused on the hippocampus, where exercise-induced neurogenesis [105] and growth factor expression [106] have been proposed as potential mediators, although not without controversy [107]. Other proposed mechanisms include exercise-driven changes in the hypothalamic–pituitary–adrenal axis that regulates the stress response [97], and altered activity of dorsal raphe serotonin neurons implicated in mediating learned helplessness behaviors [102]. It is important to note that the translatability of animal studies is dependent on the animal model of depression and how well it parallels the human condition–an area that remains under active investigation.

A key mechanism mediating these broad benefits of exercise on the brain is induction of central and peripheral growth factors and growth factor cascades, which instruct downstream structural and functional change. In addition, exercise reduces peripheral risk factors such as diabetes, hypertension and cardiovascular disease, which converge to cause brain dysfunction and neurodegeneration. A common mechanism underlying the central and peripheral effects of exercise might be related to inflammation, which can impair growth factor signaling both systemically and in the brain. Thus, through regulation of growth factors and reduction of peripheral and central risk factors, exercise ensures successful brain function [94].

Expressive therapies

Creativity interventions have been shown to positively affect mental and physiological health indicators in older adults. Developing creative coping strategies can enable older adults to adapt more effectively to physical, psychological and psychosocial changes that occur during old age. The process of creating and one's attitude toward life may be more important than the actual product or tangible outcome. Addams-Price concludes that late-life creativity reflects aspects of late-life thinking: synthesis, reflection and wisdom [108]. From a problem-solving perspective, creativity is an asset in older adulthood, given the number of health, functional and financial limitations likely to occur [109]. Many older adults might not describe themselves as creative and would be reluctant to engage in typical creative endeavors, such as painting or drawing.

Art & music therapy

Drawing, painting and sculpting help many people to reconcile inner conflicts, release deeply repressed emotions, and foster self-awareness, as well as personal growth. Some mental health providers use art therapy as both a diagnostic tool and as a way to help treat disorders such as depression, abuse-related trauma and schizophrenia. Music or sound therapy has been used to treat disorders such as stress, grief, depression, loneliness, and cognitive and functional decline.

The largest study of creativity to date is Cohen's investigation of the impact of professionally conducted cultural programs on older adults [110]. This study involved 150 treatment and 150 control participants aged 65 years and older, who were matched for health and functioning. Control participants were permitted to engage in their routine activities; however, none of them became involved in rigorous and sustained participation in art programs during the course of the study. The treatment group reported better health 1 year after baseline starting point measures; the control group reported their health was not as good 1 year postbaseline measures [202]. Furthermore, the intervention group reported an average of 9.27 doctor visits per year while the control group reported an average of 13.19 visits per year. Both groups had more visits when compared with baseline, but the control group's visits increased at a greater rate [202]. Medication use increased at a greater rate in the control group as compared with the intervention group. The average number of medications reported by the intervention group at the 1-year follow-up was 6.97, while the average number of medications reported by the control group at the 1-year follow-up was 8.48. Mental health was positively affected by the intervention as well; an examination of the means revealed that the intervention group revealed significantly lower levels of depression compared with the control group after 1 year. The intervention also group had a self-reported morale score that was significantly higher (higher morale) than the control group (14.07 and 13.07, respectively) 1 year later. In addition to older adults' enjoyment, the physiological benefits of creativity, combined with the mental health advantages, are key reasons for the use of creative activities in older adults. These findings provide overwhelming support for this notion, linking the engaging nature, physical and mental health benefits of creativity [202].

Dance & movement therapy

The underlying premise to dance/movement therapy is that it can help a person integrate the emotional, physical and cognitive facets of 'self.' A recent study designed a multimodal program aimed at influencing a group of 75 older adult participants' purpose in life, depression and hypochondriasis, by targeting physical, mental and spiritual wellbeing [111]. Interventions included rhythm and dance exercises; general physical exercises; recreational exercise outdoors; relaxation exercises; a creativity enhancement seminar; a seminar on psychology and philosophy of life; and a seminar on contact with other people and communication. The group sessions were conducted 2 days per week over a period of 4 months. A purpose in life, depression and hypochondria were three parameters of wellbeing that were measured pre- and

post-intervention. The purpose in life scale (PIL) measured purpose in life, the GDS assessed depressive symptoms, and the hypochondriasis scale institutional geriatric (HIP) determined the presence of hypochondria. The first day each week consisted of 1 h of some form exercise and a 2 h seminar. The second day each week was comprised of 1 h of relaxation, 1 h of exercise and 2 h of a seminar about stimulating creativity. Significant changes in test scores were observed over time. Mean PIL scores increased from preintervention to postint-ervention, suggesting greater purpose in life, and these scores remained elevated at 6 months postintervention. Scores for the GDS and the HIP decreased from preintervention to postint-ervention, indicating a decrease in depressive symptoms and hypochondriasis, and continued to be significantly reduced 6 months postinter-vention. Outcomes suggested that interventions were successful in improving quality of life as evidenced by an increased purpose in life and decreased depression and hypochondriasis.

Those who prefer more structure or who feel they have ‘two left feet’ gain the same sense of release and inner peace from the Eastern martial arts, such as Tai Chi. There is considerable evidence that Tai Chi has positive health benefits; physical, psychosocial and therapeutic [112]. Furthermore, Tai Chi does not only consist of a physical component, but also sociocultural, meditative components that are believed to contribute to overall wellbeing. Tai Chi exercise is chosen by the elderly for its gentle and soft movements. Besides the physical aspect, the benefits they describe include lifestyle issues, as well as psychological and social benefits [113,114]. Evidence highlights that the improvements in physical and mental health through the practice of Tai Chi among the older adults are related to their perceived level of quality of life [115]. Findings from numerous studies support the belief that the practice of Tai Chi has multiple benefits to practitioners that are not only physical in nature. It is recommended as a strategy to promote successful cognitive and emotional aging.

Conclusion

In summary, late-life mood and cognitive disorders are the most common reasons for using complementary and alternative therapies. The amount of rigorous scientific data to support the efficacy of complementary therapies in the treatment of depression is extremely limited. The areas with the most evidence for beneficial effects are exercise, herbal therapy (*Hypericum perforatum*), the use of fish oil, and, to a lesser extent, acupuncture and relaxation therapies. There is a need for further research involving randomized, controlled trials into the efficacy of complementary and alternative therapies in the treatment of depression and cognitive impairment in later life, and the development of effective treatment approaches for these serious conditions.

Future perspective

The public health significance of late-life mood and cognitive disorders is rapidly growing with the mounting number of elderly persons. The cost of care for the victims of mental and cognitive illnesses will increase exponentially in the next several decades. The available standard treatments and preventive strategies have only limited efficacy. At the same time, the interest and use of CAM is rising among aging persons. The currently available evidence of the efficacy of CAM interventions is limited owing to the serious methodological limitations and the lack of understanding of Asian medicine. Only true integration of the specific outcomes, increasing the understanding of various approaches and application of this in clinical research will be likely to benefit researchers, clinicians and older adults. The number of studies of various CAM interventions and translational research is steadily rising, and will probably lead to a merger of the methodologies and approaches of the Eastern and Western medicine.

Executive summary

Trends in use of complementary & alternative medicine in the USA

- Late-life mood disorders and cognitive aging are the most common reasons for using complementary and alternative therapies.
- An alternative approach to mental healthcare is one that emphasizes the interrelationship between mind, body and spirit.
- Despite the increasing use of complementary and alternative medicine (CAM) by individuals, the scientific support for its efficacy is limited. The treatments with the best evidence of effectiveness are St John's wort, exercise, cognitive behavior therapy and light therapy. There is some limited evidence to support the effectiveness of acupuncture, massage therapy, relaxation therapy, *S*-adenosylmethionine, folate and yoga breathing exercises.
- The principal uses in older adults include stress reduction, antiaging effects of CAM for the prevention of diseases of aging, memory enhancement and treatment of various neuropsychiatric disorders, such as depression, anxiety, insomnia, pain and many other specific indications.

Complementary & alternative medicine use in late-life mood & cognitive disorders

- Mood and cognitive impairment are the most frequently occurring psychiatric syndromes in older adults. Mood disturbances are commonly observed in patients with neurodegenerative disorders including probable Alzheimer's disease (AD), Parkinson's and poststroke depression. Depression in later life is a treatable condition.

Diet & the use of nutritional & herbal supplements

- Adjusting both diet and nutrition may help some people with mental illnesses manage their symptoms and promote recovery. Herbel supplements, B-complex vitamins, riboflavin, magnesium and thiamine are used to treat anxiety, depression and memory loss. There is a significant amount of evidence supporting the use of *Hypericum perforatum* (St John's wort) for depression, and omega-3 fatty acids and gingko biloba for dementia.
- Ginkgo biloba leaf extract is among the most widely sold herbal dietary supplements in the USA. Its purported biological effects include: scavenging free radicals; lowering oxidative stress; reducing neural damages, reducing platelets aggregation; anti-inflammation; antitumor activities; and antiaging. Ginkgo biloba has been widely used for many years by people with symptoms attributed to 'cerebrovascular insufficiency', but the results are inconsistent.

Use of nutritional supplements

- Folate, tryptophan and phenylalanine have been used and studied as adjuncts to enhance the effectiveness of conventional antidepressants in the treatment of depression.
- A high dietary ratio of omega-6 to omega-3 has been linked to vulnerability to many physical and mental disorders. Reported health benefits include improvements in mood in unipolar and bipolar disorders, as well as dementia. Fish oil and omega-3 fatty acids lead to reductions in cardiovascular risk and depression. There is increased interest in the use of omega -3 fatty acid

supplementation for other the use of omega psychiatric illnesses and prevention of AD.

- *S*-adenosylmethionine is derived from the amino acid L-methionine through the one-carbon cycle and it is a methyl donor involved in the synthesis of the monoaminergic neurotransmitters. SAMe dosages of 200–1600 mg/day (orally or parenterally) have been shown be superior to placebo and as effective as tricyclic antidepressants in alleviating depression, although some individuals may require higher doses. SAMe may have a faster onset of action than conventional antidepressants and may potentiate the effect of tricyclic antidepressants or of serotonin reuptake inhibitors.

Culturally based healing arts

- Culturally based healing includes traditional Asian medicine (such as acupuncture, shiatsu and reiki), Indian systems of healthcare(such as Ayurveda and yoga), and Native American healing practices (such as the sweat lodge and talking circles). All incorporate wellness is a state of balance between the spiritual, physical and mental/emotional 'selves'; an imbalance of forces within the body is the cause of illness; herbal/natural remedies, combined with sound nutrition, exercise and meditation/prayer, will correct this imbalance.
- Ayurveda is a comprehensive natural healthcare system that originated in India more than 5000 years ago. Ayurvedic medicine is described as 'knowledge of how to live'. It incorporates an individualized regimen, such as diet, meditation, herbal preparations or other techniques to treat a variety of conditions, including depression, to facilitate lifestyle changes, and to teach people how to release stress and tension through yoga or transcendental meditation. There are encouraging results for its effectiveness in treating various ailments, including chronic disorders associated with the aging process. Pilot studies of depression, anxiety, sleep disorders, hypertension, diabetes mellitus, PD and AD yielded positive results.
- Acupuncture is the Chinese practice of inserting needles into the body at specific points to manipulate the body's flow of energy to balance the endocrine system. This manipulation regulates functions such as heart rate, body temperature and respiration, as well as sleep patterns and emotional changes. Compared with other empirically validated treatments, acupuncture designed specifically to treat major depression produced results that are comparable in terms of rates of response and of relapse or recurrence, and wellbeing.

Yoga & meditation

- Yoga, the ancient Indian system of healthcare, uses breathing exercises, posture, stretches and meditation to balance the body's energy centers. Mindful physical exercise is a special kind of physical exercise with an additional element on the state of mind. It has recently emerged as a therapeutic intervention for improving psychosocial wellbeing of older individuals. Scientific evidence shows that medical conditions such as hypertension, cardiovascular disease, insulin resistance, depression and anxiety disorders respond favorably to the mindful physical exercises.

Relaxation & stress reduction techniques: biofeedback

- Biofeedback assists in learning to control muscle tension and involuntary body functioning, such as heart rate and skin temperature, and can be a path to mastering one's fears. It is used in combination with, or as an alternative to, medication to treat disorders such as anxiety, panic and phobias. For example, a person can learn

to ‘retrain’ his or her breathing habits in stressful situations to induce relaxation and decrease hyperventilation. Some preliminary research indicates that it may offer an additional tool for treating depression and in improving cognitive performance.

- Massage therapy uses rubbing, kneading, brushing and tapping a person’s muscles in order to help release tension and pent emotions. It has been used to treat trauma-related depression and stress, and anxiety, depression, general health and positive wellbeing.

Exercise

- Human and animal studies demonstrate that exercise targets many aspects of brain function providing broad effects on overall brain health. The benefits of exercise have been best defined for learning and memory, protection from neurodegeneration and alleviation of depression, particularly in elderly populations.

Expressive therapies

- Expressive therapies use creativity interventions that have been shown to positively affect mental and physiological health indicators in older adults. Developing creative coping strategies can enable older adults to adapt more effectively to physical, psychosocial and psychosocial changes that occur during old age.
- Drawing, painting and sculpting help many older people to reconcile inner conflicts, release deeply repressed emotions, and foster self-awareness, as well as personal growth. Some mental health providers use art therapy as both a diagnostic tool and as a way to help treat disorders such as depression. Music or sound therapy has been used to treat disorders such as stress, grief, depression, loneliness, cognitive and functional decline.

Dance & movement therapy

- Dance and movement therapy can help a person integrate the emotional, physical and cognitive facets of ‘self’ by targeting physical, mental and spiritual wellbeing. Interventions included rhythm and dance exercises; general physical exercises; recreational exercise outdoors; relaxation exercises; a creativity enhancement seminar; a seminar on psychology and philosophy of life; and a seminar on contact with other people and communication.
- Tai Chi has positive health benefits; physical, psychosocial and therapeutic, and improves perceived level of quality of life. Findings from numerous studies support the belief that the practice of Tai Chi has multiple benefits to practitioners that are not only physical in nature. It is recommended as a strategy to promote successful cognitive and emotional aging.

Conclusion

- There is a need for further research involving randomized, controlled trials into the efficacy of complementary and alternative therapies in the treatment of depression and cognitive impairment in later life, including the development of effective treatment approaches for these serious conditions.

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Table 1

Complementary and alternative medicine interventions for the treatment of late-life affective and cognitive disorders.

Mode of intervention	Postulated mechanism of action	Scientific evidence		Main adverse effects and drug interactions
		Depression	Dementia and cognition	
St John's wort	MAOI and reduced monoamine reuptake, and decreased amyloid production in rodent models of AD	Close to 40 RCTs	Positive animal studies	Mania; serotonergic syndrome; photosensitivity; multiple drug interactions with HIV protease inhibitors, warfarin, digoxin, oral contraceptives and anticonsvulsants
Omega-3 fatty acids (fish oil)	Mood stabilization, memory enhancement, neuroprotection, and reduction in amyloid production	Several RCTs are mixed or negative in the effect on mood and wellbeing	Several RCTs are mixed or negative in the effect on cognition	Fishy aftertaste; gastrointestinal distress; increased effect of warfarin and NSAIDs
SAMe	Cofactor in neurotransmitter synthesis and methylation homocysteine to methionine	Several RCTs, Parenteral SAMe is superior to placebo	Animal studies are suggestive of potential use; no human studies available	Mania; gastrointestinal distress; headache interaction with SSRIs
Folate and B12	Cofactor in neurotransmitter synthesis, methylation homocysteine to methionine and precursor to SAMe	Folic acid is an effective adjunct	RCTs are suggestive of usefulness in prevention of cognitive decline and improved memory performance	Mania induction; interaction with SSRIs
Gingko biloba	Scavenging free radicals; lowering oxidative stress; reducing neural damages; increased blood flow to brain	Several RCTs in postmenopausal women, and for sexual side effects of antidepressants: mixed results	Mixed and negative results in RCTs of dementia and other cognitive disorders	Increased bleeding time; allergic reactions
Ayurveda	Indian treatment system with the use of herbs, diet and lifestyle to achieve balance in cognition and wellbeing	Few studies suggestive of positive effect	Few RCTs; suggestive of positive effect	Consistent with the above side effect of herbals
Acupuncture	Balancing energy flow through the meridians in the body	Small RCTs with poor controls, randomization and blinding and inconclusive results	A few trials: improved memory and other cognitive tests in AD/VAD	Needle phobia; bleeding
Yoga	Postures, breath, meditation- rebalancing the mind–body connections	Reduced depression and enhanced wellbeing in a few studies	A few uncontrolled studies showed improved attention and memory in nondemented adults	None
Biofeedback	Retraining of the autonomic nervous system or alpha-brain waves	No data available	Alpha peak in brain waves is associated with enhanced cognitive performance	None
Spirituality	Lowers stress and enhances cognition via church attendance and prayer	Improves depression in practitioners	Enhances cognitive performance in those who attend church	None
Exercise	Improved cardiovascular function, release of endorphins, increased energy and mental stimulation	Improved mood and wellbeing, especially in minor depression	Modest improvement in cognition in dementia	None
Expressive therapies (art, music and dance)	Allows expression of emotional and cognitive facets of self	Improves mood and stress reduction	Can help expression in those with language and memory impairment	None

AD: Alzheimer's disease; MAOI: Monoamine oxydase inhibitor; NSAID: Nonsteroidal anti-inflammatory drug; RCT: Randomized, controlled trial; SAMe: S-adenosyl-l-methionine; SSRI: Serotonin-specific reuptake inhibitor; VAD: Vascular dementia.