



Nutrition and Lifestyle Intervention on Mood and Neurological Disorders

Gary Null, PhD¹, Luanne Pennesi, RN, MS¹,
and Martin Feldman, MD^{2,y}

Abstract

This group study explored how an intervention of diet and lifestyle, including a vegan diet, fruit and vegetable juicing, nutritional supplements, regular exercise, and destressing techniques, would affect 27 subjects with anxiety, depression, poor memory, dementia, Alzheimer's disease, Parkinson's disease, history of stroke, or multiple sclerosis. Several subjects had overlapping conditions. Videotaped testimonials were obtained describing subjective results. Testimonials stated multiple benefits across all conditions addressed by the study, with subjects often reporting substantial benefits. These results demonstrate that an intervention of diet, juicing, supplements, exercise, and lifestyle may provide considerable benefits for all conditions addressed.

Keywords

neurological, diet, lifestyle, depression, anxiety

Received December 17, 2015. Accepted for publication February 6, 2016.

Within a given year (12-month prevalence), 18.1% of the US adult population will have experienced an anxiety disorder,¹ with 4.1% classified as severe.¹ A total of 22.8% of the population has experienced anxiety disorder at some point in their lives.² The 12-month prevalence of major depression for adults in 2013 in the United States was 6.7%, or 15.7 million persons.³

An estimated 5.3 million or 1.6% of Americans of all ages have Alzheimer's disease in 2015, and without breakthroughs in prevention or treatment, such numbers may nearly triple by 2050.⁴ For US residents over age 70 years, rates for Alzheimer's, vascular dementia, and all-cause dementia are 9.74%, 2.43%, and 13.93%, respectively.⁵ In 2010, approximately 630 000 people in the United States had diagnosed Parkinson's disease, with diagnosed prevalence likely to double by 2040.⁶ Every year, more than 795 000 people in the United States have a stroke.⁷ Using data from 2000 and earlier, best available estimates for multiple sclerosis prevalence in the United States range from 211 000 to 400 000.^{8,9}

Exercise has shown effects on depression.¹⁰ It has shown effects on cognition in healthy subjects¹¹ and motor function and dementia.¹² However, a meta-analysis showed a lack of effect on dementia.¹³ Studies showed positive effect on brain mitochondrial biogenesis.^{14,15}

Antioxidants b-carotene and vitamins C and E have shown positive association related to Alzheimer's risk.¹⁶⁻¹⁸ Antioxidants have shown benefit for depression,¹⁹ and antioxidant status has shown association with depression.²⁰ Vitamin C has shown positive effects on anxiety but not on depression in one study²¹ and positive effects on anxiety in another.²²

Coenzyme Q10 has produced benefits or shown positive association regarding Parkinson's in multiple studies.²³⁻²⁸ Serum and dietary magnesium have shown inverse association with depression.^{29,30} Omega-3 fatty acids have shown benefit for depression.^{31,32} They affected brain structures alone,³³ and in combination with exercise and stimulation.³⁴ Omega-3 fatty acids showed a possible role in preventing cognitive decline and dementia.³⁵ Quercetin, with epicatechin or curcumin, showed neuroprotective effects.^{36,37}

Folate has shown help for depression.³⁸ Low folate and B₁₂ levels were associated with depression in older women.³⁹ B vitamins showed benefit on mild cognitive impairment in a small study,⁴⁰ but not on cognitive decline in Alzheimer's in another study.⁴¹ B vitamins appear to slow brain atrophy in elderly with mild cognitive impairment.⁴² Omega-3 fatty acids and B vitamins may need to work together to ameliorate brain atrophy.⁴³ Studies showed association with homocysteine, low B₁₂, and low folate with cognitive impairment and Alzheimer's.⁴⁴⁻⁴⁶

Zinc showed benefits for depression,⁴⁷ and deficiency is associated with neurodegenerative disorders.⁴⁸ Coenzyme

¹ Fairleigh Dickinson University, Teaneck, NJ, USA

² Mount Sinai School of Medicine, New York, NY, USA
yDeceased

Corresponding Author:

Gary Null, PhD, 135 Madison Avenue, 12th Floor, New York, NY 10016, USA.
Email: Jeremy@garynull.com

Q10, and dietary antioxidants including vitamins A, C, and E, have shown neuroprotective effects in relation to Parkinson's disease.⁴⁹ For multiple sclerosis, evidence exists for benefits from a variety of nutritional interventions including zinc, essential fatty acids, vitamin/mineral supplementation, and antioxidants.⁵⁰⁻⁵²

Materials and Methods

Subjects

Subjects were recruited from announcements on Dr Null's radio program, drawn from the general public. A group of 10 men and 17 women undertook the program, 9 with emotional disorders including anxiety, depression, and with some overlapping: 16 with issues of low memory, dementia, Alzheimer's disease, Parkinson's disease, history of stroke, and related issues. Program entry required a letter from an MD confirming the conditions. Four subjects with cognitive issues were represented at meetings by family as proxy, who would administer protocols to the subjects. Subjects were instructed to maintain regular contact with their physicians. Only their MD was to determine if medications were to be altered or eliminated.

Study Design

This was a lifestyle modification study on the impact of lifestyle and diet on individuals suffering mainly from cognitive decline, Parkinson's disease, anxiety, or depression. The study consisted of instruction on the necessary components of a healthy lifestyle: proper diet, juicing, supplements, detoxification exercise, destressing, environmental hygiene, and examination of beliefs and attitudes. Information on the prescribed intervention was given in weekly sessions of 2½ hours each, over a period of 3 months from the first meeting to the last. Twenty-seven persons initially presented at the first meeting. Medical supervision was provided by Dr Martin Feldman, MD, associate professor of medicine at Mt Sinai hospital in New York, and Luanne Pennesi, RN, a nurse practitioner with 36 years of experience including clinical nurse supervisor at Long Island Jewish hospital. Those in attendance on the final day who did not follow the protocol reported no improvement.

Protocol

Diet. Diet prescribed was an alkalizing anti-inflammatory vegan diet with 75% raw and 25% lightly cooked foods. It required complete elimination of certain foods, especially pro-inflammatory foods or food preparations, including refined carbohydrates and any wheat, gluten, dairy, meat, poultry, or shellfish. No caffeine, alcohol, refined sugar, or artificial sweeteners or chemicals such as additives, preservatives, coloring agents or flavorings, and no carbonated beverages, including sodas and seltzer were included. No conventional table salt, microwaved, deep fried, toasted foods, or nightshade vegetables were allowable. Those allowable were the following:

High-quality protein from vegetarian sources such as legumes, nuts, seeds, and grains: brown rice, Essene bread, millet, amaranth, buckwheat, and quinoa. Protein intake ideally was 0.9 g/kg of body weight (40-60 g high-quality protein for women and 60-80 g for men). Fiber intake was at least 35 to 50 g.

Beverages included herbal teas, nondairy milks: almond milk, rice, or oat milk, bottled or filtered water, fresh squeezed organic fruit juice, coconut milk, and coconut water.

Sweeteners raw honey, molasses, brown rice syrup, raw palm sugar, natural fruit sweeteners, and stevia.

Oils: grapeseed, sesame, extra virgin olive oil, coconut, macadamia and mustard seed oils in moderate amounts. Foods were to be cooked at low heat temperatures.

Nine to 12 servings of nutrient-dense fruits and vegetables (preferably organic) per day. Additionally, one serving of sea vegetables daily.

Fruits for anti-inflammation: fresh or frozen berries daily, purple or red grapes, apple, melons, kiwi, citrus, star fruit, papaya, berries, and pomegranate.

Herbs and spices: cayenne, curcumin, basil, rosemary, oregano, thyme, chili peppers, anise, cinnamon, horseradish, wasabi, mustard, dill weed, fennel, and spearmint.

Protein smoothie for breakfast, to include berries, 20 to 25 g of vegetable protein from powder: pea, rice, or hemp, 1000 to 2000 mg vitamin C, a handful of walnuts, rice or almond, or oat milk, 1 teaspoon chia powder or fennel seeds and 1 teaspoon coconut oil.

Juicing

Sixteen ounce glasses: celery cucumbers apple or watermelon, grapefruit, or lemon.

Also bok choy, cabbage, cilantro, parsley, kale, collard greens, carrots, beets, and chard.

Dilute green vegetables with water.

Apple seeds removed, citrus can be juiced whole with skin and lemon.

Two juices per day the first week, then increased frequency by one per week: 3 per day the second week, 4 per day the third week.

Morning drink of juice of a lemon, tablespoon of apple cider vinegar, and half teaspoon of manuka honey.

Two 12-ounce glasses of coconut water per day.

Supplements. Can be taken with protein shake, throughout day, or with food for sensitivities. Subjects were not required to take all supplements suggested.

Calcium citrate/magnesium citrate 1000 mg/1000 mg

B complex 50 mg

B₁₂ methylated

Omega-3 fatty acids 2000 mg

Coenzyme Q10 200 mg

Vitamin C 4000 mg in divided doses

Vitamin E mixed tocopherols 400 mg twice daily

Tocotrienols 200 mg

Zinc 20 mg

Vitamin A as b-carotene 15 000 IU

Quercetin 1000 mg in divided doses

Potassium 500 mg in divided doses, mainly as coconut water

Detoxification. This step is addressed on multiple levels in all parts of the protocol, avoiding pro-inflammatory diet items, use of juicing and supplements to eliminate toxins from the body, environmental hygiene

to eliminate ambient toxins, and in elimination of toxic beliefs, attitude, or relationships.

Exercise. Typical prescribed exercise was aerobic exercise such as power walking 45 to 60 minutes 5 days per week, and 3 days per week 30 minutes resistance exercise. Additional instruction was given for types of exercises that could be done in a seated position for those with significantly limited mobility.

Destressing. Examples discussed included daily yoga, meditation, tai chi, guided imagery, and mindfulness in nature.

Environmental Hygiene

- ﷲ Declutter living space.
- ﷲ Keep floors and surfaces with safe cleansers: can use hydrogen peroxide, rubbing alcohol.
- ﷲ Remove indoor pollution sources, including outgassing furniture, carpet, and building materials.
- ﷲ Use water filter, and veggie wash or apple vinegar to clean produce.
- ﷲ Avoid secondhand smoke.
- ﷲ Recommend houseplants or air filter for oxygen, purifying.

Beliefs and Attitudes for Self-Actualization. Participants were encouraged to examine core values, life purpose, potential for helping others, and to avoid conditioned responses and negative or self-limiting thinking.

Outcome Measures

Of those completing the study, 21 videotaped testimonials were obtained. Subjects were asked to identify conditions they or family members they represented had at the beginning and their symptoms, and changes in symptoms over the course of the study.

Videotaped Results (Edited for Clarity)

Anxiety and Depression

Sandra: Extreme Anxiety.

I came in with extreme anxiety. Completely closed in from the world—closed out from the world and now I'm able to sleep. I have freedom that I didn't have in an extremely long time. I was able to ride the subway and cross bridges. And even today it was extremely emotional for me to come here because I actually made it from my door to this door by myself and that's such a big achievement. So I want to say thank you. I'm high with the positive, very high and a lot more energy.

Leslie: Depression for Over 15 Years.

I was suffering from depression for over 15 years. I'm feeling much better; 100 percent I would say. My energy level is improved. I sleep better. I'm less fatigued and I have an overall positive attitude now.

Monica: Depression and Anxiety.

I've been suffering from depression and anxiety. Ever since I've started this program, I've been feeling so much better; so much more positive and no depression. I'm off the medication. It's just wonderful. This is great. I've been encouraging my husband, also, to be on the protocol. He has been, as well. We've been just together working on it and just feeling great.

Michael: Anxiety and Depression.

I came here for sometimes debilitating anxiety and depression. . . . I'd say, surprisingly, my vision improved. My skin cleared up. I feel like I'm a better husband, better father, better friend. . . . I lost probably seven pounds of pure fat and I got stronger. . . . I got stronger. I shattered a time on a three mile run. (Anxiety and depression) are just gone . . . it's lifted, . . . it was such a crutch and such an excuse, and now that it's gone, it's like I have to recreate myself. Definitely sharper, better memory. I have a tom rotator cuff and the pain has really subsided. I don't want to have surgery on it. It's lifted, as well. So, across the board, again, I feel really blessed to have met everybody, and I thank you all.

Carl: Debilitating Depression, Suicidal Tendency.

When I first started coming here, I was suicidal, suicidal, suicidal. I could hardly talk. I was diagnosed with depression. I was on Wellbutrin and lithium. Now I am only on lithium. But the antidepressant is gone, and lo and behold, I feel actually somewhat better without the damn thing. I'm not going to sleep with the prayer for the next day not to happen. I have a job interview this coming week. There are two toxic people in my life that are no longer in my life. I'm lonely, but they're gone because Gary said it's better to have no relationship than to have those that don't honor you. I can now have a conversation. I don't know what the reason is but there is a reason to live now. My concentration is a little bit better. Digestion is unbelievably better. . . . I'm on my way and I'm glad I've been here.

Marcella: Major Depression, Cognitive Decline, and Chronic Pain.

I came here for major depression and chronic pain. I've had two laminectomies due to a job injury, and my depression I've been suffering with it for quite a few years. . . . And since I came to the study, it's been giving me more insight into the things that I can do with myself. It has built my self-esteem. I've been feeling a lot more energy. I'm in physical therapy now . . . and I'm trying to do a lot more things. My cognitive functioning has increased. That was one of my big problems . . . and I feel a lot better. My sleep pattern has just started to improve. . . . I was having a lot of difficulties sleeping. So, I'm doing a lot better and I'm very thankful.

Rina: Depression and Anxiety.

I came in here with depression and anxiety, which I've suffered for about the past eight years. . . . I have a lot more focus. I'm much happier and much less stress, calmer and much more hopeful about

the future. I've lost about ten pounds and went down a jeans size. So, that was great.

Tammy: Anxiety and Memory.

I have much more memory than I was—did before. I was always a very sort of healthy kind of person, but now I'm more focused. I listen. I follow the protocol 110 percent. My memory is better. I've lost fears. I've been in a lot of different kind of music. I was with Motown and I have hit records and all that stuff and they didn't pan out the way I wanted them to. So I was looking. I was having fear. I'm taking care of my mother and having fear of the future. Now I have no fear. I believe that I can do. I believe and I know that I'm the magnificent manifestation of all that is. [Applause] I'm all right. I'm all right. It's been wonderful.

Neurological Conditions

Tammy: Dementia.

I'm here for my mom. Anyway, my mother was suffering from short-term memory. She was headed to—for dementia and everything. She had a heart condition. She has arthritis. She was very lethargic, poor sleeping habits. She wouldn't eat. She would fuss with me if I tried to give her something. I had to trick her to eat healthy. No exercise. She's non-ambulatory. She walks with a walker, but she walks. I mean like 50—50 yards—50 feet and she's out of breath and it would take. Whenever I would take her to the doctor, it was an ordeal. Now it's different. She remembers. She didn't, but now she remembers things. Her speech is more fluent because she also was suffering from two minor strokes years ago that caused her to stammer, to stutter a lot. Now she's more fluent. She's eating. She's drinking green juices, yeah. You know. I mean kale and all of the stuff. She's excited now because she's lost over 20 pounds. She can walk. We had rugs that we couldn't remove off the floor because she needed something to grip her—grip her feet. Now she's told me last week, "Let's take these rugs up. I can feel the bottom of the floor now." So her feet, the swelling has gone down in her legs. She doesn't have the pain in her feet that she used to have. She takes charge. She's more confident in that it's up to her. She can make a change in herself. She can do it and that was fantastic.

Margaret: Dementia.

I've been coming here for several weeks for a friend of mine. She is somebody that has early dementia and it got so that she couldn't come to the class because she didn't have the stamina to come. But I have seen such improvement in her. I don't live with her, but I'm very close with her. She takes the juices all the time. She walks more. She's more alert. She surprises me because I'll ask her how so and so, somebody she forgot about. "Oh, yeah, I know who they are. You think I don't know who they are, but I do." She goes to like a senior center, where she does exercising. Her appetite has improved an awful lot. She takes a juicing. Her medications have been cut down. She sleeps better than I do, and her whole personality has changed, and I just hope that we can keep this going with her. Maybe with all that she's doing we can get her to do more. I know

with the early dementia it's not going to be that we can expect her to be like she was before, but, at least, if she can take what we've given her and just if we can get her to stay at a certain plateau and you don't see the crash. That's what I'm hoping for her.

Joan: Alzheimer's.

I'm here with my sister Sonia and we came here for my mom, who's here. My mother is 86 years old. Seven years ago she was diagnosed with Alzheimer's. Her short-term memory was really horrible. And, also, if you remember when I used to bring her in here, she would sleep most of the time. She was just zoned out. Now she is in my business all the time. "What are you doing? Why are you doing this?" She's in it. She's with us. She sleeps like a baby. Getting the sugar out of her diet was hell. She fights like a badger for those Snickers bars, but now I have her on no sugar and she's lost about 15 pounds. So, this has been a blessing.

Javier: Stroke.

I had a stroke on the 4th of July last year. I came in like very weak. I couldn't like stand and I had my cane more often, and I barely use a cane now just for—and I even walked or jogged, actually, twice around Central Park Lake two weeks in a row. Something I couldn't even do when I was like 16 years old. Yeah, everything is like I think feeling much better. I think I'm definitely on my way to 100 percent. I just have to stay focused on the vegan trip, and I'm just very proud of all that. I have more energy. I'm sleeping better. The pain has gone down as well on the right side, which is great. Everything is great. Yeah, especially, like on positivity. I'm 1000 percent more positive. I think I was a very angry person.

Ron: Multiple Sclerosis.

Twenty-seven years ago I was diagnosed by the medical experts as having multiple sclerosis, and they said, "I'm sorry. Get your affairs in order. There's nothing we can do for you." I had to look elsewhere aka I happened upon Gary and Luanne, and they put me on a protocol to eliminate fatigue, to eliminate numbness, to improve my cognitive abilities. And I have been working with Gary and Luanne for about 25 to 27 years and this has been a great journey. I feel great. I feel confident. I'm working full time. I'm actually going to be retiring shortly and I'm looking for another gig. So, who knows what can come about, but thank you for everything. My energy levels have gone up. My cognitive abilities have gone up. I don't feel fatigued any longer. I am able to walk two miles per day and that's 25 minutes in the morning and 25 minutes in the afternoon. And I'm doing that every single day, consistently, for a couple of years now and my energy levels are through the roof and I'm feeling great.

Aaron: Parkinson's Disease.

I was diagnosed last October, with early stage Parkinson's disease. I had the symptoms for six months. I think I've had an improvement in my complexion and my memory and cognition. And I've lost approximately five pounds. I've been able to deal without taking medication most of the time.

Monique Parkinson's Disease

I have Parkinson's disease I was diagnosed with it in 1999. And sure enough, it's helping me. So, this has been 12 weeks that I've had to a lot do and I have some more stuff to do, but I feel myself getting better. I'm walking better. Exercising every day and my chair exercises with my weight lifts. I'm sleeping better. I'm not screaming in the middle of the night scaring my husband to death. I'm feeling better. I'm feeling positive and I just have to say thank you.

Results

Fifteen of 21 subjects videotaped reported substantial results, shown here, for conditions of concern. Of those not reporting substantial condition specific benefits, all reported side benefits and satisfaction with their participation. Five subjects with mood disorders reported major reversals in their conditions, and 2 of them eliminated one or all medications. Three other subjects reported considerable mood disorder improvement.

Three subjects with dementia or Alzheimer's reported sizable improvement for family represented, with one individual's medications reduced. A stroke survivor formerly with difficulty standing reported almost eliminating needing a cane, and jogging over a mile. Two subjects with Parkinson's reported improvements in activity, memory, reduction in medication, or sleep. A subject with multiple sclerosis stated improvement in cognition, activity, and energy. Other benefits reported overall included weight loss, pain reduction, more physical activity, better interpersonal relationships, and improvement of appetite.

Discussion

Of the 27 subjects beginning the study group, 21 gave videotaped testimonials, all of them stating some benefits and satisfaction with their participation. A few original participants did not complete the study. Of all those beginning the study, a majority, 15 subjects, reported substantial results for conditions of concern.

The study ambitiously addressed a very broad range of both mood and neurological conditions without concentrating on any condition or physiology in particular. This truly holistic intervention provided wide ranging nutritional and lifestyle support, for mind and body, to show therapeutic benefit for multiple specific conditions.

Limitations

The study was a relatively small group, with a short duration. It is our hope that larger studies of 3, 6, and 9 months and 1 year durations with larger groups will be conducted.

Conclusion

Given the increasing number of individuals afflicted with mood and cognitive disorders, this lifestyle and behavior

modification protocol should be considered an important alternative approach.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Ethical Approval

The study did not required ethical approval as it did not involve the introduction or use of any drug or medical device. It was strictly a lifestyle and behavioral modification program and there was no medical intervention involved.

References

1. Kessler RC, Chiu WT, Demler O, Merikangas KR, Walters EE. Prevalence, severity, and comorbidity of twelve-month DSM-IV disorders in the National Comorbidity Survey Replication (NCS-R). *Arch Gen Psychiatry*. 2005;62:617-627.
2. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication (NCS-R). *Arch Gen Psychiatry*. 2005;62:593-602.
3. National Institutes of Health. Major depression among adults. <http://www.nimh.nih.gov/health/statistics/prevalence/major-depression-among-adults.shtml>. Accessed February 25, 2016.
4. Alzheimer's Association. 2015 Alzheimer's disease facts and figures. <http://www.alz.org/facts/>. Accessed February 25, 2016.
5. Plassman BL, Langa KM, Fisher GG, et al. Prevalence of dementia in the United States: the aging, demographics, and memory study. *Neuroepidemiology*. 2007;29:125-132. doi:10.1159/000109998.
6. Kowal SL, Dall TM, Chakrabarti R, Storm MV, Jain A. The current and projected economic burden of Parkinson's disease in the United States. *Mov Disord*. 2013;28:311-318. doi:10.1002/mds.25292.
7. Centers for Disease Control and Prevention. Stroke facts. <http://www.cdc.gov/stroke/facts.htm>. Accessed February 25, 2016.
8. Noonan CW, Kathman SJ, White MC. Prevalence estimates for MS in the United States and evidence of an increasing trend for women. *Neurology*. 2002;58:136-138.
9. National Multiple Sclerosis Society. Estimating the prevalence of MS. <http://www.nationalmssociety.org/About-the-Society/MS-Prevalence>. Accessed February 25, 2016.
10. Rethorst CD, Trivedi MH. Evidence-based recommendations for the prescription of exercise for major depressive disorder. *J Psychiatr Pract*. 2013;19:204-212. doi:10.1097/01.pra.0000430504.16952.3e.
11. Lucas SJ, Ainslie PN, Murrell CJ, Thomas KN, Franz EA, Cotter JD. Effect of age on exercise-induced alterations in cognitive executive function: relationship to cerebral perfusion. *Exp Gerontol*. 2012;47:541-551. doi:10.1016/j.exger.2011.12.002.

12. Schwenk M, Dutzi I, Englert S, et al. An intensive exercise program improves motor performances in patients with dementia: translational model of geriatric rehabilitation. *J Alzheimers Dis*. 2014;39:487-498. doi:10.3233/JAD-130470.
13. Forbes D, Forbes SC, Blake CM, Thiessen EJ, Forbes S. Exercise programs for people with dementia. *Cochrane Database Syst Rev*. 2015;(4):CD006489. doi:10.1002/14651858.CD006489.pub4.
14. Marques-Aleixo I, Santos-Alves E, Balça MM, et al. Physical exercise improves brain cortex and cerebellum mitochondrial bioenergetics and alters apoptotic, dynamic and auto(mito)phagy markers. *Neuroscience*. 2015;301:480-495. doi:10.1016/j.neuroscience.2015.06.027.
15. Steiner JL, Murphy EA, McClellan JL, Carmichael MD, Davis JM. Exercise training increases mitochondrial biogenesis in the brain. *J Appl Physiol* (1985). 2011;111:1066-1071. doi:10.1152/jappphysiol.00343.2011.
16. de Oliveira BF, Veloso CA, Nogueira-Machado JA, et al. Ascorbic acid, alpha-tocopherol, and beta-carotene reduce oxidative stress and proinflammatory cytokines in mononuclear cells of Alzheimer's disease patients. *Nutr Neurosci*. 2012;15:244-251. doi:10.1179/1476830512Y.0000000019.
17. Polidori MC, Ruggiero C, Croce MF, et al. Association of increased carotid intima-media thickness and lower plasma levels of vitamin C and vitamin E in old age subjects: implications for Alzheimer's disease. *J Neural Transm (Vienna)*. 2015;122:523-530. doi:10.1007/s00702-014-1357-1.
18. Li FJ, Shen L, Ji HF. Dietary intakes of vitamin E, vitamin C, and b-carotene and risk of Alzheimer's disease: a meta-analysis. *J Alzheimers Dis*. 2012;31:253-258. doi:10.3233/JAD-2012-120349.
19. Réus GZ, Dos Santos MA, Abelaira HM, et al. Antioxidant treatment ameliorates experimental diabetes-induced depressive-like behavior and reduces oxidative stress in brain and pancreas [published online October 3, 2015]. *Diabetes Metab Res Rev*. doi:10.1002/dmrr.2732.
20. Beydoun MA, Beydoun HA, Boueiz A, Shroff MR, Zonderman AB. Antioxidant status and its association with elevated depressive symptoms among US adults: National Health and Nutrition Examination Surveys 2005-6. *Br J Nutr*. 2013;109:1714-1729.
21. Mazloom Z, Ekramzadeh M, Hejazi N. Efficacy of supplementary vitamins C and E on anxiety, depression and stress in type 2 diabetic patients: a randomized, single-blind, placebo-controlled trial. *Pak J Biol Sci*. 2013;16:1597-1600.
22. de Oliveira IJ, de Souza VV, Motta V, Da-Silva SL. Effects of oral vitamin C supplementation on anxiety in students: a double-blind, randomized, placebo-controlled trial. *Pak J Biol Sci*. 2015;18:11-18.
23. Yang X, Zhang Y, Xu H, et al. Neuroprotection of coenzyme Q10 in neurodegenerative diseases. *Curr Top Med Chem*. 2016;16:858-866.
24. Shults CW, Oakes D, Kieburtz K, et al; Parkinson Study Group. Effects of coenzyme Q10 in early Parkinson disease: evidence of slowing of the functional decline. *Arch Neurol*. 2002;59:1541-1550.
25. Hargreaves IP, Lane A, Sleiman PM. The coenzyme Q10 status of the brain regions of Parkinson's disease patients. *Neurosci Lett*. 2008;447:17-19. doi:10.1016/j.neulet.2008.09.069.
26. Müller T, Büttner T, Gholipour AF, Kuhn W. Coenzyme Q10 supplementation provides mild symptomatic benefit in patients with Parkinson's disease. *Neurosci Lett*. 2003;341:201-204.
27. Mancuso M, Orsucci D, Volpi L, Calsolaro V, Siciliano G. Coenzyme Q10 in neuromuscular and neurodegenerative disorders. *Curr Drug Targets*. 2010;11:111-121.
28. Yoritaka A, Kawajiri S, Yamamoto Y, et al. Randomized, double-blind, placebo-controlled pilot trial of reduced coenzyme Q10 for Parkinson's disease. *Parkinsonism Relat Disord*. 2015;21:911-916. doi:10.1016/j.parkreldis.2015.05.022.
29. Cheungpasitporn W, Thongprayoon C, Mao MA, et al. Hypomagnesaemia linked to depression: a systematic review and meta-analysis. *Intern Med J*. 2015;45:436-440. doi:10.1111/imj.12682.
30. Miki T, Kochi T, Eguchi M, et al. Dietary intake of minerals in relation to depressive symptoms in Japanese employees: the Furukawa Nutrition and Health Study. *Nutrition*. 2015;31:686-690. doi:10.1016/j.nut.2014.11.002.
31. Rondanelli M, Giacosa A, Opizzi A, et al. Long chain omega 3 polyunsaturated fatty acids supplementation in the treatment of elderly depression: effects on depressive symptoms, on phospholipids fatty acids profile and on health-related quality of life. *J Nutr Health Aging*. 2011;15:37-44.
32. Van Oudenhove L, McKie S, Lassman D, et al. Fatty acid-induced gut-brain signaling attenuates neural and behavioral effects of sad emotion in humans. *J Clin Invest*. 2011;121:3094-3099. doi:10.1172/JCI46380.
33. Witte AV, Kerti L, Hermannstädter HM, et al. Long-chain omega-3 fatty acids improve brain function and structure in older adults. *Cereb Cortex*. 2014;24:3059-3068. doi:10.1093/cercor/bht163.
34. Köbe T, Witte AV, Schnelle A, et al. Combined omega-3 fatty acids, aerobic exercise and cognitive stimulation prevents decline in gray matter volume of the frontal, parietal and cingulate cortex in patients with mild cognitive impairment [published online October 1, 2015]. *Neuroimage*. doi:10.1016/j.neuroimage.2015.09.050.
35. Solfrizzi V, D'Introno A, Colacicco AM, et al. Dietary fatty acids intake: possible role in cognitive decline and dementia. *Exp Gerontol*. 2005;40:257-270.
36. Nichols M, Zhang J, Polster BM, et al. Synergistic neuroprotection by epicatechin and quercetin: activation of convergent mitochondrial signaling pathways. *Neuroscience*. 2015;308:75-94. doi:10.1016/j.neuroscience.2015.09.012.
37. Waseem M, Parvez S. Neuroprotective activities of curcumin and quercetin with potential relevance to mitochondrial dysfunction induced by oxaliplatin [published online May 29, 2015]. *Protoplasma*. doi:10.1007/s00709-015-0821-6.
38. Fava M, Mischoulon D. Folate in depression: efficacy, safety, differences in formulations, and clinical issues. *J Clin Psychiatry*. 2009;70(suppl 5):12-17. doi:10.4088/JCP.8157su1c.03.
39. Petridou ET, Kousoulis AA, Michelakos T, et al. Folate and B₁₂ serum levels in association with depression in the aged: a

- systematic review and meta-analysis [published online June 8, 2015]. *Aging Mental Health*. doi:10.1080/13607863.2015.1049115.
40. de Jager CA, Oulhaj A, Jacoby R, Refsum H, Smith AD. Cognitive and clinical outcomes of homocysteine-lowering B-vitamin treatment in mild cognitive impairment: a randomized controlled trial. *Int J Geriatr Psychiatry*. 2012;27:592-600. doi:10.1002/gps.2758.
 41. Aisen PS, Schneider LS, Sano M, et al. High-dose B vitamin supplementation and cognitive decline in Alzheimer disease: a randomized controlled trial. *JAMA*. 2008;300:1774-1783. doi:10.1001/jama.300.15.1774.
 42. Smith AD, Smith SM, de Jager CA, et al. The accelerated rate of brain atrophy in elderly with mild cognitive impairment can be slowed by treatment with homocysteine-lowering B vitamins. *PLoS One*. 2010;5:e12244. doi:10.1371/journal.pone.0012244.
 43. Jemerén F, Elshorbagy AK, Oulhaj A, Smith SM, Refsum H, Smith AD. Brain atrophy in cognitively impaired elderly: the importance of long-chain ω -3 fatty acids and B vitamin status in a randomized controlled trial. *Am J Clin Nutr*. 2015;102:215-221. doi:10.3945/ajcn.114.103283.
 44. Chen H, Liu S, Ji L, et al. Associations between Alzheimer's disease and blood homocysteine, vitamin B₁₂, and folate: a case-control study. *Curr Alzheimer Res*. 2015;12:88-94.
 45. Kim G, Kim H, Kim KN, et al. Relationship of cognitive function with B vitamin status, homocysteine, and tissue factor pathway inhibitor in cognitively impaired elderly: a cross-sectional survey. *J Alzheimers Dis*. 2013;33:853-862. doi:10.3233/JAD-2012-121345.
 46. Kim H, Kim G, Jang W, Kim SY, Chang N. Association between intake of B vitamins and cognitive function in elderly Koreans with cognitive impairment. *Nutr J*. 2014;13:118. doi:10.1186/1475-289.
 47. Ranjbar E, Kasaei MS, Mohammad-Shirazi M, et al. Effects of zinc supplementation in patients with major depression: a randomized clinical trial. *Iran J Psychiatry*. 2013;8:73-79.
 48. Prasad AS. Zinc: an antioxidant and anti-inflammatory agent: role of zinc in degenerative disorders of aging. *J Trace Elem Med Biol*. 2014;28:364-371. doi:10.1016/j.jtemb.2014.07.019.
 49. Sutachan JJ, Casas Z, Albarracín SL, et al. Cellular and molecular mechanisms of antioxidants in Parkinson's disease. *Nutr Neurosci*. 2012;15:120-126. doi:10.1179/1476830511Y.0000000033.
 50. Salari S, Khomand P, Arasteh M, Yousefzamani B, Hassanzadeh K. Zinc sulphate: a reasonable choice for depression management in patients with multiple sclerosis: a randomized, double-blind, placebo-controlled clinical trial. *Pharmacol Rep*. 2015;67:606-609. doi:10.1016/j.pharep.2015.01.002.
 51. Shinto L, Calabrese C, Morris C, Sinsheimer S, Bourdette D. Complementary and alternative medicine in multiple sclerosis: survey of licensed naturopaths. *J Altern Complement Med*. 2004;10:891-897.
 52. Farinotti M, Vacchi L, Simi S, Di Pietrantonj C, Brait L, Filippini G. Dietary interventions for multiple sclerosis. *Cochrane Database Syst Rev*. 2012;(12):CD004192. doi:10.1002/14651858.CD004192.pub3.