The Relationship Between Parkinson Disease And The Lifestyle Of Patient

Mernan Alsharif

ABSTRACT
Background: Parkinson's disease (PD) is described as a progressive neurodegenerative disease related to age that influences the quality of life. This disease doesn't have a treatment but the medications and lifestyle can reduce the progression of the disease.
Aim: The aim of this review is to focus on the lifestyle of the patient to improve the prognosis of the patient.
Methods: We performed a PubMed search for research papers published in English between 2000 and 2017. I employed a combination of search terms like :("Parkinson disease and lifestyle ", "Parkinson disease diet " and "Parkinson and smoking"). The review categorized the literature review into risk factor and preventive factor.
Conclusion: Lifestyle factor can surely affect PD patient but in different percentages. most of these factors are not truly understood why they affect PD.

1 INTRODUCTION

Parkinson's disease (PD) is a neurodegenerative disease that is related to age, associated with impairment in the mental ability and develop dementia, with more obvious motor features [1] It also influences the lifestyle, leads to depression, motor dysfunctions, social isolation, inactivity and all factors which affect the quality of individuals life with the disease.[2,3]in and almost 25% of new patient diagnosed with PD [1]

It is a common neurodegenerative disease and its classified as the second after Alzheimer's disease in the occurrence [4] . Globally its incidence rate range from to 19 per 100,000 patient and a prevalence to 230 : 100,000 population [5]. Different risk and protective agents of PD have been investigated over many decades, however the reason remains largely unclear [6]. There is a great focus in identifying the risk in individuals early, to slow down or suppress neurodegeneration . While genetic and environment are often contribute to PD risk such as coffee/tea , smoking, and alcohol consumption for a period have been the interesting of research for decades [7,8] and that is unlike to the first publish of a lower mortality from Parkinson disease (PD) in group of smokers in 1959 , multiple studies proved that there is reduction in risk . A lower risk of PD in group of coffee consumptions has also been demonstrated , although the relation is not as strong as that for smokers. And inverse association between PD and alcohol consumption has been suggested [9,10,11,12,13]
Lately , non-motor signs of PD have been recalled by scientists and clinicians as early signal of PD, and they're detrimental factors in the lifes PD patients. It is essential to comprehensively understand the behavioral assessments, from the simplest certain symptoms to the tangled neuropsychological tasks.[14] also Some studies suggested that reduce endogenous estrogen amount increase possibility of PD while therapies with estrogen decrease possibility of PD in women .[15,16,17]

In some studies on PD have seen obvious improvements of muscles strength, walking performance , balance, cardio-respiratory fitness and QOL after exercise therapy.

Additionally , animal research suggest that exercise has a neuroprotective out come in PD, however this have to be validate in human studies [18,19]
Some study see that there should be intervention from the policies that aimed to improve and estimate QoL and seek for mental, social and physical well-being. For this aim , there is need for methods that can raise health in people with PD by an integrated approach .

Those information about PD patients, exclusively those related to the lifestyle , and physical therapy could assist in reduce such changes .[2,3]

2 OBJECTIVES

Focusing in the lifestyle factors that affecting Parkinson disease patients and how they improve the ability of the patient to live for a long time with minimal compliance on other and have good health as possible in non-medical way adjacent to the treatment especially that the reason of the disease is unknown yet and Restrict the causes that lead to Parkinson disease and how to minimize the environment that lead to .

3 REVIEW OF LITERATURE

The etiology of Parkinson's disease (PD) is still mainly unknown and accordingly the disease cannot be prevented effectively [20]
Major discoveries have profoundly changed our understanding of Parkinson's disease and its determinants. Whereas genetic studies have revealed the heterogeneity of Parkinson's disease and provided insights into its pathogenesis and etiology, [21] epidemiological investigations have provided robust evidence that behavioral and environmental factors have a key role in the disease pathogenesis and progression. This evidence is strengthened and complemented by observations that 90%

of Parkinson's disease cases have no identifiable genetic cause,[22] and that many factors associated with an altered risk of Parkinson's disease have neuroprotective or neurotoxic properties in animal models of the disease. [23] The combination of genetic predisposition and environmental exposure, however is evident . Environmental exposures, especially those based on individual choices which therefore can be modified, are important targets for our research.[20]

3.1 Risk factors

3.1.1 Stress

Chronic stress, on the other hand, either due to major life events or due to minor but frequent 'irritations and frustrations' causes a prolonged activation of the hypothalamic–pituitary–adrenal (HPA)[24] axis and triggers 'allostatic load', a failure of adequate coping mechanisms to reduce stress.[25] This can cause 'lifestyle diseases' such as type 2 diabetes mellitus, gastric ulcers or hypertension.[26]

A convincing link between chronic stress and neurodegeneration has been now established in patients with Alzheimer's disease. Emotionally stressed patients have a 2.7% higher risk of developing the disease and stressed dementia patients have a more rapid disease progression.[27]

A recent case report suggested that major stress[28] may have triggered PD in a young woman and stress-induced striatal damage, with subsequent worsening of motor symptoms has been also found in several animal models of PD.

Elevated glucocorticoid levels in rodent models worsened motor performance and higher corticosterone levels led to a greater permanent loss of nigral neurons. [30] 6-Hydroxydopamine (6-OHDA)-lesioned rats moved more slowly, froze more often and became rigid when challenged with stressors but reverted to normal when left alone in their home cage.[31] Foot shock, tail pinch or other stressors have all been shown to increase striatal dopamine release and turnover in rodents[32] and it has been suggested that this could excite striatal dopamine nerve terminals to death through increased oxidative stress[33]

Chronic stress can lead to reduced dopaminergic activity within the ventral tegmental area in rodents[34] and cause increased cortisol levels, and higher salivary cortisol levels compared with matched controls have been described in PD patients.[35] In rats, chronic stress significantly decreased dopamine levels in the frontal cortex, striatum and the hippocampus.[36]

It is possible, however, that proneness to emotional stress might be the first sign of a neurodegenerative disease and changes in prefrontal, parietal or limbic networks lead to an impairment in coping with stressful life events. Possible mechanisms underlying stress-induced neuronal degeneration 1. Stress reduces regulatory T-lymphocytes by 50% in patients who suffered from posttraumatic stress disorder[37]and a similar profound reduction has been found in PD.[38] Dysfunction of regulatory T-lymphocytes might contribute to dopaminergic cell loss and vaccination in animal models of PD with these regulatory lymphocytes can attenuate nigrostriatal degeneration.[39]

Chronic stress has been also found to induce the proinflammatory networks of cytokines and chemokines, which in turn activate the HPA axis.[40]Upregulation of cytokines has been linked with sudden death after major emotional trauma[41]and increased concentrations of tumor necrosis factor, interleukins and β 2 macroglobulin have been reported in the substantia nigra of PD patients.[42] Further, dysregulation of the HPA axis can cause dendritic remodeling, dysfunction of neurogenesis, apoptosis in hippocampal neurons and result in increased oxidative stress.[27]

Catecholamines such as dopamine are inert when stored in vesicles, but it is possible that in susceptible patients chronic stress shifts catecholamines into the cytosol where they become toxic via auto-oxidation. Oxidation of catecholamines leads to quinones which can cause lipid peroxidation and membrane disruption[44] and might ultimately cause neurodegeneration. Support for this hypothesis comes from additional preclinical studies, which have shown that chronic stress induces oxidative stress and increased protein and lipid peroxidation.[45]

3.1.2 Pesticides

The hypothesis that exposure to pesticides and other environmental chemicals increases Parkinson's disease risk was suggested by the discovery of the neurotoxic effects of a metabolite of 1-methyl,-4-phenyl-1,2,3,6-tetra hydro pyridine (MPTP) , which is converted in the body to a pro-parkinsonian molecule with a structure similar to the herbicide parquets.[46] In the HAAS cohort, Parkinson's disease risk increased with increasing duration of work in plantations (RR 1·9 for 20 or more years vs none, p for trend=0·006) [47]. In the Agricultural Health Study, Parkinson's disease risk increased monotonically with increasing number of days of exposure to pesticides; the RR was 2·3 for more than 397 days versus less than 64 days of lifetime exposure (p for trend=0·009). [48]

3.1.3 Cancer

An increased risk of Parkinson's disease among individuals with melanoma is well documented.[49]In a large Danish study including over 8000 patients with Parkinson's disease, a diagnosis of melanoma was associated with a 44% increased risk of developing Parkinson's disease. [50]

3.1.4 Alcohol

Overall, the results of longitudinal studies support a modestly lower Parkinson's disease risk among drinkers as compared with non-drinkers[51], a result consistent with the urate-elevating effects of alcoholic beverages[52] (RR 0·86, 95% CI 0·75–1·0; p=0·05 comparing the highest and lowest categories of intake in a meta-analysis of longitudinal studies). However, in a study based on the Swedish National Inpatients Register and including over 1000 cases of Parkinson's disease, alcohol misuse (defined as hospital admission with a diagnosis of alcohol use disorder) has been associated with an increased Parkinson's disease risk (RR 1·4, 95% CI 1·3–1·5; p<0·0001).[53]

3.1.5 Nutrients That May Be Associated With An Increased Risk Or Progression Of PD

3.1.5.1 Dairy products

Risk of Parkinson's disease is increased among individuals with high milk and dairy consumption.[54] Although the findings from multiple cohorts and countries are more consistent with the increased Parkinson's disease risk being associated with the urate-lowering effects of dairy products.[55]

3.1.6 Other factors

There are many putative risk factors for Parkinson's disease for which evidence is still sparse or inconsistent. These include early life factors such as season of birth, birthweight, parental age[56] and several infections such as measles (inverse association),[57] infections of the CNS,[58] hepatitis C,[59] and Helicobacter pylori.[60] Influenza has been associated with an increased risk of parkinsonism, but not of Parkinson's disease. Manganese can cause parkinsonism,[61] but evidence on Parkinson's disease risk remains inconclusive. [62] long-term exposure to some specific metals such as manganese, copper, mercury, lead, iron, zinc, aluminum, amalgam and the combination of metals has been reported to be a risk factor for PD in some case reports and case control studies [63]

3.2 Protective factors

3.2.1 Physical activity

An inverse relation between amount of physical activity and Parkinson's disease risk was first prospectively reported in the Nurses' Health Study and HPFS,[64]and later substantiated in five additional longitudinal studies (the Harvard Alumni Health Study,[65] the CPS-IIN,[66] the NIH-AARP Diet and Health Study,[67] the Finnish Mobile Clinic study,[68] and the Swedish National March Cohort). The combined results of these studies show that frequent moderate or vigorous physical activity is associated with a 34% (95% CI 22–43) reduction in Parkinson's disease risk.[69]That Parkinson's disease risk in late adult life was strongly inversely associated with physical activity during high school and college (figure 2),[64] or at age 35–39 years,[67] argues against reverse causation. Although the possibility that individuals predisposed to Parkinson's disease tend to avoid strenuous physical activity in early adult life cannot be excluded, these results are consistent with a neuroprotective effect of physical activity, an interpretation supported by experimental results from animal models of Parkinson's disease . [70,71] Among the proposed mechanisms for this neuroprotective effect are an increase in serum urate, an increased released of neurotrophic factors (e.g., BDNF), upregulation of PGC1α, and regulation of dopamine turnover. The potential benefits of exercise in individuals with Parkinson's disease are an area of active investigation,[72] including randomized trials.[73]

The Feldenkrais method is an approach that seeks to balance the systems in a dynamic and multidimensional way. All parts of the body are involved in body movements, including tactile, proprioceptive, visual, and vestibular systems.[74]

An underlying principle of the Feldenkrais method is that the processes of thinking, feeling, and doing are all interrelated to components of human functioning. To resolve any component, medical practitioners have to address all of them. This concept of unity of mind and body distinguishes the Feldenkrais method from more traditional approaches to improving movement.[75]

Few studies demonstrate how good physical therapy practice is for treatment of PD.[76] Therefore, the current study has suggested an exercise program based on the Feldenkrais method, which focuses on a set of movements that favor motor action that is more functional, more harmonious, and easier to perform.

The natural trajectory of disability in PD affects daily living activities and interferes in mobility and QoL.[77] Thus, offering exercises that motivate action and generate self-confidence and self-control in PD patient is very important to the instigation of emotional states that trigger the intentional movements nicely. The Feldenkrais method favors the intentional movement in an easy and pleasurable way, and then it triggers emotional aspects related to the ability to perform daily activities easily. And After the sessions of exercises based on the Feldenkrais method, the treatment group showed better results than the control group regarding QoL. Moreover, the rate of depression decreased, and the mental state score increased. The current study's findings suggest that the practice of exercises based on the Feldenkrais method could contribute greatly to QoL in PD, which indicates the importance of interventions that work with awareness through movement to the promotion of wellness for this population.[78]

3.2.2 Smoking

Cigarette smoking is the most preventable cause of death in the United States today. Cigarette smoking has been studied in relation to various neurological disorders, such

as Alzheimer's disease and Parkinson's disease. However, the relationship between cigarette smoking and PD remains to be controversial. Several epidemiological studies have found a negative association between cigarette smoking and PD. It is reported that patients who smoke are 50% less likely to have PD when compared to their non-smoking counterparts. This suggests that cigarette smoking might exert a neuroprotective effect. The hypothesis is that cigarette smoking protects against neurodegeneration thereby preventing PD. This is a review of cigarette smoking and PD.[79]

Cigarette smoke has also been shown to inhibit monoamine oxidase (MAO) activity, and MAO is known to breakdown dopamine (Fowler et al., 2000)[80]. Several studies also suggest that nicotine stimulates dopamine release (Janson et al., 1992; Westfall et al., 1967; Clarke et al., 1985)[81,82,83]; thereby conceivably suppressing early signs of PD. Numerous studies have also shown that cigarette smoke contains more than 10 free radicals per puff (Church and Pryor, 1985; Bluhn et al., 1971; Forbes et al., 1967; Pryor, 1992; Pryor and Ston., 1993; Pryor et al., 1990).[84,85,86,87,88,89] However, although cigarette smoke contains several free radicals, it also contains carbon monoxide (CO), and CO seems to be protective against hydrogen peroxide (H2 O2) induced membrane damage (McKenney et al., 1990; Metz et al., 1974; Sagone et al., 1975).[90,91,92] CO also inhibits neural MAO-B-associated metabolism of dopamine to produce H2 O2 and possibly creates a protective nigral "reducing environment" (Baron, 1986)[93], therefore suppression of free radical generation in early life could possibly lead to reduced risk of PD by preserving dopamine producing cells.

3.2.3 Nutrients That May Be Associated With A Decreased Risk Or Progression Of PD

3.2.3.1 Coffee and Caffeine

A neuroprotective effect of caffeine, an adenosine receptor antagonist, is well documented in experimental models of Parkinson's disease, and is probably mediated by adenosine A receptor blockade.[94,95] This effect is 2A stronger in male than in female mice and, as in women, there seems to be an interaction between caffeine and estrogens in rodents.[96] Although caffeine is the most probable neuroprotective component of coffee, other constituents (e.g., cafestol) might also contribute.[97,98]Low doses of caffeine have symptomatic benefits on freezing of gait,[99]and bradykinesia or rigidity.[100,101] More selective A2A receptor antagonists (e.g., istradefylline and tozadenant) provide symptomatic benefit in clinical trials among levodopa-treated Parkinson's disease patients.[102,103] The possibility that caffeine (a non-specific adenosine antagonist) or more selective A2A receptor antagonists have neuroprotective effects has not been rigorously addressed in trials in individuals with Parkinson's disease. Considering the well-established safety profile of caffeine and its probable beneficial effects in the prevention of conditions common among individuals with Parkinson's disease, such as depression,[104] its potential neuroprotective effects among individuals who are not usual caffeine consumers deserve further investigation.

Caffeine consumption

In a study the total caffeine consumption per day was calculated with the Caffeine Consumption Questionnaire [105]. The questionnaire investigated daily number of servings for common sources of caffeine (i.e. coffee, tea, energy drinks, chocolate) during the previous year ("on average over the past 1 year"), and also included decaffeinated beverages, as most of them are not actually caffeine-free [106]. Then, the daily amount of caffeine was calculated .

Kaplan-Meier curves for the need for L-Dopa treatment in relation to caffeine intake. Kaplan-Meier plots estimating the probability of the need for L-Dopa treatment in relation to caffeine consumption categorized on the median value for graphical purposes. P-values and hazard ratios (HR) are shown from Cox regression analysis. The dashed line represents caffeine consumption lower than the median value (<270.0 mg per day), whereas the solid line represents caffeine consumption higher than the median value (≥270.0 mg per day). [107]

3.2.3.2 Green and black tea

Parkinson's disease risk is lower among tea drinkers than non-drinkers, although this association is more apparent in individuals who are not coffee drinkers (RR 0·4, 95% CI 0·2–2·12; p for trend=0·02 for regular tea drinkers vs nondrinkers in the HPFS[108] and RR 0·4, 95% CI 0·2–0·8 for ≥3 cups of tea per day vs non-drinkers in the Finnish cohort).[109] In a cohort study in Singapore, consumption of black tea was associated with a reduced risk of Parkinson's disease (RR=0·29 for the highest vs lowest of intake, 95% CI 0·13–0·67; p for trend=0·0006), but green tea was not. Because the association persisted after adjustment for total caffeine intake, the authors concluded that components of black tea other than caffeine might contribute to reduce Parkinson's disease risk.[110] This preliminary finding— which seems to contradict early experimental studies suggesting protective effects of green tea components such as epicatechin and epigallocatechin gallate needs to be substantiated [111].

3.2.3.3 Phytochemicals

The health benefits associated with the intake of phytochemical Cals present in fruits and vegetables leads to decreased functional decline associated with aging and may slow the progression of PD [112]. Epidemiological studies found that high intake of fruits, vegetables and fish was inversely associated with PD risk [113,114]. Dietary patterns, characteristic of a Mediterranean diet, are emerging as a potential neuroprotective alternative for PD [115].

Epidemiological studies have found a decrease in PD risk in individuals who consume foods containing carotenoids

and β-carotene [116].Carotenoids possess antioxidant properties; they act as a reducing agent by protecting lipids through oxidation interference and free radical entrapment.[117] In mice, pretreatment with β-carotene partially protected against MPTP-induced neurotoxicity [118,119] but not in primates [120]. Lycopene, another carotenoid compound, reduces oxidative stress and cognitive decline in a rotenone-induced rodent model of PD [121]. One should be cautious however about applying conclusions from animal models about the bene- fits of carotenoids to humans, since most animals do not absorb or metabolize carotenoids in a similar manner [122].

Riboflavin is an integral component of the coenzymes flavin adenine dinucleotide and flavin mononucleotide. Flavin coenzymes participate in oxidation–reduction reactions where they are a major source of energy and are critical for carbohydrate, fat and protein metabolism [123]. It has been suggested that riboflavin may be involved in glutathione depletion, cumulative mitochondrial DNA mutations, disturbed mitochondrial protein complexes, and abnormal iron metabolism [124]. Despite these characteristics, some studies found that riboflavin is not associated with the risk of PD ([125,126]

3.2.3.4 Omega-3 (DHA)

Omega-3 polyunsaturated fatty acids (PUFAs) appear to be neuroprotective for several neurodegenerative diseases [127]. There have been no studies in PD patients that address whether omega-3s are neuroprotective, however, one study showed that supplementation with omega-3 PUFA reduced depression in PD patients [128].
Current research focuses specifically on the omega-3 fatty acid docosahexaenoic acid (DHA). DHA is an essential factor in brain growth and development [129] and has anti-inflammatory potential due to its ability to inhibit cyclooxygenase-2 [130]. DHA protects neurons against cytotoxicity, inhibition of nitrogen oxide (NO) production, and calcium (Ca2+) influx. DHA also increases the activities of antioxidant enzymes glutathione peroxidase and glutathione reductase [131].

3.2.3.5 Soy (GENISTEIN)

In PD, genistein treatment resulted in dopaminergic neuron protection from lipopolysaccharide (LPS)-induced injury via inhibition of microglia activation [132]. Genistein pretreatment improved spatial learning and memory in parkinsonian rats [133] and restored tyrosine hydroxylase (TH), dopamine transporter (DAT) and Bcl-2 mRNA expression in the midbrain of MPTP-treated animals [134].

4 CONCLUSION

Intervention is required in the early stages of PD to improve and maintain QoL. there is a definite link between cigarette smoking and PD. there is a negative association between smoking and PD. but the mechanism by which this occurs is un-clear. evidence is sufficiently strong to promote physical activity and, arguably, moderate doses of caffeine, for primary prevention of Parkinson's disease. poor diet may lead to increased oxidative stress, which could impede the antioxidant defense system. In contrast, a well-balanced diet rich in a variety of foods, including numerous servings of vegetables and fruits (especially those containing nicotine) and moderate amounts of omega-3 fatty acids, tea, caffeine provide neuroprotection.

ACKNOWLEDGEMENT

I appreciate all the hard works that have been done by the researchers to come out with these valuable pieces of information. And I would thank my friend ghadeer for being part of my journey In medical school.

REFERENCES

[1] John V, Catherine S, David J et al ,The effects of cognitive reserve and lifestyle on cognition and dementia in Parkinson's disease—a longitudinal cohort study . Int J Geriatr Psychiatry . 2016; 31: 13–23
[2] Tickle-Degnen L, Ellis T, Saint-Hilaire MH, et al . Self management rehabilitation and health-related quality of life in Parkinsons disease: a randomized controlled trial. Mov Disord. 2010;25(2): 194-204.
[3] Tomlinson CL, Patel S, Meek C, et al. Physiotherapy intervention in Parkinsons disease: systematic review and meta-analysis. BMJ. August 2012;345:e5004.
[4] Nussbaum RL, & Ellis CE , Alzheimer's disease and Parkinson's disease. N Engl J Med. 2003 ; 348 : 1356-1364.
[5] Muangpaisan W, Mathews A, Hori H, & Seidel D , A systematic review of the worldwide prevalence and inci- dence of Parkinson's disease. J Med Assoc Thai. 2011; 94, 749-755.
[6] Jannetta PJ, Whiting DM, Fletcher LH et al , Parkinson's dis- ease: An inquiry into the etiology and treatment. Neurol Int. 2011; 3, 24-27.
[7] Costa J, Lunet N, Santos C et al , Caffeine exposure and the risk of Parkinson's disease: A sys- tematic review and meta-analysis of observational studies. J Alzheimers Dis . 2010 ; 1 :221-238.
[8] Kiyohara C, & Kusuhara S (2010) Cigarette smoking and Parkinson's disease: A meta-analysis. Fukuoka Igaku Zasshi, 102, 254-265.
[9] Dorn HF. Tobacco consumption and mortality from cancer and other diseases. Public Health Rep. 1959;74(7):581–593.
[10] Chen H, Huang X, Guo X, et al. Smoking duration, intensity, and risk of Parkinson disease. Neurology. 2010;74(11): 878–884.
[11]]Thacker EL, O'Reilly EJ, Weisskopf MG, et al. Temporal relationship between cigarette smoking and risk of Parkinson disease. Neurology. 2007;68(10):764–768.
[12] Ascherio A, Zhang SM, Hernán MA, et al. Prospective study of caffeine consumption and risk of Parkinson's disease in men and women. Ann Neurol. 2001;50(1):56–63.
[13] Sääksjärvi K, Knekt P, Rissanen H, et al. Prospective study of coffee consumption and risk of Parkinson's disease. Eur J Clin Nutr. 2008;62(7):908–915.
[14] Asakawa T , Fang H , Sugiyama k , Human Behavioral Assessments in Current Research of Parkinson's Disease . neuroscience and biobehavior review 7634(16)30167-1
[15] Benedetti MD, Maraganore DM, Bower JH, et al. Hys- terectomy, menopause, and estrogen use preceding Par- kinson's disease: an exploratory case control study. Mov Disord . 2001; 16: 830–837.
[16] Currie LJ, Harrison MB, Trugman JM, Bennett JP, Wooten GF. Postmenopausal estrogen use affects risk for Parkinson disease. Arch Neurol. 2004 ; 61: 886–888.
[17] Ragonese P, D'Amelio M, Salemi G, et al. Risk of Par- kinson disease in women: effect of reproductive charac- teristics. Neurology. 2004 ; 62: 2010–2014.
[18] Lau YS, Patki G, Das-Panja K, etal , Neuroprotective effects and mechanisms of exercise in a chronic mouse model of parkinson's disease with moderate neurodegeneration. Eur J Neurosci. 2011;33(7):1264-1274.
[19] Ahlskog JE. Does vigorous exercise have a neuroprotective effect in

parkinson disease? . Neurology. 2011;77(3):288-294.
[20] Lang AE, Lozano AM. Parkinson's disease. First of two parts. N Engl J Med. 1998;339(15):1044–53.
[21] Singleton AB, Farrer MJ, Bonifati V. The genetics of Parkinson's disease: progress and therapeutic implications. Mov Disord 2013; 28: 14–23.
[22] Kalia LV, Lang AE. Parkinson's disease. Lancet 2015; 386: 896–912.
Klein C, Westenberger A. Genetics of Parkinson's disease. Cold Spring Harb Perspect Med 2012; 2: a008888.
[23] Ascherio A, Schwarzschild MA . The epidemiology of Parkinson's disease: risk factors and prevention. Lancet Neurol 2016; 15: 1257–72
[24] McEwen BS. Physiology and neurobiology of stress and adaptation: central role of the brain. Physiol Rev 2007;87:873–904.
[25] McEwen BS. Mood disorders and allostatic load. Biol Psychiatry 2003;54:200–7.
[26] Liu J, Mori A. Stress, aging, and brain oxidative damage. Neurochem Res 1999;24:1479–97.
[27] Rothman SM, Mattson MP. Adverse stress, hippocampal networks, and Alzheimer's disease. Neuromolecular Med 2010;12:56–70.
[28] Zou K, Guo W, Tang G, et al. A Case of early onset Parkinson's disease after major stress. Neuropsychiatr Dis Treat 2013;9:1067–9.
[29] Smith LK, Jadavji NM, Colwell KL, et al. Stress accelerates neural degeneration and exaggerates motor symptoms in a rat model of Parkinson's disease. Eur J Neurosci 2008;27:2133–46
[30] Snyder AM, Stricker EM, Zigmond MJ. Stress-induced neurological impairments in an animal model of parkinsonism. Ann Neurol 1985;18:544–51.
[31] Pei Q, Zetterstrom T, Fillenz M. Tail pinch-induced changes in the turnover and release of dopamine and 5-hydroxytryptamine in different brain regions of the rat. Neuroscience 1990;35:133–8.
[32] Hastings TG, Lewis DA, Zigmond MJ. Role of oxidation in the neurotoxic effects of intrastriatal dopamine injections. Proc Natl Acad Sci USA 1996;93:1956–61.
[33] Moore H, Rose HJ, Grace AA. Chronic cold stress reduces the spontaneous activity of ventral tegmental dopamine neurons. Neuropsychopharmacology 2001;24:410–19.
[34] Djamshidian A, O'Sullivan SS, Papadopoulos A, et al. Salivary cortisol levels in Parkinson's disease and its correlation to risk behaviour. J Neurol Neurosurg Psychiatry 2011;82:1107–11.
[35] Rasheed N, Ahmad A, Pandey CP, et al. Differential response of central dopaminergic system in acute and chronic unpredictable stress models in rats. Neurochem Res 2009;35:22–32.
[36] Sommershof A, Aichinger H, Engler H, et al. Substantial reduction of naive and regulatory T cells following traumatic stress. Brain Behav Immun 2009;23:1117–24.
[37] Baba Y, Kuroiwa A, Uitti RJ, et al. Alterations of T-lymphocyte populations in Parkinson disease. Parkinsonism Relat Disord 2005;11:493–8.
[38] Reynolds AD, Stone DK, Hutter JA, et al. Regulatory T cells attenuate Th17 cell-mediated nigrostriatal dopaminergic neurodegeneration in a model of Parkinson's disease. J Immunol 2010;184:2261–71.
[39] Reynolds AD, Stone DK, Hutter JA, et al. Regulatory T cells attenuate Th17 cell-mediated nigrostriatal dopaminergic neurodegeneration in a model of Parkinson's disease. J Immunol 2010;184:2261–71.
[40] Haddad JJ, Saade NE, Safieh-Garabedian B. Cytokines and neuro-immune-endocrine interactions: a role for the hypothalamic-pituitary-adrenal revolving axis. J Neuroimmunol 2002;133:1–19.
[41] Steptoe A, Brydon L. Emotional triggering of cardiac events. Neurosci
[42] Hirsch EC, Hunot S. Neuroinflammation in Parkinson's disease: a target for neuroprotection? Lancet Neurol 2009;8:382–97.
[43] Goldstein DS. Stress, allostatic load, catecholamines, and other neurotransmitters in neurodegenerative diseases. Endocr Regul 2011;45:91–8.
[44] Lucca G, Comim CM, Valvassori SS, et al. Effects of chronic mild stress on the oxidative parameters in the rat brain. Neurochem Int 2009;54:358–62
[45] Langston JW, Ballard P, Tetrud JW, Irwin I. Chronic Parkinsonism in humans due to a product of meperidine-analog synthesis. Science 1983; 219: 979–80.
[46] Petrovitch H, Ross GW, Abbott RD, et al. Plantation work and risk of Parkinson disease in a population-based longitudinal study. Arch Neurol 2002; 59: 1787–92.
[47] Weisskopf MG, Knekt P, O'Reilly EJ, et al. Persistent organochlorine pesticides in serum and risk of Parkinson disease. Neurology 2010; 74: 1055–61.
[48] Guilarte TR, Nihei MK, McGlothan JL, Howard AS. Methamphetamine-induced deficits of brain monoaminergic neuronal markers: distal axotomy or neuronal plasticity. Neuroscience 2003; 122: 499–513.
[49] Liu R, Gao X, Lu Y, Chen H. Meta-analysis of the relationship between Parkinson disease and melanoma. Neurology 2011; 76: 2002–09.
[50] Olsen JH, Friis S, Frederiksen K. Malignant melanoma and other types of cancer preceding Parkinson disease. Epidemiology 2006; 17: 582–87.
[51] Zhang D, Jiang H, Xie J. Alcohol intake and risk of Parkinson's disease: a meta-analysis of observational studies. Mov Disord 2014; 29: 819–22.
[52] Yamamoto T, Moriwaki Y, Takahashi S. Effect of ethanol on metabolism of purine bases (hypoxanthine, xanthine, and uric acid). Clin Chim Acta 2005; 356: 35–57.
[53] Eriksson AK, Löfving S, Callaghan RC, Allebeck P. Alcohol use disorders and risk of Parkinson's disease: findings from a Swedish national cohort study 1972-2008. BMC Neurol 2013; 13: 190
[54] Chen H, Zhang SM, Hernán MA, Willett WC, Ascherio A. Diet and Parkinson's disease: a potential role of dairy products in men. Ann Neurol 2002; 52: 793–801.
[55] Choi HK, Atkinson K, Karlson EW, Willett W, Curhan G. Purine-rich foods, dairy and protein intake, and the risk of gout in men. N Engl J Med 2004; 350: 1093–103.
[56] Gardener H, Gao X, Chen H, Schwarzschild MA, Spiegelman D, Ascherio A. Prenatal and early life factors and risk of Parkinson's disease. Mov Disord 2010; 25: 1560–67.
[57] Sasco AJ, Paffenbarger RS Jr. Measles infection and Parkinson's disease. Am J Epidemiol 1985; 122: 1017–31.
[58] Fang F, Wirdefeldt K, Jacks A, Kamel F, Ye W, Chen H. CNS infections, sepsis and risk of Parkinson's disease. Int J Epidemiol 2012; 41: 1042–49.
[59] Wu WY, Kang KH, Chen SL, et al. Hepatitis C virus infection: a risk factor for Parkinson's disease. J Viral Hepat 2015; 22: 784–91.
[60] Nielsen HH, Qiu J, Friis S, Wermuth L, Ritz B. Treatment for Helicobacter pylori infection and risk of Parkinson's disease in Denmark. Eur J Neurol 2012; 19: 864–69.
[61] Racette BA. Manganism in the 21st century: the Hanninen lecture. Neurotoxicology 2014; 45: 201–07.
[62] Li X, Sundquist J, Sundquist K. Subsequent risks of Parkinson's disease in patients with autoimmune and related disorders: a nationwide epidemiological study from Sweden. Neurodegener Dis 2012; 10: 277-84.
[63] Lai B, Marion S, Teschke K, Tsui J. Occupational and environmental risk factors for Parkinson's disease. Parkinsonism & Related Disorders. 2002;8(5):297-309.
[64] Chen H, Zhang SM, Schwarzschild MA, Hernán MA, Ascherio A. Physical activity and the risk of Parkinson disease. Neurology 2005; 64: 664–69.
[65] Logroscino G, Sesso HD, Paffenbarger RS Jr, Lee IM. Physical activity and risk of Parkinson's disease: a prospective cohort study. J Neurol Neurosurg Psychiatry 2006; 77: 1318–22.
[66] Thacker EL, Chen H, Patel AV, et al. Recreational physical activity and risk of Parkinson's disease. Mov Disord 2008; 23: 69–74.
[67] Xu Q, Park Y, Huang X, et al. Physical activities and future risk of Parkinson disease. Neurology 2010; 75: 341–48.
[68] Sääksjärvi K, Knekt P, Männistö S, et al. Reduced risk of Parkinson's disease associated with lower body mass index and heavy leisure-time physical activity. Eur J Epidemiol 2014; 29: 285–92.
[69] Yang F, Trolle Lagerros Y, Bellocco R, et al. Physical activity and risk of Parkinson's disease in the Swedish National March Cohort. Brain 2015; 138: 269–75.
[70] CohenAD,TillersonJL,SmithAD,SchallertT,ZigmondMJ. Neuroprotective effects of prior limb use in 6-hydroxydopamine-treated rats: possible role of GDNF. J Neurochem 2003; 85: 299–305.
[71] Zigmond MJ, Smeyne RJ. Exercise: is it a neuroprotective and if so, how does it work? Parkinsonism Relat Disord 2014; 20 (suppl 1): S123–27.
[72] Hirsch MA, Iyer SS, Sanjak M. Exercise-induced neuroplasticity in human

Parkinson's disease: what is the evidence telling us? Parkinsonism Relat Disord 2016; 22 (suppl 1): S78–81.

[73] van Nimwegen M, Speelman AD, Overeem S, et al, and the ParkFit Study Group. Promotion of physical activity and fitness in sedentary patients with Parkinson's disease: randomised controlled trial. BMJ 2013; 346: f576.

[74] Connors KA, Galea MP, Said CM. Feldenkrais method balance classes improve balance in older adults: a controlled trial. Evid Based Complement Alternat Med. 2011;2011:873672.

[75] Stephens J, Davidson J, Derosa J, Kriz M, Saltzman N. Lengthening the hamstring muscles without stretching using "awareness through movement." Phys Ther. 2006;86(12):1641-1650.

[76] Tomlinson CL, Patel S, Meek C, et al. Physiotherapy versus placebo or no intervention in Parkinsons disease. Cochrane Database Syst Rev. August 2012;8:CD002817.

[77] Dowding CH, Shenton CL, Salek SS. A review of the health-related quality of life and economic impact of Parkinsons disease. Drugs Aging. 2006;23(9):693-721.

[78] Teixeira-Machado L , Araujo FM , Cunha FA . Feldenkrais Method-based Exercise Improves Quality of Life in Individuals With Parkinson's Disease: A Controlled, Randomized Clinical Trial . Altern Ther Health Med. 2015;21(1):8-14.

[79] Miller L, Das S. Cigarette Smoking and Parkinson's Disease. EXCLI Journal. 2007;93-99(1611-2156).

[80] Fowler JS, Wang GJ, Volkow ND, Franceschi D, Logan J, Pappas N, Shea C, MacGregor RR, Garza V. Smoking a single cigarette does not produce a measurable reduction in brain MAO B in non-smokers. Am J Psychiartry 2000; 157 (11): 1864-6

[81] Janson AM, Fuxe K, Goldstein M. Differential effects of acute and chronic nicotine treatment of MPTP- (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) induced degeneration of nigrostriatal dopamine neurons in the black mouse. Clin Investig 1992; 70:232-38

[82] Westfall TC, Fleming RM, Fudger MF, Clark WG. Effect of nicotine and related substance upon amine levels in the brain. Ann NY Acad Sci 1967;142:83-100

[83] Clarke PBS, Hommer DW, Pert A, Skirboll LR. Electrophysiological actions of nicotine on substantia nigra single units. Br J Pharmacol 1985; 85:827-35

[84] Church T, Pryor WA. Free-radical chemistry of cigarette smoke and its toxicological implications. Environ Health Perspect 1985; 64:111-26

[85] Bluhm, AC, Weistein J, Sonsa JA. Free radicals in tobacco smoke. Nature 1971; 229: 500.

[86] Forbes WF, Robinson JC, Wright GF. Free radicals of biological interests. Electron spin resonance spectra of tobacco smoke condensates. Can J Biochem 1967; 5:1087-98

[87] Pryor WA. Biological effects of cigarette smoke, wood smoke, and the smoke from plastics: The use of electron spin resonance. Free Radic Biol Med 1992; 13:659-76

[88] Pryor WA, Ston K. Oxidants in cigarette smoke: Radicals, hydrogen peroxides, peroxynitrate, and peroxtnitrite. Ann NY Acad Sci 1993; 686:12-28

[89] Pryor, WA, Church DF, Evans MD, Rice WY, Jr., Hayes JR. A comparison of the free radical chemistry of tobacco burning cigarettes and cigarettes that only heat tobacco. Free Radic Biol Med 1990; 8:275-79

[90] McKenney J, Valeri CR, Mohandas N, Fortier N, Giorgio A, Snyder LM. Decreased in vivo survival of hydrogen peroxide-damaged baboon red blood cells. Blood 1990; 76:206- 11

[91] Metz EN, Balcerzak SP, Sagone AL, Jr. Regeneration of reduced glutathione in erythrocytes: stoichiometric and temporal relationship to hexose monophosphate shunt after sulfhydryl inhibition. Blood 1974; 44:691-97

[92] Sagone AL, Balcerzak Sp, Metz EN. The response of red cell hexose monophosphate shunt after sulfhydryl inhibition. Blood 1975; 45:49-54

[93] Baron JA. Cigarette smoking and Parkinson's disease. Neurology 1986; 36:1490-96

[94] Kachroo A, Irizarry MC, Schwarzschild MA. Caffeine protects against combined paraquat and maneb-induced dopaminergic neuron degeneration. Exp Neurol 2010; 223: 657–61.

[95] Xu K, Xu YH, Chen JF, Schwarzschild MA. Neuroprotection by caffeine: time course and role of its metabolites in the MPTP model of Parkinson's disease. Neuroscience 2010; 167: 475–81.

[96] Xu K, Xu Y, Brown-Jermyn D, et al. Estrogen prevents neuroprotection by caffeine in the mouse 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine model of Parkinson's disease. J Neurosci 2006; 26: 535–41.

[97] Trinh K, Andrews L, Krause J, et al. Decaffeinated coffee and nicotine-free tobacco provide neuroprotection in Drosophila models of Parkinson's disease through an NRF2-dependent mechanism. J Neurosci 2010; 30: 5525–32.

[98] Lee KW, Im JY, Woo JM, et al. Neuroprotective and anti-inflammatory properties of a coffee component in the MPTP model of Parkinson's disease. Neurotherapeutics 2013; 10: 143–53.

[99] Kitagawa M, Houzen H, Tashiro K. Caffeine in Parkinson's disease: comment on its importance and the dose proposal. Mov Disord 2012; 27: 808.

[100] Postuma RB, Lang AE, Munhoz RP, et al. Caffeine for treatment of Parkinson disease: a randomized controlled trial. Neurology 2012; 79: 651–58.

[101] Schwarzschild MA. Caffeine in Parkinson disease: better for cruise control than snooze patrol? Neurology 2012; 79: 616–18.

[102] Kondo T, Mizuno Y, and the Japanese Istradefylline Study Group. A long-term study of istradefylline safety and efficacy in patients with Parkinson disease. Clin Neuropharmacol 2015; 38: 41–46.

[103] Hauser RA, Olanow CW, Kieburtz KD, et al. Tozadenant (SYN115) in patients with Parkinson's disease who have motor fluctuations on levodopa: a phase 2b, double-blind, randomised trial. Lancet Neurol 2014; 13: 767–76.

[104] Lucas M, Mirzaei F, Pan A, et al. Coffee, caffeine, and risk of depression among women. Arch Intern Med 2011; 171: 1571–78.

[105] K.L. Shohet, R.E. Landrum, Caffeine consumption questionnaire: a standardized measure for caffeine consumption in undergraduate students., Psychol. Rep. 89 (2001) 521–6. doi:10.2466/pr0.2001.89.3.521.

[106] C. Ojeda-López, A. Cervantes-Arriaga, M. Rodríguez-Violante, T. Corona, Caffeine drinking, cigarette smoking, and dopaminergic replacement therapy dose in Parkinson's disease, Neurol Sci. 34 (2013) 979–983. doi:10.1007/s10072-012- 1180-0.

[107] Moccia M, Erro R, Picillo M, Vitale C, Longo K, Amboni M et al. Caffeine consumption and the 4-year progression of de novo Parkinson's disease. Parkinsonism & Related Disorders. 2016;32:116-119.

[108] Ascherio A, Zhang SM, Hernán MA, et al. Prospective study of caffeine consumption and risk of Parkinson's disease in men and women. Ann Neurol 2001; 50: 56–63.

[109] Hu G, Bidel S, Jousilahti P, Antikainen R, Tuomilehto J. Coffee and tea consumption and the risk of Parkinson's disease. Mov Disord 2007; 22: 2242–48

[110] Tan LC, Koh WP, Yuan JM, et al. Differential effects of black versus green tea on risk of Parkinson's disease in the Singapore Chinese Health Study. Am J Epidemiol 2008; 167: 553–60.

[111] Levites Y, Weinreb O, Maor G, Youdim MB, Mandel S. Green tea polyphenol (-)-epigallocatechin-3-gallate prevents N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-induced dopaminergic neurodegeneration. J Neurochem 2001; 78: 1073–82.

[112] Liu, R. H. (2003). Health benefits of fruit and vegetables are from additive and synergistic combinations of phytochemicals. Am. J. Clin. Nutr. 78, 517S-520S.

[113] Gao, X., Chen, H., Fung, T. T., Logroscino, G., Schwarzschild, M. A., Hu, F. B., et al. (2007). Prospective study of dietary pattern and risk of Parkinson disease. Am. J. Clin. Nutr. 86, 1486–1494.

[114] Okubo, H., Miyake, Y., Sasaki, S., Murakami, K., Tanaka, K., Fukushima, W., et al. (2012). Dietary patterns and risk of Parkinson's disease: a case-control study in Japan. Eur. J. Neurol. 19, 681–688. doi: 10.1111/j.1468-1331.2011.03600.x

[115] Alcalay, R. N., Gu, Y., Mejia-Santana, H., Cote, L., Marder, K. S., and Scarmeas, N. (2012). The association between Mediterranean diet adherence and Parkinson's disease. Mov. Disord. 27, 771–774. doi: 10.1002/mds.24918

[116] Miyake, Y., Fukushima, W., Tanaka, K., Sasaki, S., Kiyohara, C., Tsuboi, Y., et al. (2011a). Dietary intake of antioxidant vitamins and risk of

Parkinson's disease: a case-control study in Japan. Eur. J. Neurol. 18, 106–113. doi: 10.1111/j.1468-1331.2010.03088.x

[117] Paiva, S. A., and Russell, R. M. (1999). Beta-carotene and other carotenoids as antioxidants. J. Am. Coll. Nutr. 18, 426–433. doi: 10.1080/07315724.1999.10718880

[118] Perry, T. L., Yong, V. W., Clavier, R. M., Jones, K., Wright, J. M., Foulks, J. G., et al. (1985). Partial protection from the dopaminergic neurotoxin N-methyl-4- phenyl-1,2,3,6-tetrahydropyridine by four different antioxidants in the mouse. Neurosci. Lett. 60, 109–114. doi: 10.1016/0304-3940(85)90229-0

[119] Yong, V. W., Perry, T. L., and Krisman, A. A. (1986). Depletion of glutathione in brainstem of mice caused by N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine is prevented by antioxidant pretreatment. Neurosci. Lett. 63, 56–60. doi: 10.1016/0304-3940(86)90012-1

[120] Perry, T. L., Yong, V. W., Hansen, S., Jones, K., Bergeron, C., Foulks, J. G., et al. (1987). Alpha-tocopherol and beta-carotene do not protect marmosets against the dopaminergic neurotoxicity of N-methyl-4-phenyl- 1,2,3,6-tetrahydropyridine. J. Neurol. Sci. 81, 321–331. doi: 10.1016/0022-510X(87)90106-7

[121] Kaur, H., Chauhan, S., and Sandhir, R. (2011). Protective effect of lycopene on oxidative stress and cognitive decline in rotenone induced model of Parkinson's disease. Neurochem. Res. 36, 1435–1443. doi: 10.1007/s11064-011-0469-3

[122] Paiva, S. A., and Russell, R. M. (1999). Beta-carotene and other carotenoids as antioxidants. J. Am. Coll. Nutr. 18, 426–433. doi: 10.1080/07315724.1999.10718880

[123] Massey, V. (2000). The chemical and biological versatility of riboflavin. Biochem. Soc. Trans. 28, 283–296. doi: 10.1042/0300-5127:0280283

[124] Coimbra, C. G., and Junqueira, V. B. (2003). High doses of riboflavin and the elimination of dietary red meat promote the recovery of some motor func- tions in Parkinson's disease patients. Braz. J. Med. Biol. Res. 36, 1409–1417. doi: 10.1590/S0100-879X2003001000019

[125] Abbott, R. D., Ross, G. W., White, L. R., Sanderson, W. T., Burchfiel, C. M., Kashon, M., et al. (2003). Environmental, life-style, and physical precursors of clini- cal Parkinson's disease: recent findings from the Honolulu-Asia Aging Study. J. Neurol. 250(Suppl. 3), III30–III39. doi: 10.1007/s00415-003-1306-7

[126] Murakami, K., Miyake, Y., Sasaki, S., Tanaka, K., Fukushima, W., Kiyohara, C., et al. (2010b). Dietary intake of folate, vitamin B6, vitamin B12 and riboflavin and risk of Parkinson's disease: a case-control study in Japan. Br. J. Nutr. 104, 757–764. doi: 10.1017/S0007114510001005

[127] Bousquet, M., Calon, F., and Cicchetti, F. (2011a). Impact of omega-3 fatty acids in Parkinson's disease. Ageing Res. Rev. 10, 453–463. doi: 10.1016/j.arr.2011.03.001

[128] Da Silva, T. M., Munhoz, R. P., Alvarez, C., Naliwaiko, K., Kiss, A., Andreatini, R., et al. (2008). Depression in Parkinson's disease: a double-blind, randomized, placebo-controlled pilot study of omega-3 fatty-acid supplementation. J. Affect. Disord. 111, 351–359. doi: 10.1016/j.jad.2008.03.008

[129] Horrocks, L. A., and Yeo, Y. K. (1999). Health benefits of docosahexaenoic acid (DHA). Pharmacol. Res. 40, 211–225. doi: 10.1006/phrs.1999.0495

[130] Massaro, M., Habib, A., Lubrano, L., Del Turco, S., Lazzerini, G., Bourcier, T., et al. (2006). The omega-3 fatty acid docosahexaenoate attenuates endothe- lial cyclooxygenase-2 induction through both NADP(H) oxidase and PKC epsilon inhibition. Proc. Natl. Acad. Sci. U.S.A. 103, 15184–15189. doi: 10.1073/pnas.0510086103

[131] Wang, J. Y., Sekine, S., and Saito, M. (2003). Effect of docosahexaenoic acid and ascorbate on peroxidation of retinal membranes of ODS rats. Free Radic. Res. 37, 419–424. doi: 10.1080/1071576031000070084

[132] Wang, X., Chen, S., Ma, G., Ye, M., and Lu, G. (2005). Genistein protects dopamin- ergic neurons by inhibiting microglial activation. Neuroreport 16, 267–270. doi: 10.1097/00001756-200502280-00013

[133] Sarkaki, A., Badavi, M., Aligholi, H., and Moghaddam, A. Z. (2009). Preventive effects of soy meal (+/- isoflavone) on spatial cognitive deficiency and body weight in an ovariectomized animal model of Parkinson's disease. Pak. J. Biol. Sci. 12, 1338–1345. doi: 10.3923/pjbs.2009.1338.1345

[134] Liu, L. X., Chen, W. F., Xie, J. X., and Wong, M. S. (2008). Neuroprotective effects of genistein on dopaminergic neurons in the mice model of Parkinson's disease. Neurosci. Res. 60, 156–161. doi: 10.1016/j.neures.2007.10.005