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Diet and the Risk of Parkinson's Disease — Research Suggests Dietary Interventions May Prevent It and Lessen Symptom Severity
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Parkinson's disease (PD) is a chronic and progressive movement disorder affecting nearly 1 million people in the United States, making it the second most common neurodegenerative disorder after Alzheimer's disease.[1] First described almost 200 years ago by James Parkinson, PD has no cure, and therapies to lessen symptoms are limited.

The condition involves the malfunctioning and death of neurons, primarily in an area of the brain called the substantia nigra, where the neurotransmitter dopamine is produced. Under normal conditions, dopamine sends messages to the part of the brain that controls movement and coordination. As PD progresses, dopamine production decreases, affecting movement and coordination.

A hallmark of PD, Lewy bodies are the clumping of the protein alpha-synuclein in the substantia nigra. Loss of cells in other areas of the brain, including the brain stem and the olfactory bulb, also may play a role in PD. Though symptoms vary from person to person, they often include stiffness, slowness, impaired balance, and tremor of the hands, arms, legs, jaw, and face.[2,3]

What Causes PD?
There's no single cause of PD. A variety of factors with complex interactions are thought to be responsible for both the disease's development and progression. Despite years of research, the exact causes are unknown. However, it has been suggested that the disease is caused by some combination of genetic predisposition and environmental factors, such as exposure to certain pesticides and heavy metals.[4] Some genetic mutations appear to be inherited, such as in early-onset PD, but these affect only a small number of families, and not everyone who inherits the genetic mutation will develop the disease.[4]

In addition, environmental factors may affect the risk of developing PD by causing altered gene expression, a process known as epigenetics, rather than a genetic mutation.[5] Age, however, is a clear risk factor. While the general population has a 1% to 2% chance of developing PD, those older than age 60 have a 2% to 4% chance of developing the disease.4 Currently, there's no genetic screening for PD.[4]

Moreover, there's no single test for diagnosing PD. However, there's a collection of symptoms and various diagnostic tests, including CT scans, that can be used in combination to rule out other conditions and point to PD. A neurologist will take a detailed medical history to eliminate the possibility that medications are causing PD-like symptoms and perform a neurological

examination to determine whether gait, agility, and balance are normal by comparing findings with a rating scale. Ultimately, a neurologist may prescribe medications for PD to determine whether symptoms improve.[4]

Diet's Role

A body of research suggests that what individuals eat and drink and the supplements they take also may affect the risk of developing PD and its progression. However, dietary factors are difficult to accurately assess.

Plant-Based Diets

Individual foods and food groups have been studied to determine whether they may be associated with the development of PD. One prospective study of men and women found no association with any single food group or the quality of diet and the occurrence of PD.[6] However, other studies suggest a diet high in fish, vegetables, whole grains, fruits, and legumes may be protective.[7,8] A case-control study in Japan found an almost 50% lower risk of developing PD among those who ate a diet characterized by a high intake of vegetables, seaweed, legumes, mushrooms, fruit, and fish compared with those whose diets included the lowest amounts of these foods.[8]

The association between overall dietary patterns and the risk of PD also was examined as part of the prospective Health Professionals Follow-Up Study and the Nurses' Health Study. Researchers found that dietary patterns characterized by high intakes of fruits, vegetables, fish, legumes, nuts, and soy were associated with a 25% to 30% lower risk of developing PD.[9] It's unknown whether individual nutrients, such as vitamins C and E and carotenoids, which are concentrated in plant-based diets, are responsible for the observed association because of their role in protecting cells against oxidative damage.

Inflammation also has been implicated in the pathogenesis of PD. Adherence to a Mediterranean diet, which is plant based and rich in monounsaturated fats, fish, and seafood, may reduce inflammation.[10] However, those who follow diets that aren't rich in plant foods haven't been found to have a greater risk of developing PD.[8]

Nevertheless, it has been suggested that consuming a mostly plant-based diet may be helpful in the management of PD patients' motor performances.[9] Polyphenols are found in a variety of fruits, vegetables, herbs, cocoa, teas, wines, and juices as well as supplements, and it has been suggested that they may be effective as preventive agents.

As a whole, polyphenols constitute a huge group of molecules. Phenolic acids account for about one-third of the total dietary intake of polyphenols; flavonoids account for the remaining two-thirds. To put the complexity of polyphenols into perspective, more than 5,000 flavonoid compounds have been identified.[11]

A clinical trial to determine which polyphenols and at which doses may be effective to benefit patients with PD would be a monumental task. Though they haven't been proven effective in humans, some polyphenols, such as catechins, caffeic acid, and curcumin, are effective in alleviating and protecting against neurodegenerative processes in cell cultures and

animals.[12,13] While several clinical trials are under way to test the effectiveness of polyphenol supplements in the treatment of Alzheimer's disease, there are none yet to study polyphenols and PD.[12]

Dietary Restriction and Ketogenic Diets

Long-term reduction in calorie intake has been associated with extended life span in animals and has been proposed to counteract the loss of functioning neurons in animals with neurodegeneration such as occurs with PD.[14] In addition, overweight in midlife has been identified as a risk factor for PD, independent of other risk factors. Researchers found those with a BMI of 30 had twice the risk of developing PD than those with a BMI of less than 23.[15] Researchers have offered several theories to explain why calorie restriction protects neurons, including decreased production of free radicals and regulations of gene expression.[14]

Researchers also have explored the effect of diet on PD's progression. In rats with chemically induced PD, dietary restriction has been found to reduce the destruction of dopamine-producing neurons.[16] In monkeys, low-calorie diets lessened the severity of PD-related neurochemical deficits and motor dysfunction.[16]

Similarly, ketogenic diets, which have been found effective in the treatment of epilepsy, may have similar beneficial effects in lessening the symptoms associated with PD. A ketogenic diet is a high-fat (about 80% of calories), low-carbohydrate diet that forces the body to burn fats rather than carbohydrates for energy; ketones are a metabolic product of the diet. An elevated level of ketones in the blood (ketosis) may alleviate symptoms. It has been suggested that increasing blood ketone concentrations to a therapeutic level requires a diet consisting of 4 parts fat and 1 part carbohydrate-protein mixture.[17] However, the diet is difficult to follow for long periods of time and can result in elevated blood lipid levels.[18]

One small clinical study testing the ketogenic diet's effects on PD symptoms found that after 28 days on the diet patients experienced an average 43% reduction in the Unified Parkinson's Disease Rating Scale scores, the most commonly used rating scale for the course of PD.[19] All patients reported their improvement as moderate to very good. However, because it was a small, uncontrolled study, the authors noted that a placebo effect couldn't be ruled out. One author went so far as to suggest that a medium-chain-triglyceride–based supplement, which encourages ketonemia, may benefit patients with PD as it has in patients with Alzheimer's disease.[20,21]

The most prominent theory on the cause of Alzheimer's disease suggests that the accumulation and aggregation of beta-amyloid proteins into plaque is toxic to neurons. Ketonemia may reduce the risk of Alzheimer's disease by protecting against the toxic effects of these beta-amyloid proteins on neurons[22] and by preventing free-radical damage, which also may be one of its protective actions in PD. However, there have been no well-controlled trials in humans.[14]

Coffee and Tea

Coffee consumption is one of the most studied dietary factors related to the development of PD. Researchers have found that caffeine has a neuroprotective effect in animals with

chemically induced PD and may explain the apparent protective effect in humans.[23,24] Several studies have found that people who consume caffeinated coffee or tea tend to have a lower risk of developing PD and a delayed onset of the disease, but the findings haven't been consistent.

A systematic review and meta-analysis of 26 studies found a 25% lower risk of PD among caffeine consumers. The results also indicated that the higher the intake of caffeine, the lower the risk of PD.[25] The association was weaker when only women were considered.

One cohort study found that after adjustment for age, smoking, and alcohol intake, coffee consumption was associated with a decreased risk of death from PD in men. In postmenopausal women, the association was influenced by the use of estrogen replacement therapy. Women who never used estrogen replacement therapy and drank four or more cups of coffee per day had nearly one-half the risk of dying from PD compared with nondrinkers. However, there was a 31% increased risk among those who drank four or more cups of coffee per day and used estrogen replacement therapy. The authors suggested that the caffeine in coffee reduces the risk of PD but noted that this hypothetical preventive effect in women may be blocked in those taking estrogen replacement therapy.[26]

One prospective study of men and women found that an unusually high intake of coffee (10 or more cups per day) was associated with an almost 75% reduced risk of developing PD compared with no coffee intake. The association was stronger among those who were overweight and those with the lowest serum cholesterol levels.[27]

While research has found an association between specific patterns of obesity (central obesity and higher triceps skinfold)[28,29] and PD, it's unknown why coffee drinking may affect overweight men and women differently. An earlier meta-analysis found an overall 32% lower risk of PD among coffee drinkers compared with non-coffee drinkers.[30] The effect appears to be dose dependent, and rather than directly affecting the development of PD, it may suppress its clinical expression.[31,32]

It has been suggested that not all coffee drinkers are less vulnerable to PD and that the difference may be the result of genetic makeup.[33] A recent study indicated genetic factors may indeed influence the effects of coffee on risk.[34] However, these findings haven't been consistent. One retrospective study found that consuming more than three cups of coffee per day advanced the onset of PD by almost five years.[35]

Studies from Japan, Finland, and Israel have investigated the association between tea consumption and PD. A Finnish study found that those who consumed three cups of tea per day had nearly a 60% lower risk of developing PD than nondrinkers.[36] In a study of Japanese subjects, the highest consumption of black, Japanese, and Chinese tea was associated with a 61% to 62% lower risk of developing PD compared with the lowest consumption.[37] An Israeli study didn't find that tea consumption lowered the overall risk of PD development, but that consumption of more than three cups of tea per day delayed the onset of motor symptoms by almost eight years.[35]

Dairy Foods

Four prospective studies have suggested an association between the consumption of dairy foods and a higher risk of PD development, particularly in men.[6,38-40] Increased risk among dairy consumers ranged from 10% to 230%. The greatest associated rise in risk was found in those who consumed more than 16 oz of dairy per day compared with those who consumed no dairy.[39] A meta-analysis of the studies found a 60% increased risk in men and women combined, an 80% greater risk in men, and a 30% higher risk in women consuming the most dairy compared with those who consumed the least.[38] A prospective study from Finland found a positive association only in women.[6] However, a recent case-control study from Japan found no association between intake of dairy products, regardless of gender.[4]1 None of the studies looked at the effect of dairy consumption on symptoms or progression of the disease.

Supplements

The combined analysis of the Health Professionals Follow-Up Study and the Nurses' Health Study examined whether taking multivitamin supplements affected the risk of PD development and found a small 2% lower risk among multivitamin supplement users.[9]

In a large cohort study in Finland, those with the highest serum vitamin D concentrations had a 67% reduced risk of PD compared with those with the lowest serum levels.[42] In another study, supplemental vitamin D use was associated with a 20% to 30% lower risk of developing PD for doses up to 399 IU/day and more than 400 IU/day, respectively, compared with nonuse.[28] In addition, one review of the research suggested that moderate amounts of vitamin D in the diet may help protect against the progression of PD.[43] No recommendations have been made, however, for supplementation of vitamin D for either PD prevention or treatment.

For those already diagnosed with PD, supplementation with antioxidants has been suggested as an appropriate therapy to possibly prevent or reduce disease progression by preventing the death of dopamine-producing neurons, but this hasn't been proven.[44] Coenzyme Q10 (CoQ10) is a potent antioxidant and important for the activity of enzymes in dopamine-producing cells. With PD, levels of CoQ10 and enzyme activity in cells are reduced.[3] Doses of up to 1,200 mg/day of CoQ10 have been associated with less disability in PD patients, with the greatest benefit associated with the highest dose.[3] However, not all studies have found CoQ10 to be beneficial.[45] It has been suggested as a therapeutic agent that warrants further study.[3,46]

Supplemental vitamin E wasn't found to affect the risk of developing PD. However, risk was found to be lower in men and women with high dietary intakes of vitamin E.[47] Large doses of supplemental vitamin E (2,000 to 3,200 IU/day) have been studied for their effect on PD progression but mostly have been found to be ineffective.[48,49]

Physical Activity

With regard to physical activity, research suggests moderate to vigorous exercise may have a neuroprotective effect, reducing the risk of PD development, slowing progression, and improving mobility in those already diagnosed with the disease.[50]

In rats with chemically induced PD, treadmill exercise was found to suppress the loss of dopamine-producing neurons.[51] In another animal study, exercise strengthened weakened muscles and partially recovered the loss of dopamine-producing neurons in rats.[52]

In a large population of US older adults aged 50 to 71 who had been studied prospectively, higher levels of moderate to vigorous physical activity from the age of 35 to 39 or in the 10 years before the study were associated with a 40% future lower risk of PD compared with those who were inactive.[53] A recent review also suggests that higher levels of moderate to vigorous physical activity in mid or later life are associated with lower PD risk.[50]

While a direct cause and effect relationship hasn't been proven between physical activity and a reduced risk of PD, the evidence is more clear that physical activity benefits patients with PD. Research indicates that cardiovascular fitness improves cognition among PD patients.[54] Cognitive impairment occurs in about 25% of patients with early PD and eventually develops into dementia in most patients over the long term.[55,56] The Parkinson's Disease Foundation recommends regular physical activity to maintain and increase mobility among PD patients.[2] Three 20-minute exercise sessions per week have been recommended as a reasonable goal. Ideally, an exercise program would include aerobic, strengthening, and stretching exercises.[57]

Protein and Parkinson's Symptoms

Levodopa (L-dopa) is the drug most often prescribed to alleviate tremors common in PD patients. L-dopa is a large neutral amino acid that depends on the same transport system as other neutral amino acids found in the diet. As a result, amino acids in dietary protein may compete with L-dopa for intestinal absorption and transport across the blood-brain barrier. It has long been suggested that either restricting or redistributing dietary protein during the day can enhance L-dopa's effectiveness. In fact, current guidelines from the American Academy of Neurology recommend a diet in which protein is redistributed throughout the day, with a low-protein intake at breakfast and lunch, and a high-protein intake at dinner, the logic being that motor impairment is less important in the evening and at bedtime than it is during the day.[58]

However, the effectiveness of following a protein-restricted diet while taking L-dopa appears to be highly variable, depending on the stage of the disease and the ability to adhere to the diet in the long term.[59] In addition, dosages of L-dopa may have to be adjusted to improve efficacy because of the decrease in protein intake. This diet therapy typically has been suggested in the later stages of PD as the effectiveness of L-dopa wanes and fluctuations in motor ability increase. However, the diet may provide an alternative to increasing L-dopa dosages and be more beneficial when the intervention is begun in the early stages of PD and neurons retain some ability to store L-dopa.[59]

Research suggests that protein needs for the elderly—the population most affected by PD—may be almost twice that (about 1.5 g/kg/day) of those who are younger (0.8 g/kg/day) to maintain muscle mass.[60] It may be difficult to meet that higher recommendation if most protein intake is restricted to a single meal and since long-term effectiveness of a protein redistribution diet hasn't been established.[59] However, one study found that no significant loss of fat-free mass among PD patients occurred following one month on a minimal protein intake.[61]

The availability of low-protein food products makes it easier for patients to adhere to low-protein meals. Several companies offer a variety of products (see below).

Future Hope

The research strongly suggests an association between diet and the risk of developing PD later in life. However, the specific dietary prescription to reduce risk, at which stage of life, and for whom it should be prescribed hasn't yet been identified. However, based on the research to date, maintaining a healthy weight by following a calorie-controlled diet throughout life is prudent. In addition, a plant-based diet has shown some promise and is a rich source of polyphenols, a class of compounds suggested to be beneficial in preventing neurodegeneration.

While it isn't recommended for nondrinkers to begin drinking coffee, there appears to be no reason for regular coffee drinkers to be concerned about increased risk as a result of their coffee consumption; they may, in fact, experience reduced risk. Adequate intake of vitamin D is recommended to support bone health and has been associated with a lower risk of a variety of conditions and diseases, and also may decrease PD risk.

For treatment of patients diagnosed with PD, several supplements, such as CoQ10, polyphenols, and vitamin D, are potential subjects of future research, but not enough is known to make supplement recommendations.

Regular physical activity, which is recommended for overall good health, also may provide some protection against the development of PD and contribute to an improvement in motor abilities.

For patients taking L-dopa, a restricted protein diet or a diet involving the redistribution of protein may help enhance the medication's effectiveness, but any change in protein intake must be made in consultation with the treating physician in case adjustments to L-dopa dosage are required.

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Companies Offering Low-Protein Food Products

- Applied Nutrition Corp (www.medicalfood.com)
- Cambrooke Foods (www.cambrookefoods.com)
- Dietary Specialties online store (www.dietspec.com)
- Med-Diet (www.med-diet.com)
- My Special Diet (www.myspecialdiet.com)
- PKU Perspectives (www.pkuperspectives.com)
- Taste Connections, LLC (www.tasteconnections.com)

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Examination

1. Parkinson's disease (PD) involves the malfunctioning and death of neurons, primarily in which area of the brain where the neurotransmitter dopamine is produced?
A. Occipital lobe
B. Cerebellum
C. Substantia nigra
D. Temporal lobe

2. Which of the following factors is proven to increase the risk of developing PD?
A. Being female
B. Being over the age of 60
C. History of smoking
D. Tea consumption

3. Research suggests that caffeine reduces the risk of PD in women, but this hypothetical benefit may be prevented by the use of estrogen replacement therapy.
A. True
B. False

4. Based on the information in this article, which of the following statements is true?
A. All cases of PD are caused by an inherited genetic mutation.
B. The inherited genetic mutation for PD is rare.
C. Environmental factors are not believed to increase the risk of developing PD.
D. The child of a parent with PD has a 50% chance of developing the disease.

5. People over the age of 60 have what percentage risk of developing PD?
A. 1% to 2%
B. 2% to 4%
C. 4% to 6%
D. 8% to 10%

6. The risk of developing PD has been found to double in those with a BMI that is greater than:
A. 25.
B. 28.
C. 30.
D. 32.

7. People with PD have been found to have higher serum levels of vitamin D.
A. True
B. False

8. Research suggests moderate-to-vigorous exercise in general may have a neuroprotective effect against PD development. However, a recent review reported that higher levels of moderate-to-vigorous activity is associated with a lower PD risk during which stage of life?
A. Childhood
B. Adolescence
C. Young adulthood
D. Mid or later life

9. Which dietary pattern has been associated with a reduced risk of developing PD?
A. Vegan diet
B. Low-fat diet
C. Plant-based diet
D. Western diet

10. Which supplement has shown early promise for treatment of PD?
A. Coenzyme Q10
B. Calcium
C. Zinc
D. Vitamin C