



REVIEW ARTICLE

Part Two: Habit and Customs, Obesity and Parkinson's Disease

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Abstract

Objective: To establish correlation between lifestyles, obesity and the risks of Parkinson's disease (PD).

To ascertain the effect of PD on Body mass index (BMI).

Methods: Keyword used in searching for similar articles on PubMed were, Obesity, hyperlipidemia, Metabolic syndrome (MetS), Neurodegenerative disorders, Parkinson's diseases (PD). Papers from 2014-2019 related were compiled. Cases at Zhenjiang First people's hospital similar was compiled to draw conclusions. I evaluated the association between years of diagnosis (YOD) of PD and BMI for both male and female patients and compared to controlled groups. There was a statistically significance between YOD of PD and BMI.

Conclusion: Meta-analysis showed that YOD is inversely proportional to BMI.

Parkinson's Disease in China

The rapid growth in China's economy caused an increase in the risk factors for PD such as obesity [5] and the prevalence was estimated as 18 per 100,000 people in a survey in Shanghai, China. Age adjusted rates give more restricted range of 72-258.8 per 100,000 people. Most of the reports recorded overall crude report ratio of between male and female of all ages 100 and 200 per 100,000 people [6]. PD is common among old people and as the population of China continues to be majorly Old, we can conclude that in the next decade the prevalence of PD in China will grow exponentially.

Risk Factors for PD

Nutrition

Some motor symptoms such as dyskinesia increases energy expenditure and some of the medications affects food intake, cognitive impairment can also increase chances of malnutrition, If the diagnosis was made at an older age and the patient has no caregiver, they tend to have higher neurologic and depression score causing for a higher dose of daily levodopa, this predicts malnutrition [7-9], patients like these are at high risk of losing weight and malnourishment has a negative feedback effect on the neurological status.

A systematic review reported a malnutrition prevalence ranges from 0%-24%, while 3%-60% of PD patients were found to be at risk [10]. Factors that influences appetite are early satisfaction, constipation, dysphagia

Introduction

Following Alzheimer's disease, Parkinson's disease (PD) is the second most common age-related neurodegenerative disorder. The motor-related symptoms include bradykinesia, rigidity, tremor and postural instability, while metabolic imbalances, psychiatric and cognitive disorders are typical of the non-motor symptoms [1]. The pathology of PD is yet to be understood but some studies showed that the risk factors were age, obesity, environmental toxins, genetics, physical inactivity [2-4]. Weight loss correlates with the progression of PD, in our study we were able to ascertain that lowest BMI was in the most advanced stage.



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having a significant influence on food intake.

Appetite can be improved by reducing the daily protein intake and also by redistribution while focusing on intake of plant-based protein to improve fiber intake, if the dietary intervention allows reducing total levodopa intake, it should be applied also to nonfluctuating patients. A non-fluctuating patient are those that can reduce levodopa total intakes. Although levodopa is associated with weight loss, other dopaminergic agents can cause weight gain, and an increase risks of compulsive behavior, such as compulsive eating [11-13].

Genetics

About 5-10% of patients suffers from a monogenic form of PD where autosomal dominant mutations in *SNCA*, *LRRK2*, and *VPS35* and autosomal recessive mutations in *PINK1*, *DJ-1*, and *Parkin* cause the disease with high penetrance [14]. The genetic connection of PD is complex with contribution from certain gene mutations, Mendelian factor such as *SNCA*, *LRRK2*, *Parkin*, *Pink1* and non-Mendelian factors (e.g. single nucleotide polymorphisms), Glucocerebrosidase gene mutations (Gaucher disease) are currently the strongest genetic risk factor for PD, the recognition of α -synuclein mutations as a uncommon origin of disease and the understanding that this protein is an important factor of all PD in the form of Lewy bodies and Lewy neurites [15,16].

Monogenic loci: Autosomal dominant mutations

Mutations in the alpha-synuclein gene (*SNCA*) is uncommon and also point mutations in addition with all locus multiplication, duplication is evidence in family members that is compatible with autosomal dominant inheritance, phenotypes (including myoclonus, severe autonomic dysfunction and dementia in addition to parkinsonism), and looks similar to diffuse Lewy body disease or multiple system atrophy. The patients with *SNCA* duplications display a classical PD phenotype. Most common known cause of autosomal dominant in PD is the mutation in leucine-rich repeat kinase 2 (*LRRK2*) This gene has 51 exons, encoding a very large protein, termed *Lrrk2* (dardarin), this contains two predicted enzyme domain namely (GTPase and kinase) and multiple protein-protein interaction domains showing almost 10% of the patients with familial PD and a clear autosomal dominant pattern of inheritance. In some studies, approximately up to 70% of people age 80 years has an incomplete and age-related penetrance estimated for commonest Gly2019Ser mutation. Dopamine neuron loss and a change in glial cell (gliosis) in the substantia nigral is a common feature in patients with *LRRK2* mutation, with Lewy body found in these patients [16].

Autosomal recessive forms

PRKN(parkin, *PARK2*), *PINK1* (*PARK6*), and *DJ-1* (*PARK7*)

no atypical clinical forms presentation, mutations in each cause rare form of parkinsonism with an early onset (< 30 years) clinical features is presented as pyramidal, dystonic, ocular movement, and cognitive disturbances. Mutations in *PINK1* and *PARK7* accounts for up to 1-8%, and 1-2% of the sporadic cases with early-onset. Mutations in *parkin* accounts for half of the category of the disease onset which is usually before the age of 45 years, and also ~15% of the sporadic cases with onset before 45 [16].

Recently discovered gene mutation

Vacuolar protein sorting (*VPS35* c.1858G > A; p. Asp620Asn) *VPS35* is a central component of the tripartite retromer cargo-recognition complex, consisting of *VPS35*, *VPS29* and *VPS26a* or *b*, that together form the luminal structure for transport of specific membrane-associated proteins. To date, the role of retromer within neurons is poorly described but the linkage of *VPS35p*, D620N to Parkinson's disease is likely to be a catalyst for future research. Dynactin *DCTN1* mutations provide an elegant opportunity to understand the selective vulnerability of different neuronal population to a neurodegenerative disease, eIF4G1 were genetically linked to autosomal dominant late-onset Parkinson's disease with brainstem Lewy body pathology [16].

Metabolic syndrome (Mets)

The component of Mets are Diabetes mellitus (DM), Central Obesity, Glucose intolerance, Dyslipidemia along with elevated triglycerides, low high density lipoprotein (L-HDL) cholesterol, microalbuminuria, Low density lipoprotein (LDL), cholesterol particles, High blood pressure (HBP), Endothelial dysfunction, high waist circumference, oxidative stress, inflammation, tumors, neurodegeneration, and atherosclerosis-based ischemic cardio- or cerebral-vascular disease. Studies has shown that increased oxidative stress is the core and a general character of metabolism-related disease, making it a risk factor for PD [17]. Fat and Obesity has been reported to have an association with PD, Obesity at middle age increases the chances of neurodegenerative diseases and excessive consumption of glucose had neurotoxicity [18-21]. Hyperhomocysteinemia and Endothelial Dysfunction are risk factors for neurodegenerative diseases [22,23]. Stress to the endoplasmic reticulum (ER) and inflammation results in pathogenesis of PD [24-26].

Environmental factors

There was a connection established between PD and Pesticide this was suspected in 1983, when a chemical found in paraquat (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) (MPTP), was said to cause acute Parkinsonism [27]. Studies that reported exposures used it as an estimate for pesticide expo-

sure effect on PD but it's difficult to pin point because PD occurs late in life [28,29]. Some self-reported cases, job exposures to toxins, geographical location was also reported in some patients [30-33].

A study reported association of direct pesticide application defined broadly and specifically, well-water consumption, and farming residences and occupations with PD were evaluated in 319 cases from 308 families and 296 relative and other controls, of the controls, 252 were relative controls from the 308 families with at least one case, and these relative controls included 237 siblings, 10 parents or children, and 5 cousin or avuncular relatives (uncles/aunts/nephews/nieces). The remaining 44 controls were ascertained as spouse or other unrelated controls or as relative controls in families with no environmental risk factor data available on the case(s). Only 39 of the 319 cases (12%) reported having symptoms of PD for two years or less [32,34,35].

Autoimmune disease

Amyotrophic, lateral sclerosis and multiple sclerosis were associated with risk of PD, these diseases were said to have common pathological features such as inflammation, genetic mutation, improper protein aggregates and biochemical defect that leads to cell death [36]. Some studies assumed PD to be an autoimmune disease because of the signs of neuroinflammation and peripheral immune infiltration, a Swedish study found that patients with autoimmune diseases and those with higher socio-economic status had a higher risk of Parkinson's disease [37,38]. Reiter's disease was connected to the highest risk for PD and an increased risk was also noted during 1-4 years follow up of ankylosing spondylitis [39].

Body Mass Index (BMI)

Several reports have had it that patients with $25 \text{ BMI} \leq 25 \text{ kg/m}^2 < 30 \text{ kg/m}^2$ was a risk factor for PD, an association was established between waist circumference and PD amongst non-smokers, increased triceps skin-fold thickness, which is an indicator of obesity of the periphery was said to be associated to an increased risk of PD [40-43].

Common view

Chen, et al. [2] found that $25 \leq \text{BMI} < 30$ might have an increased risk of PD compared to $\text{BMI} < 25$ in cohort studies but in case-controlled studies $25 \leq \text{BMI} < 30$ was not a risk factor for PD compared to Cohort studies.

A report in Mexico pointed out that overweight and obesity is common amongst PD patients, while Underweight and malnutrition were well documented among these patients during the course of the disease. A cross-sectional study including 177 healthy controls and 177 PD patients attending a tertiary care center record-

ed a statistically significant difference between BMI between controls and PD patients (29.1 ± 5.4 versus 27.2 ± 4.7 , $p < 0.001$). In the PD Group, two patients were underweight, 32.7% were within normal range, 46.9% had overweight, and 19.2% were obese. Overweight and normal weight were more prevalent in the PD Group ($p = < 0.01$ and < 0.001 , respectively) when compared to controls. He concluded that overweight/obesity are common among patients with PD, while underweight is almost negligible [6].

Conclusion

PD has been attributed to several metabolic diseases, genetic affiliations, Neurological disease as its risk factors, either of these has just given clue to ascertain a possibility of the disease in the future, might not necessarily be true if close attention is paid to avoid the avoidable risk factors that are glaring, and the non-avoidable, life style modification should be employed to help prevent future PD, Since the main cause is yet to be established we recommend close monitoring of at risk people to reduce the eventuality of PD. Attention should be paid to these metabolic diseases that not only disrupt the system but also affects the medication used decreasing the chances of proper PD management. Neurologist should work hand in hand with endocrinologist and nutritionist to follow up on PD patients for proper management and prognosis.

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