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Smell Loss (Anosmia) and Cerebrovascular Disease in Comparison in a Cohort of Patients with Parkinson's Disease

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Abstract

Loss of smell (anosmia) is a frequently found symptom in Parkinson's disease. Moreover, numerous studies have highlighted a significant incidence of cerebrovascular disease in patients with Parkinson's disease. The smell disorder has been framed as an indicator of a sensory pathological process consistent with the hypothesis of the origin of the disease from the peripheral and visceral nervous system, according to Braak theory. In this study, we sought a correlation between vascular damage, a possible contributing factor for 'central' type neurodegeneration, and anosmia in a cohort of 118 patients with Parkinson's disease of the outpatients' clinic for Movement Disorders. In this investigation we calculated the absolute and relative percentages of the two considered parameters for the total population and the subpopulations respectively; thereafter we performed the statistical analysis for cerebrovascular disease and anosmia with the chi-square test, which showed no correlation. This finding corroborates the idea of different and independent mechanisms of pathogenic processes and compromises the symptom anosmia as a unique marker or predictor of the disease.

Keywords: Anosmia; Parkinson's disease; L-Dopa; Stroke; Cerebrovascular disease; Vascular parkinsonism; Pathogenesis

Introduction

There are many studies on the etiopathogenesis of Parkinson's disease (PD), but to date there are no univocal models that can lead to a single cause or pathogenic mechanism, and apart from the investigation of genetic or toxic variants, the cases most commonly encountered in clinical practice are universally accepted as probably due to multifactorial causes and in high degree linked to aging factors. In particular, the scientific debate is divided between the hypotheses of a "central descending" origin of neurodegeneration, in which the loss of dopaminergic receptor function originates from the encephalic network, and a "peripheral ascending" origin (Braak's hypothesis) in which the pathological alpha-synuclein and degenerative components originates at the gastrointestinal level and the process then extends to the Central Nervous System (CNS) [1,2]. The latter case makes an elegant compatibility with the neurovegetative disorders present in PD as well as in related neurodegenerative forms. In recent studies by this Author, parameters of general occurrence in groups of patients with PD such as cerebrovascular disease (CVD) and its significant, non-random, incidence have been statistically evaluated. In agreement with Braak's hypothesis, another parameter that is highlighted by researchers is the frequency of the loss of smell (anosmia) in patients affected by PD, which can even precede the clinical onset of the disease by many years. This symptom has also been taken into consideration as a biomarker or predictor of the disease. In the present study the Author investigated the statistical relation between CVD and smell loss or impairment in a population of patients taken in charge on the basis of data retrospectively analyzed from the database of the PD Center of Albano Laziale. The incidence of the symptom anosmia hyposmia was firstly evaluated in the total population of patients diagnosed with PD. External causes of hyposmia, such as infectious or head traumas' outcomes or other local pathologies, were previously considered and excluded. The incidence of hyposmia symptom was then studied in ratio to cerebrovascular damage in PD patients with imaging lesions of CVD. The incidence of hypoanosmic or not PD patient's

with\without CVD was then evaluated by means of percentages on total population and subpopulations; afterwards statistical tests analysis was performed.

Methods

A total population of 130 patients with a definite diagnosis of Parkinson's disease, carried out through clinical-instrumental investigations, including objective examination, score scale examinations (mainly Unified Parkinson's Disease Rating Scale, UPDRS, and Mini Mental State Evaluation, MMSE), brain magnetic resonance (RM imaging), Iodine Ioflupane-123I scintigraphy (daTscan), was initially available. Among these we counted 118, after excluding the cases in which some of the parameters necessary for the study were missing in the data stored in the database of the Center for Movement Disorders between 2014 and 2024. The cohort includes a large age range due to the heterogeneity of patients' age at the different time of taking in charge, and to the duration of taking in charge, generally rather long (between 3 and 12 years). The computer storage program used includes in the data screen several parameters, among which the presence absence of the symptom anosmia hyposmia, recorded, similarly to other parameters, as an 'absolute' value (yes\no) for each patient when certainly related to the disease and not to other causes (such as infectious or head traumas' outcomes or other pathologies). All the data could be extracted and processed 'off-line' with an excel system, able to select the subpopulations and the parameters chosen for the statistical analysis. As already mentioned, some of the cases in the subgroups were lacking of sure information, therefore they were not counted into the numbers for the analysis (Table1). We calculated the absolute percentage of patients reporting the symptom anosmia in the total population of PD patients and the absolute percentage of patients with CVD in the total population with PD, respectively. CVD was defined based on the finding of multifocal Fazekas type 2\3 damage, or as a result of stroke with the support of brain MRI and/or CT scan, with the same criteria as previous research. Then, the percentage of subjects with anosmia affected by CVD on the total subpopulation of anosmic subjects and that of anosmic subjects without CVD were calculated. Conversely, the percentage of anosmic patients on the total subpopulation of PD patients with CVD and that of anosmic subjects on total PD subpopulatin without CVD were calculated as well (Table 2). Afterwards we applied a statistical analysis by the Chi-Square Calculator contingency table considering subjects with CVD as the independent variables, to check eventually a correlation with the anosmic condition (Table 3).

Results

Table 1: *The absolute numbers of cross-referenced patients' subpopulations.*

CVD	ANOSMIA	n°
Yes	Yes	39
Yes	No	59
No	Yes	11
No	No	9
V	No	4
No	V	2
V	Yes	3
Yes	V	1
V	V	2

Description: CVD= cerebrovascular disease; V=not known; in the first column are listed numbers with respect the finding or not of vascular damage as in the text description; in the second column numbers with smell loss

Table 2: *The values of the calculated percentages.*

anosmic subjects on total PD population	50\118	=42.37%
subjects with CVD on total PD population	98\118	=83%
anosmic subjects with CVD on anosmic PD subjects' subpopulation	39\50	=78%
anosmic subjects without CVD on anosmic PD subjects' subpopulation	11\50	=22%
anosmic subjects on PD subpopulation with CVD	39\98	=39.8%
Anosmic subjects on total PD subpopulatin without CVD	11\20	=55%

Description: scheme of the relative percentages of the subpopulations of subjects with PD. PD: Parkinson's disease, CVD: cerebrovascular disease. See text for discussion

On (Table 1) there are the absolute numbers of cross-referenced patients' subpopulations, showing the missing values for a total of 12 subjects on 130. The values of the calculated percentages are shown on (Table 2). The results of the statistical analysis with the Chi Square Calculator are shown in (Table 3).

***Table 3**: The results of the statistical analysis with the Chi Square Calculator.*

Results			
	anosmia Yes	**anosmia No**	***Row Totals***
CVD Yes	39 (41.53) [0.15]	59 (56.47) [0.11]	98
CVD No	11 (8.47) [0.75]	9 (11.53) [0.55]	20
Column Totals	50	68	118 (Grand Total)
The chi-square statistic is 1.5725. The p-value is .20985. The result is not significant at $p < .05$.			

The chi-square statistic is 1.5725. The p-value is 0.20985. The result is not significant at $p < .05$ showing a lack of correlation between the incidence of CVD and that of anosmia.

Discussion

Despite the amount of studies on the etiopathogenesis of Parkinson's disease, to date there are no univocal interpretation or scientific models that allow us to identify a cause or a univocal mechanism, but apart from the genetic variants' description, the cases commonly encountered in clinical practice as idiopathic are universally accepted as probably of multifactorial origin. Various pathogenic models have been speculated to explain neurodegeneration, calling into question the histopathological findings of anomalous molecular structures (TAU proteins, alpha synuclein, neurofibrils, Lewy bodies, etc.) in nervous tissue of affected patients [2-6]. Recently Braak's theory has highlighted a possible primary role of the peripheral visceral component as the starting mechanism for the central neurodegenerative process, leading to the hypothesis of the "ascending track" in the development of Parkinson's disease. In the scenario of neurovegetative symptoms, the loss of smell has raised the attention of many researchers, as it can precede the onset of the extrapyramidal symptoms by many years, bringing them to consider it as a predictor of PD. Indeed, it has also been taken into consideration as a possible biomarker of the disease [7,8]. In more recent times, studies have been conducted on the possible role of cerebrovascular damage in PD [9-12]. In particular, a significant incidence of CVD has been observed in patients affected by the common, non-genetic form of PD, through statistical analysis on cohort' patients or descriptions of single clinical cases [11,12]. The 'central' oxidative mechanism due to vascular impairment is therefore listed as a possible contributing factor to pathogenesis of PD, through a direct or indirect mechanism of the dopamine receptor network damage. This configuration is commonly clearly distinguished from the so-called vascular Parkinsonism, in which a poor response to dopaminergic therapy suggests in clinical practice a probable structural disruption of the extrapyramidal system, although with clinical phenomena superimposable to idiopathic PD. However, this clear distinction has recently been questioned with articles by several authors who report a good response to dopaminergic therapy in patients classified as having vascular parkinsonism, in which the clinical features did not allow a redefinition as PD (for example in patients with abrupt onset of the syndrome after a stroke, but with good response to dopaminergic therapy) [11, 13-15]. The aim of this retrospective study was to investigate the statistical relationship between the two parameters CVD and anosmia by means of the data extracted from the patients' population in charge in the clinic for Parkinson's disease and Movement Disorders. This in order to speculate whether there is any link or if there are possible independent or concurrent pathogenic mechanisms for idiopathic PD genesis. Although an initial look draws attention to the relevance of the numbers (patients with CVD and anosmia 39, patients with CVD without the symptom 59, patients with the symptom without CVD 11), which highlight a consistent coexistence of the two parameters, albeit with a prevalence of CVD alone (59 patients), the cross-statistical study did not give a positive result to confirm any significantl linkage (see table3, p=.20985). Again in this study the numbers show an absolute prevalence of the CVD in the observed population (98 out of 118, equal to 83%), if compared with the incidence of the anosmia symptom (50 out of 118, equal to 42.4%), while anosmic patients affected also by CVD resulted 39 on total subpopulation with anosmia (50), i.e. 78%. In other words, especially in light of the statistical verification, in this study CVD and anosmia seem to be independent parameters and therefore, they can be said not correlated or linked, although a concurrence in PD pathogenesis cannot be excluded, consistently with the multifactorial explanation. Ultimately, this finding can be considered a further confirmation of the non-exclusiveness of Braak's 'ascending' theory, being able to orient oneself towards the 'central' origin of the disease in a predominant part of the cases and assuming that CVD is indeed a critical factor in PD pathogenesis. Finally, it is well known to clinicians that olfactory disorder is not a constant but has a relatively low incidence in "sporadic" PD, which undermines its use as an absolute biomarker.

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References

1. Braak H, Bohl JR, Müller CM, Rüb U, de Vos RA, Del Tredici K, et al. Stanley Fahn Lecture 2005: The staging procedure for the inclusion body pathology associated with sporadic Parkinson's disease reconsidered. Mov Disord. 2006; 21: 2042-2051.
2. Tofaris GK. Initiation and progression of α synuclein pathology in Parkinson's disease. Cell Mol Life Sci. 2022; 79.
3. Colosimo C, Hughes AJ, Kilford L, Lees AJ. Lewy body cortical involvement may not always predict dementia in Parkinson's disease. J Neurol Neurosurg Psychiatry. 2003; 74: 852-856.
4. Garcia-Reitböck P, Anichtchik O, Bellucci A, Iovino M, Ballini C, Fineberg E, et al. SNARE protein redistribution and synaptic failure in a transgenic mouse model of Parkinson's disease. Brain. 2010; 133: 2032-2044.
5. Tofaris GK, Reitböck PG, Humby T, Lambourne SL, O'Connell M, Ghetti B, et al. Pathological changes in dopaminergic nerve cells of the substantia nigra and olfactory bulb in mice transgenic for truncated human alpha-synuclein (1–120): implications for Lewy body disorders. J Neurosci. 2006; 26: 3942-3950.
6. Li J, Uversky VN, Fink AL. Effect of familial Parkinson's disease point mutations A30P and A53T on the structural properties, aggregation, and fbrillation of human alpha-synuclein. Biochemistry. 2001; 40: 11604-11613.
7. Haehner A, Boesveldt S, Berendse HW, Mackay-Sim A, Fleischmann J , Silburn PA, et al. Prevalence of smell loss in Parkinson's disease – A multicenter study. Parkinsonism related disorders. 2009; 15: 490-494.
8. Ponsen MM, Stoffers D, Booij J, Berthe LF, Eck-Smit V, Erik Ch, et al. Idiopathic hyposmia as a preclinical sign of Parkinson's disease. 2004; 56: 173-181.
9. Freeze B, Pandya S, Zeighami Y, Raj A. Regional transcriptional architecture of Parkinson's disease pathogenesis and network spread. Brain. 2019; 142: 3072-3085.
10. Jenner P, Olanow CW. The pathogenesis of cell death in Parkinson's disease. Neurology. 2006; 66.
11. Zarola F. Vascular Parkinsonism sensitive to Rotigotine therapy is found in aged patients: a clinical case description. Acta Biomed. 2018; 89: 99-100.
12. Zarola F. Incidence of brain vascular damage in a population with parkinson's disease: statistical comparison by age subassemblies with age homogeneous control groups. Cureus. 2020; 12.
13. Zarola F. Vascular Parkinsonism: A Clinical Study of Response to Dopaminergic Therapy and Patterns of Brain Vascular Lesions in a Group of Patients. Insights Neuro Oncology. 2022; 5.
14. Zarola F. Retrospective comparative study of Dopaminergic Therapy's efficacy's persistence between a group of patients with Parkinson's disease and a group with Vascular Parkinsonism. Int J Clin Epidemio. 2024; 3.
15. Zarola F. Retrospective Analysis of Diabetes Comorbidity in Populations with Movement Disorders Related to Parkinson's disease. J Aging Sci. 2021.