The risk of occupational and environmental exposure to develop Parkinson's Disease in the province of Rome, Italy.

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## Introduction

Typically late-onset form of idiopathic PD (onset after age 55 years) is the product of an interaction between environmental contributors and (epi)genetic risk factors carried by the host. The risk factors associated with PD can be divided into two general categories: personal health and habits, and external environment. External environmental factors may be easily measured in terms of place of residence and occupation. Indeed, these conditions serve as surrogate markers for toxicant exposures, in particular they are representative of the exposure to pesticides, organic solvents and heavy metals. Since these external factors are modifiable risk factors, their analysis is crucial for the identification of prevention strategies. The province of Rome is an urban area in the center of Italy, whose prevalence ratio of PD for the total population is $173.5 / 100000$ inhabitants, in line with the range of European prevalence. In this study we estimate the risk of environmental and occupational exposure to develop Parkinson's Disease (PD) in a population of inhabitants the province of Rome by a combined (epidemilogical-biochemical) approach.

## Subjects and Methods

Cohort: we enrolled 178 consecutive subjects ( 89 PD patients and 89 controls) afferent to Policlinico Tor Vergata, Rome.
Epidemilogical analysis: each subject underwent a questionnaire by which environmental and/or occupational exposure was investigated. Data collected included: demographics, familiar history of PD, occupations; occupational exposure to pesticides/toxicants/metals; environmental exposure (residence close to toxicants/pesticides sources and use for leisure of toxicants/pesticides/metals); personal habits (smoking/alcohol intake/dental fillings). The grade of association between PD and exposure was calculated by chi-square-test. A more detailed analysis of the risk due to different kinds of exposure was measured by means of binary-logistic-regression, taking demographics, familial history and personal habits as covariates.
Biochemical analysis: serum samples were collected from eligible and consenting subjects (63 PD, 41 controls) and dosage of iron, copper, manganese and magnesium was performed, through Inductively-Coupled-Plasma-Mass-Spectrometry (ICP-MS), as measurement of metal accumulation. The differences in metals serum concentration between the groups were calculated by the multivariate-analysis-of-covariance (MANCOVA) according to exposure and taking in consideration demographics, familial history and personal habits.

Results

| Parkinson's D. | Male | Female | Total |
| :---: | :---: | :---: | :---: |
| Not Exposed | 25 | 23 | 48 |
| Environemental | 8 | 2 | 10 |
| Occupational | 17 | 6 | 23 |
| Both Exposure | 8 | 0 | 8 |
| Exposed | 33 | 8 | 41 |
| Total |  |  | 89 |



| Healthy S. | Male | Female | Total |
| :---: | :---: | :---: | :---: |
| Not Exposed | 28 | 37 | 65 |
| Environemental | 3 | 5 | 8 |
| Occupational | 9 | 0 | 9 |
| Both Exposure | 7 | 0 | 7 |
| Exposed | 19 | 5 | 24 |
| Total |  |  | 89 |

Healthy Subjects


| Risk Factors | Odd Ratio | p value |
| :---: | :---: | :---: |
| Not Exposed (0) | 0.001 | ns |
| Environemental (1) | 0.000002 | ns |
| Occupational (2) | 0.009 | $\mathbf{0 . 0 5 3}$ |
| Both Exposure (3) | . | . |
| Age | 0.953 | ns |
| Age x 0 | 1.098 | ns |
| Age x 1 | 1.207 | $<0.05$ |
| Age x 2 | 1.088 | ns |
| Age x 3 | . | . |
| Male | 0.488 | $\mathbf{0 . 0 5 6}$ |
| Female | . | . |
| No Alcool | 3.21 | $<0.01$ |
| Alcool | . | . |

The proportion of exposed subjects resulted significantly higher in PD group. Particularly, the interaction between age and environmental exposure significantly increases the risk of PD. Conversely, the environmental or occupational exposures per se do not seem major risk factors of PD. Interestingly, no alcohol consumption was associated with the risk to develop PD.


## Discussion

Our findings do not support a role as major risk factors for occupational or environmental exposure per se to develop PD in the province of Rome. These data are in agreement with previous epidemiological investigations that, similarly, did not provide support for an increased chance on developing PD after direct occupational exposure to solvents or metals. However, here we highlight that the combination of multiple factors may lead to develop the disease. Indeed, in our study-cohort we found an higher prevalence of exposed subjects in the PD group and also that that the interaction of aging and environmental exposition increases the risk of PD. The measurement of blood concentration of metals did not show significant differences between the two groups. In our population, metal levels were not affected by the kind of exposure and did not represent a risk factor for PD. Finally we further confirmed the inverse association of PD risk with alcohol intake.

