

Project Summary

NOT CONFIDENTIAL		
Title of the project PARKINSONISM AND PARKINSON'S DISEASE		
Acronym of the project GEOPARKINSON		
Type of contract	RTD	
Contract number QLK4-CT-1999-01133	Duration 59 Months	EU contribution €1.104.453
Commencement date 1 February 2000		Period covered by the Final report 1 February 2000 - 31 January 2005
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Key words Parkinson's disease, chemical exposure, polymorphisms.		
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List of participants

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Objectives:

To investigate whether exposure to chemicals increases the risk of developing parkinsonism or Parkinson's Disease. To determine the role of a number of genes known to influence metabolism of chemicals in modifying these risks.

Results and Milestones:

The research was a multi-centre case-control study, prevalent cases of parkinsonism and controls being recruited in the five participating countries (Scotland, Italy, Sweden, Romania and Malta). Recruitment was completed in October 2004 and all available data from the five centres entered on an Access database. In all we recruited 959 prevalent cases of parkinsonism (of whom 767 had Parkinson's disease) and 1989 age and gender balanced controls.

Genetic analyses of the polymorphisms of interest in the 15 candidate genes studied are now complete. We genotyped *CYP2D6*, *PON1*, *GSTM1*, *GSTT1*, *GSTM3*, *GSTP1*, *NQO1*, *CYP1B1*, *MAO-A*, *MAO-B*, *SOD 2*, *EPHX*, *DAT1*, *DRD2*, and *NAT2*.

Analysis of both the environmental and occupational risk factors and the genetic factors is complete. Our main findings were as follows;

1. Analyses showed statistically significantly increased odds ratios for Parkinson's disease with an exposure-response relationship for pesticides.
2. A history of ever having been knocked unconscious was associated with an increased risk of the disease with an exposure response relationship.
3. We did not find a significant association between metal exposure (iron, copper, manganese) and Parkinson's disease.
4. Use of anti-depressants, sleeping tablets or medicines for anxiety was associated with an increased risk of Parkinson's disease.
5. Smoking reduced the risk of Parkinson's disease.
6. There was a modest but significant association between *MAO-A* polymorphism in males and Parkinson's disease risk.
7. Most gene-environment interaction analyses did not show significant effects.
8. There was a possible interaction between *GSTM1 null* genotype and solvent exposure that was stronger when limited to cases with Parkinson's disease.

Three papers have been published:

Simple SE, Dick F, Cherrie JW. Exposure assessment for a population-based case-control study combining a job-exposure matrix with interview data. *Scand J Work Environ Health* 2004;**30**:241-248.

Mozzoni P, De Palma G, Scotti E, Capelletti M, Mutti A. Characterization of *GSTM3* polymorphism by real-time polymerase chain reaction with LightCycler. *Anal Biochem* 2004;**330**:175-7.

Osborne A, Bell C, Grant F, Dick F, Seaton A, Haites N. A rapid method of screening for N-acetyltransferase (*NAT2*) phenotype by use of the WAVE DNA fragment analysis system. *Biochem Genet* ;**41**:405-11.

Benefits and Beneficiaries:

An exposure assessment methodology has been developed for large case-control studies. This methodology has been shown to have high intra- and inter-rater agreement for a range of agents and the concepts can be readily transferred to other centres with minimal training. It is anticipated that this exposure assessment work will benefit other researchers in occupational epidemiology. The analysis of occupational and environmental risk factors has shown a number of risk factors for Parkinson's disease with implications both for prevention of parkinsonism and for further research into the causes of Parkinson's Disease.

Future Actions (if applicable):

Two papers detailing the main results of the study are in preparation