

Familial, autosomal-dominant neurodegenerative parkinsonism with cognitive deterioration spanning five generations in a genetically isolated population of south-eastern Moravia, Czech Republic

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Background. An epidemiological study conducted over four years revealed increased prevalence of neurodegenerative parkinsonism in a small, isolated region (10 villages, with a combined population of 8664, with approx. 2927 over 50 years of age) of south-eastern Moravia, Czech Republic. The aim of this study was to obtain more detailed information on the medical history of the relatives of individuals with confirmed parkinsonism in an isolated rural population in south-eastern Moravia, Czech Republic.

Methods. We did detailed genealogical research on the families of all inhabitants with confirmed parkinsonism and compiled the pedigrees. These were modified on the basis of information from a consecutive door-to-door survey and local municipal and church registers.

Results. In the first stage, three large pedigrees with a familial occurrence of parkinsonism were found; two originated in one of the region's villages. In the second stage, these two pedigrees were combined into one large family tree.

Conclusions. The high prevalence of parkinsonism in the researched area is caused by the familial aggregation of parkinsonism that was found in two large family trees. This is probably the result of the genetic isolation of the regional population due to the very low migration rate of its inhabitants to neighboring regions in the last two centuries.

Key words: parkinsonism, cognitive deterioration, isolated population, neuroepidemiology, genealogy

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INTRODUCTION

The prevalence of parkinsonism in the population over 65 years of age is reported to be around 2.2% (ref.^{1,2}). Prevalence estimates of Parkinson's disease (PD) reported in various studies range from 0.6% to 1.8% (ref.^{1,3}). Some studies have indicated that the prevalence of both parkinsonism and Parkinson's disease in small, isolated communities is higher than in the general population^{4,5}. Detailed genealogical studies carried out in isolated communities revealed a higher frequency of familial relationships among individuals with parkinsonism than had been previously thought^{6,7}. For four years, we conducted an epidemiological and genealogical study of parkinsonism with cognitive deterioration in a remote, small, rural region (10 villages, with a combined population of 8664, 2927 over 50 years of age) in south-eastern Moravia, Czech Republic (Fig. 1). At the outset, a pilot study was conducted in one of the region's villages and extended to the remaining nine villages of the region^{8,9}. The survey included a total of 1167 probands. Parkinsonism was

confirmed in 83 of them⁹. We did a detailed genealogy on all inhabitants with confirmed parkinsonism and the family trees were compiled. Three large pedigrees with an autosomal-dominant inheritance pattern with reduced penetration of parkinsonism were identified; two of them originated in one of the region's villages (Javornik nad Veličkou, PCN CZ-69674, elevation 412 m, population 720) (ref.⁹). A consecutive door-to-door survey was initiated to acquire detailed information on the two families.

METHODS

To obtain more detailed information on the clinical history and information regarding the mutual family relationships, a door-to-door survey was conducted in the researched village. All of the steps in this phase of the study were approved by the local ethics committee of the University Hospital Olomouc; all participants directly related to the study signed informed consent forms. Genealogical data obtained previously from subjects with

confirmed parkinsonism were subsequently refined and the original pedigrees were further completed. The village was surveyed from house to house. The residents were singly questioned about the presence of parkinsonism in the family, and the existing pedigrees were presented to them. Residents were also asked in detail about the family history of neurological disease, particularly parkinsonism or dementia, and they were encouraged to add any information to the existing pedigrees. In the next phase, the municipal and parish registers were used for compiling information about births, marriages, and deaths.

RESULTS

Data on the presence of parkinsonism in relatives of the first, second, and third degree and genealogical information such as name, date, and birthplace of parents and grandparents were obtained in the course of the door-to-door survey. This information was extended to seven generations using local municipal and church registers, including those which were digitized and stored in the Moravian and Lower-Austrian land archives. Confirmed parkinsonism or historical data associated with parkinsonism in deceased relatives and ancestors were captured in four consecutive generations using the data from the village GP office register. Based on this information, two original pedigrees comprised one large family tree with an apparent autosomal-dominant inheritance pattern of parkinsonism spanning generations from 1840 to the present (Fig.2).

DISCUSSION

The tight link between the major population of the village and the familial aggregation of parkinsonism with apparent autosomal-dominant inheritance is probably the result of the historical background and specific characteristics of this region. According to historical sources, this area was inhabited by the ancestors of today's inhabitants from the end of the 18th century. The family names of



Fig. 1. Map of south-eastern Moravia with county borders. Dark gray area represents the region with its 10 villages, the village in which the large pedigree has been researched is highlighted.

HO: Hodonin county, UH: Uherske Hradiste county, KM: Kromeriz county, Hodonin: Hodonin county capital

the residents in the researched village featured in documentation from the turn of the 16th and 17th centuries are quite different from the family names listed from the 18th century to the present. The names of the families forming our large pedigree are not mentioned there even once. Paradoxically, very low migration of the local population to neighboring Moravian regions has been documented in the last two hundred years¹⁰. Marriages outside the villages were and still are rare. The village is almost entirely of the Lutheran denomination, unlike the majority of neighboring villages, which are almost entirely Roman Catholic. All these factors probably contributed to the creation of a population that is practically isolated, from a genetic point of view. Our pedigree can in its two last generations witness the fact that co-sanguine marriages may still be present. A detailed genetic and molecular-genetic analysis are currently underway in all probands

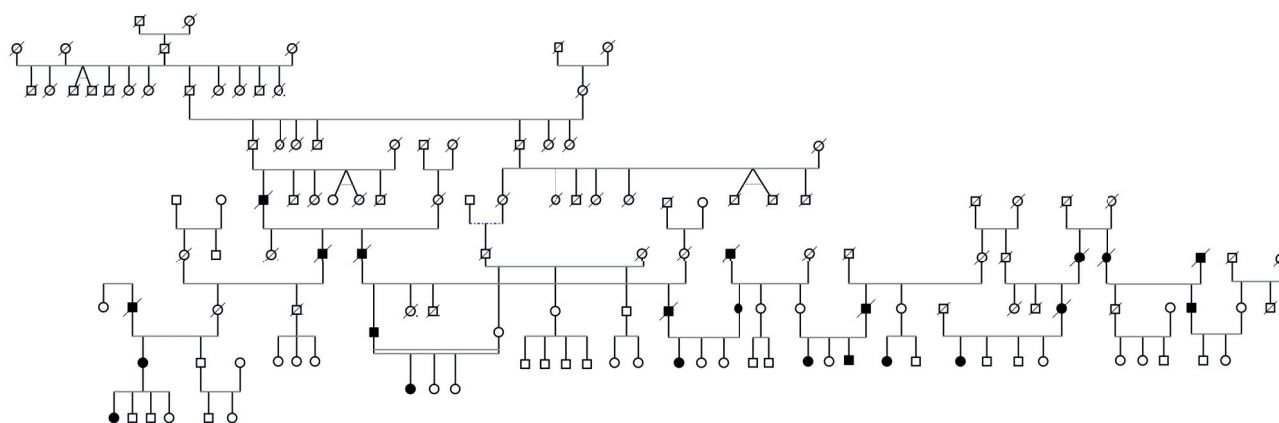


Fig. 2. Large family tree with apparent autosomal-dominant inheritance pattern of parkinsonism spanning generations from 1840 to the present.

in whom the parkinsonism symptoms were documented and in all of their blood relatives.

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Conflict of interest statement: None declared.

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