

Spatial Distribution of Parkinson's Disease Prevalence in Québec by Hydrographic Region

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ABSTRACT: The association between environmental exposures and Parkinson's disease continues to garner interest. In the late 1980s, Barbeau et al. reported in the *Canadian Journal of Neurological Sciences* a heterogeneous distribution of Parkinson's disease cases across the province of Québec by hydrographic region. Here we report the findings of a validation study based on data obtained from the Québec medication insurance program—information which was unavailable to the previous group. Similar to Barbeau et al., our analysis showed a heterogeneous distribution of cases across the province with higher prevalence in the same region of interest, in addition to other areas.

RÉSUMÉ: *Distribution géographique de la prévalence de la maladie de Parkinson selon les bassins hydrographiques du Québec.* L'association entre la maladie de Parkinson et l'exposition à divers milieux de vie continue à susciter un intérêt. À la fin des années 1980, dans le *Canadian Journal of Neurological Sciences*, Barbeau et ses collaborateurs signalaient, dans le cas du Québec, une distribution hétérogène des cas de maladie de Parkinson en fonction de ses régions hydrographiques. Dans cette étude de validation reposant sur des données obtenues auprès de la Régie de l'assurance maladie du Québec (RAMQ), nous voulons faire état ici de nos conclusions. À noter que ces données n'étaient alors pas accessibles aux précédents chercheurs. À l'instar de Barbeau et de ses collaborateurs, notre analyse a permis de montrer une distribution hétérogène de cas à l'échelle de la province, notamment une prévalence plus élevée de cas dans une région spécifique ayant suscité notre intérêt mais aussi ailleurs au Québec.

Keywords: Parkinson's disease, Epidemiology, Hydrographic basin

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Potential environmental factors involved in the development of Parkinson's disease remain under study.¹ In 1983, chemical-induced chronic Parkinsonism was described in four young Californians who injected MPTP (1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine), a synthetic by-product of a meperidine analog that transforms within astrocytes to MPP⁺, a molecule structurally similar to Paraquat.²⁻³ Proposed toxicological mechanisms associated with pesticide-induced neurodegeneration have been described,⁴ and associations between Parkinson's disease and agriculture-related risk factors such as rural-living, well-water consumption and pesticide use have garnered additional attention recently.⁵⁻⁶ In the late 80s, the *Canadian Journal of Neurological Sciences* published the findings of a descriptive study examining the spatial distribution of Parkinson's disease by hydrographic basin in rural areas of the Province of Québec.⁷ Specifically, the authors of this paper estimated the prevalence of Parkinson's disease in each basin using data compiled from doctor's visits' billing, sales of levodopa, death certificates and surveys of neurologists' practice, revealing a clustering in region 3 (please refer to Figure 1)—an area known for its apple orchards and commercial production of vegetables, the "Garden of Québec."⁷ Here we report findings of a validation of the Barbeau study using information obtained from the Québec medication insurance program, which covers all Quebecers by default (opt-out possible) after the age of 65 years.

In accordance with Barbeau's approach,⁷ we concentrated our analyses on non-urban areas. Population figures for each municipality were obtained from the Quebec institute of statistics (institute

de statistiques du Québec), and municipalities with a population over 50,000 were excluded. The remaining municipalities were grouped according to hydrographic basin using information provided by the Quebec Environmental ministry (Ministère du développement durable, environnement et lutte contre les changements climatiques). Numerator (users of levodopa and related molecules, aged 65 years and older) and denominator (enrolled individuals aged 65 years and older) information was obtained from the RAMQ (Régie de l'assurance maladies de Québec) based on these municipality groupings. RAMQ was able to locate the number of cases (for 2013, 2014 and 2015) and covered individuals aged 65 years and older (for 2014) in each municipality, presenting a sum over all the retained municipalities for each basin. These data are presented in Table 1. Note that user information is presented as an average over the 3 years provided, and that no data were available for regions 9 (James Bay and Hudson's Bay), 10 (Ungava Bay) and 11 (Labrador Sea).

A χ^2 analysis was used to evaluate the overall relationship between hydrographic basin and use of levodopa and analogs.

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Figure 1: Hydrographic regions of the province of Québec, Canada. Source: MDDELCC website: <http://www.mddelcc.gouv.qc.ca/eau/bassinversant/regionshydro/index.ht>

Following this, in order to identify regions that demarcate themselves from the others in terms of prevalence, individual χ^2 statistics were calculated to evaluate the association for each region individually versus all other regions combined. Data management was done with google spreadsheet, and all calculations were performed with the use of STATA version 14.

Total estimated Parkinson's disease prevalence across hydrographic regions was found to be 945.61 cases per 100,000 registered regime users over the age of 65 years (Table 1). The χ^2 statistic for the overall association between levodopa use and hydrographic region was statistically significant ($p < 0.0000$). Analyses for individual regions versus all regions combined showed statistically significant departures for (expressed in cases per 100,000 users, $p < 0.05$) region 3 (993.56), region 5 (820.10), region 6 (1121.61), region 8 (1087.84) and region 13 (443.92).

This study illustrates an uneven distribution of prevalent Parkinson's disease cases across the hydrographic regions of the

province of Québec, although we cannot correct for differences in age distribution between regions. It is unlikely that this pattern is due to a differential distribution of neurologists across the province. Recent medical workforce data for the province of Québec show that out of 256 adult neurologist positions available only 18 were vacant at the end of 2017, with six of these vacancies in Montérégie, an area that roughly corresponds to hydrographic region no. 3.⁸ As with the study by Barbeau et al, we found an excess of levodopa users in region 3 (Saint Laurent Sud-Ouest) in addition to some other regions. The estimated overall prevalence of Parkinson's disease in this study sits within published estimates based on the Canadian Community Health Survey.⁹ Specifically, 2010-2011 data show estimates (number of cases per 100,000 people) of 410, 1030 and 1420 for the 60-69, 70-79 and 80+ age groups, respectively.⁹ This suggests that levodopa remains a good proxy for the presence of Parkinson's disease in this age set, in line with current pharmacologic practice to treat individuals over the age of 65 years with levodopa instead of dopamine agonists.¹⁰

Table 1: Prevalence of levodopa use among registered regime users (≥ 65) by hydrographic region

| Hydrographic region | No. levodopa users (≥ 65)* | No. levodopa non-users (≥ 65)* | No. registered regimes users (≥ 65) in 2014 | Prevalence (per 100,000 registered ≥ 65 regime users) |
|-----------------------------------|-----------------------------------|---------------------------------------|--|--|
| 01 (Bale des Chaleurs et Percé) | 197.67 | 19,698 | 19,896 | 993.50 |
| 02 (Saint-Laurent sud-est) | 882.67 | 92,867 | 93,750 | 941.51 |
| 03 (Saint-Laurent sud-ouest) | 1491.67 | 148,642 | 150,134 | 993.56*** |
| 04 (Outaouais et Montréal) | 1222.33 | 126,273 | 127,495 | 958.73 |
| 05 (Saint-Laurent nord-ouest) | 784.33 | 94,858 | 95,642 | 820.10*** |
| 06 (Saguenay et lac Saint-Jean) | 247 | 21,775 | 22,022 | 1121.61*** |
| 07 (Saint-Laurent nord-est) | 94.33 | 12,796 | 12,980 | 731.83*** |
| 08 (Baie des Hannah et de Rupert) | 214 | 19,458 | 19,672 | 1087.84*** |
| 12 (îles du fleuve Saint-Laurent) | 22 | 2377 | 2399 | 917.05 |
| 13 (îles du golfe Saint-Laurent) | 11.33 | 2542 | 2553 | 443.92*** |
| Total** | 5167.33 | 541,286 | 546,453 | 945.61 |

*Calculated as the average number of registered levodopa users (first column) and non-users (second column) aged ≥ 65 for the years 2013, 2014 and 2015.

**Total for all 13 hydrographic regions excluding the northern areas 9 (Baies James et d'Hudson), 10 (Baie d'Ungava) (where no cases were reported) and 11 (Labrador sea-uninhabited), χ^2 levodopa use (≥ 65) versus region $p < 0.0000$.

*** χ^2 region versus all others, $p < 0.05$.

We did not find a correlation between the density of pesticide use in kilograms sold divided by hectares covered (kg/ha) in 1982 and the prevalence of levodopa use by hydrographic basin (data not shown).¹¹ A recent systematic review and meta-analysis examining the relationship between rural living, well-water consumption, farming and pesticide use revealed that associations were present in the literature but were inconsistent. The authors highlighted the need for a better characterization of the onset of Parkinson's disease, ideally through enrollment of individuals close to the time of diagnosis in order to ensure that exposure precedes disease onset.⁶ Indeed, the major weakness of this study is the use of prevalence data, which precludes any causal inference owing to the lack of temporal information. Further work must involve the use of incident cases, with age adjustment.

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DISCLOSURE

Neither of the authors has anything to disclose.

STATEMENT OF AUTHORSHIP

FG conceived the idea for the study, FG and SRS outlined the methods, SRS performed data cleaning and analysis and wrote the initial draft of the article. FG and SRS worked together on subsequent drafts of the paper.

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