Meta-analysis on the prevalence of selected non-motor symptoms among Parkinson’s patients and controls

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Abstract

Nonmotor symptoms (NMS) are prevalent among Parkinson's (PD) patients, and some may even precede PD motor onset. We conducted meta-analyses to estimate the prevalence of selected PD NMS before and after clinical diagnosis and among controls. We searched PubMed for English publications from 1965 through October 2012 for the following NMS: hyposmia, constipation, REM sleep behavior disorder (RBD), excessive daytime sleepiness (EDS), depression, and anxiety. Eligible studies were publications with original data on one or more of these NMS that prevalence either was presented or could be calculated for PD patients and for controls if available. For each symptom, we calculated the pooled prevalence and 95% confidence intervals using random effect models. The search generated a total of 2889 publications and data were abstracted from 304 papers, mostly reported symptoms after PD diagnosis with or without comparing to controls. After diagnosis, the prevalence of all symptoms was substantially higher in PD cases than controls: hyposmia being the most prevalent (61.1% among cases vs. 24.9% among controls), followed by constipation (45.0% vs. 22.8%), anxiety (34.2% vs. 18.7%), RBD (33.4% vs. 6.9%), and EDS (29.9% vs. 12.7%) and depression (29.1% vs. 12.6%). The limited data for NMS prior to PD diagnosis also showed much higher prevalence among future PD patients than PD-free individuals. We are currently evaluating factors (e.g. age, sex, disease duration) in relation to prevalence estimates across studies.

Introduction

- Nonmotor symptoms (NMS) are common among Parkinson’s disease patients, and some may precede PD diagnosis
- May help understand disease natural history and etiology
- Fundamentals of these symptoms are however not well understood, for example, their prevalence among PD patients before and after diagnosis and among individuals free of PD

Objective

- To estimate the prevalence of selected nonmotor symptoms before and after diagnosis among PD patients and among individuals free of PD, focusing on symptoms that may develop prior to PD diagnosis

Methods

- PubMed search for papers through Oct 2012 on hyposmia, constipation, RBD, EDS, depression, and anxiety
- Article Eligibility:
  - Original contributions in English that prevalence was either presented or could be calculated
  - Detailed inclusions and exclusions in Fig 1
- We extracted data from a total of 304 eligible studies

Statistical Analyses

- Meta-analysis of the prevalence weighted by sample sizes of individual studies
  - Separately for after and before PD diagnosis, and among corresponding controls
  - Overall prevalence and 95% confidence intervals
  - Additional analyses are in progress to examine factors that contribute to study heterogeneity and symptom prevalence

Results

Figure 1. Literature search and data extraction

Table How were symptoms measured in studies

Work-In-Progress

- Examinations of biases
- Correlations of symptom prevalence with age, sex, and disease duration
- Meta-regression analyses to identify key factors that may affect prevalence estimates of individual studies
- Sensitivity analyses to exclude studies, for example, that used only one question to screen for symptoms

Conclusions

- Our meta-analysis provided summary prevalence of selected nonmotor symptoms among PD cases and controls
- The prevalence was higher among PD cases than controls after disease diagnosis
- Data are limited for symptoms prior to PD diagnosis, the limited data support higher prevalence among cases
- Future studies should examine nonmotor symptoms prior to disease diagnosis and to understand how they can help understand the natural history and etiology of PD

Acknowledgements

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Figure 2. Prevalence of selected NMS among PD cases before diagnosis and among individuals free of PD

Table: How were symptoms measured in studies

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Test</th>
<th>Mostly used definitions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyposmia</td>
<td>Olor identification/discrimination tests, e.g. Brief Smell Identification Test</td>
<td>Standardized/normalized cutoffs</td>
</tr>
<tr>
<td>Depression</td>
<td>Multiple question inventory, e.g. Geriatric Depression Scale</td>
<td>Published criteria</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Multiple question inventory, e.g. HAM-A</td>
<td>Major depression, Minor depression, dysthymia</td>
</tr>
<tr>
<td>Excessive daytime sleepiness</td>
<td>Multiple question inventory, e.g. Epworth Sleepiness Scale</td>
<td>Any anxiety disorder</td>
</tr>
<tr>
<td>REM sleep behavior disorder</td>
<td>Published criteria</td>
<td></td>
</tr>
</tbody>
</table>

Figure 2. Prevalence of selected NMS among PD cases after diagnosis and among controls

Table: How were symptoms measured in studies

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Test</th>
<th>Mostly used definitions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correlation or slowed bowel movement frequency</td>
<td>Use of laxatives, Bowel movement frequency, Single question self-report symptom</td>
<td>Yes/no</td>
</tr>
</tbody>
</table>

Figure 1. Literature search and data extraction

2889 Total Search Results
- 517 Duplicates Excluded
- 2372 Unique References Screened

1748 References Excluded During Screening and Full Text Review
- 131 Not English
- 117 Not Human
- 1041 Off Topic
- 346 No Data
- 113 Selective Cases

304 References Abstracted by Symptom
- 47 Anxiety
- 50 Constipation
- 157 Depression
- 46 Hyposmia
- 64 Excessive Daytime Sleepiness (EDS)
- 63 REM Sleep Behavior Disorder (RBD)