Research article

Prevalence of REM sleep behavior disorder in Sun City, Arizona

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ABSTRACT

Objective: To determine prevalence of REM sleep behavior disorder (RBD) [prodromal Lewy body disease] in Sun City, Arizona.

Patients and methods: We attempted, by telephone and mail, a survey using the RBD single item question for probable RBD (pRBD) and the Innsbruck RBD Inventory. Individuals answering “yes” to 4/5 Inventory questions were considered to have high likelihood RBD (HL-RBD.)

Results: Response rate was 484/3000 individuals contacted (16%), mean age 78; 48 (9.9%) endorsed pRBD by RBD1Q; 16 (3.3%) had HL-pRBD. Prevalence of idiopathic cases (without neurodegenerative disease) was 8.8% pRBD and 2.8% HL-RBD.

Conclusion: Our estimated definite RBD prevalence of 1.7% (61.3% of HL-RBD) was similar to previous community-based studies.

1. Introduction

Idiopathic, also known as isolated, rapid-eye-movement (REM) sleep behavior disorder (iRBD) is a risk factor for neurodegenerative disease in older adults. A definite diagnosis of RBD requires the presence of recurrent vocalization or complex behaviors during REM stage sleep (not better explained by a sleep disorder, mental disorder, medication or substance abuse) with polysomnogram (PSG) confirmation (demonstrating REM sleep without atonia) [1]. RBD is considered idiopathic when secondary causes (including brainstem lesions, autoimmune disease, epilepsy, narcolepsy and other neurological disorders including manifest neurodegenerative disease) are excluded [2]. Over the last 15 years, evidence from multiple research groups world-wide has indicated that approximately 50% of those identified with iRBD will develop either parkinsonism or dementia within 10 years, with 80% or more converting after 20 years [3, 4, 5]. Most of those who die after having had iRBD will have a neuropathological diagnosis characterized by the accumulation of alpha-synuclein (synucleinopathy), primarily Parkinson disease (PD) or dementia with Lewy bodies (DLB) and less commonly multiple system atrophy (MSA). In order to plan clinical trials testing preventive therapies against these disorders, the International REM Sleep Behavior Disorder Study Group recently documented a phenoconversion rate of 6.3% per year among 1280 iRBD subjects [6]. However; only four North American academic centers from three metropolitan areas participated in this effort. Therefore, as recruitment from sleep clinics is limited by the relatively small numbers of iRBD subjects that come to medical attention, prevention trials in the United States may need to identify and recruit subjects from the general population. Screening questionnaires for identifying iRBD subjects have been developed, including a single-item questionnaire [7] and a two-step method, using an additional 5-item questionnaire that has greater specificity [8]. Recruiting iRBD directly from the elderly population might be expected to generate the needed subject numbers for prevention trials, but prevalence estimates for adults aged 50 and over have a wide range, from 0.74-13.7% [9, 10, 11, 12, 13], and come primarily from Asian and European populations. We therefore designed a survey to determine the prevalence of RBD in the North American retirement community of Sun City, Arizona.

2. Patients and Methods

The study was conducted from April 2017 through August 2018 with the oversight and approval of the Western Independent Review Board.
We obtained a commercial mailing list with the contact information for all residents of the Sun City, Arizona. We initially aimed to reach 1000 households by telephone. However; half of contacted telephone numbers were disconnected, and response rate was too low overall (about 6%), so the study was converted to a mail survey and a total of 3000 individuals were contacted by telephone or mail.

The survey began with a cover letter, explaining that the local Research Institute was conducting survey research on the effects of sleep on aging. It indicated that two copies of the survey were included and encouraged completion by all members of the household (with contact information to request additional copies.) Initial questions asked about diagnosis of PD, Alzheimer disease, or a related disorder (with write-in space to specify related disorder diagnosis). The RBD single-item questionnaire (RBD1Q), “have you ever been told, or suspected yourself, that you seem to act out your dreams (for example, punching; flailing your arms; making running movements; shouting out loud; knocking things over; jumping out of bed)” was used to screen for probable RBD (pRBD) and the Innsbruck RBD Inventory (RBD-I) was used to further screen for high-likelihood RBD (HL-RBD) [8,14]. According to recently published methodology, individuals answering “yes” to at least 4 of the 5 RBD-I questions were considered to have HL-RBD [15]. Standard demographic questions and questions about other sleep disorders, heart attack, stroke, or cancer history were included. Statistical analysis included standard descriptive statistics as well as comparison of the survey population to population from 2011-2015 US Census American Community Survey zip code 85351 census data. Chi-square goodness of fit test or exact test using Monte Carlo estimation was used to test whether the observed proportions differed from hypothesized proportions. Two sample t-test or Chi-square test or Fisher’s exact test was used to compare the demographics and medical history between patients with pRBD and without pRBD when applicable. In order to allow further confirmation of RBD diagnosis via PSG and recruitment into observational research on iRBD, individuals were asked to provide contact information if they were willing to be contacted about future research.

3. Results

Of 3000 individuals contacted, there were 484 respondents (31 reached by telephone and 453 by mail) with an overall response rate of 16%. They were 42.3% male, 57.7% female, and 96.6% Caucasian, 1.5% Hispanic or Latino. Additionally, 93% owned their homes, 48.5% were married, 30% widowed, 20.3% divorced or separated, 24% had 12-year education or equivalent, 73% at least some college or greater education and 36.4% had annual income of at least $50,000. As compared with overall Sun City US Census figures, respondents were significantly older (median age 78 compared to 73, p < 0.001), more likely to be non-Hispanic or Latino (98.5% compared to 96.3%, p = 0.02), more likely to own their homes (93.0% compared to 82.6%, p < 0.0001), less likely to be married (48.5% compared to 54.4%, p < 0.0001), more likely to have had at least some college education (73% compared to 56.7%, p < 0.0001) and more likely to have annual income of at least $50,000 (36.4% compared to 28.8%, p = 0.0075). Respondent demographics and comparison with census data are shown in Table 1.

A total of 20 (4.1%) endorsed diagnosis of neurodegenerative disease including 10 (2.1%) PD, 8 (1.7%) dementia, 7 (1.4%) other; 41 (8.6%) history of stroke, 184 (38.6%) cancer, 95 (20%) diabetes, 6 (1.2%) current sleep walking, 17 (3.5%) recent night terrors, 68 (14%) sleep apnea. A total of 5 (0.9%) had pRBD as indicated by positive response to the RBD1Q and 16 (3.3%) HL-RBD as indicated by “yes” response to 4 out of 5 responses to the RBD-I [15]. After excluding cases with diagnosis of manifest neurodegenerative disease, the overall prevalence of iRBD in our survey population with a mean age 78 was 8.8% probable iRBD by RBD1Q and 2.8% HL-iRBD. By gender, pRBD prevalence was 26/201 (12.9%) of men and 22/274 (8.0%) of women and HL-RBD prevalence 8 (4.0%) of men and 8 (2.9%) of women. Demographics and medical history of those with and without pRBD are shown in Table 2.

Of those with a positive response to the RBD1Q, 24 (50%) agreed to consent for additional contact. Of these, 1 respondent did not provide adequate contact information to reach them and 1 survey was filled out twice by one subject. 9 declined to come in for additional screening and 10 were lost to follow up (no response to phone messages/letters sent to the home.) One was screened, referred for PSG and found to have definite iRBD. Only 7 (4.3%) of HL-RBD agreed to future contact.

### Table 1. Demographics compared with census data for Sun City, Arizona.

| Age Group | Survey Population (N = 484) | Sun City Population (%) | p value |
|-----------|-----------------------------|-------------------------|---------|
| 0–24 years | 0 (0%)                      | 0.7                     | <0.0001 |
| 25–44 years | 0 (0%)                     | 2.2                     |         |
| 45–54 years | 1 (0.2%)                    | 5.2                     |         |
| 55–59 years | 8 (1.7%)                    | 6.5                     |         |
| 60–64 years | 21 (4.4%)                   | 11.4                    |         |
| 65–74 years | 122 (25.4%)                 | 31                      |         |
| 75–84 years | 213 (44.4%)                 | 30.3                    |         |
| 85 years and over | 115 (24.0%) | 12.7                   |         |

| Gender | Sun City Population (%) | p value |
|--------|-------------------------|---------|
| Male   | 201 (42.3%)             | 41      |         |
| Female | 274 (57.7%)             | 59      | 0.5599  |

| Race   | Sun City Population (%) | p value |
|--------|-------------------------|---------|
| Missing | 9                       |         |         |
| Black  | 5 (1.1%)                | 1.3     |         |
| White  | 456 (96.6%)             | 96.7    |         |
| Asian  | 4 (0.8%)                | 0.4     |         |
| Native Hawaiian or Pacific Islander | 0 (0%) | 0.2 |         |
| Other  | 6 (1.3%)                | 0.8     |         |
| Two or more races | 1 (0.2%) | 0.7 |         |

| Ethnicity | Sun City Population (%) | p value |
|-----------|-------------------------|---------|
| Missing | 80                      |         | 0.0205  |
| Hispanic or Latino | 6 (1.5%) | 3.7 |         |
| Not Hispanic or Latino | 398 (98.5%) | 96.3 |         |

| Housing Tenure | Sun City Population (%) | p value |
|----------------|-------------------------|---------|
| Missing | 29                      |         | <0.0001 |
| Rent  | 32 (7.0%)               | 17.4    |         |
| Own   | 423 (93.0%)             | 82.6    |         |

| Current marital status | Sun City Population (%) | p value |
|------------------------|-------------------------|---------|
| Missing | 0.0001                 |         |         |
| Married | 230 (48.5%)             | 54.4    |         |
| Widowed | 142 (30.0%)             | 21.8    |         |
| Divorced | 80 (16.9%)             | 15.7    |         |
| Separated | 2 (0.4%)               | 1.6     |         |
| Never married | 20 (4.2%) | 6.6 |         |

| Highest education level | Sun City Population (%) | p value |
|-------------------------|-------------------------|---------|
| Missing | <0.0001                 |         |         |
| Less than high school | 10 (2.1%)               | 9.7     |         |
| High school graduate or GED | 117 (24.9%) | 33.7 |         |
| Some college or an associate degree | 173 (36.8%) | 35.2 |         |
| Bachelor's degree | 103 (21.9%)             | 13.2    |         |
| Graduate degree | 67 (14.3%)              | 8.3     |         |

| Annual Household Income | Sun City Population (%) | p value |
|-------------------------|-------------------------|---------|
| Missing | 0.0075                 |         |         |
| $24,999 or less | 108 (27.1%)             | 32.1    |         |
| $25,000 - $49,999 | 146 (36.6%)             | 39.1    |         |
| $50,000 - $99,999 | 116 (29.1%)             | 23.5    |         |
| $100,000 or above | 29 (7.3%)               | 5.3     |         |
Table 2. Demographics and Medical History with and without pRBD.

|                      | No RBD (n = 432) | Yes- pRBD (n = 48) | Total (n = 484) | p value |
|----------------------|------------------|--------------------|-----------------|---------|
| **Age**              |                  |                    |                 |         |
| 45–54 years          | 1 (0.2%)         | 0 (0.0%)           | 1 (0.2%)        | 0.1078  |
| 55–59 years          | 6 (1.4%)         | 2 (4.2%)           | 8 (1.7%)        |         |
| 60–64 years          | 16 (3.7%)        | 5 (10.4%)          | 21 (4.3%)       |         |
| 65–74 years          | 107 (24.8%)      | 14 (29.2%)         | 121 (25.2%)     |         |
| 75–84 years          | 191 (44.2%)      | 19 (39.6%)         | 210 (44.0%)     |         |
| 85 years and over    | 107 (24.8%)      | 8 (16.7%)          | 115 (23.8%)     |         |
| **Gender**           |                  |                    |                 |         |
| Male                 | 172 (39.8%)      | 26 (54.2%)         | 201 (41.5%)     |         |
| Female               | 251 (58.1%)      | 22 (45.8%)         | 273 (56.6%)     |         |
| **Race**             |                  |                    |                 |         |
| Black                | 3 (0.7%)         | 2 (4.2%)           | 5 (1.0%)        |         |
| White                | 410 (94.9%)      | 43 (89.6%)         | 453 (94.2%)     |         |
| Asian                | 2 (0.5%)         | 2 (4.2%)           | 4 (0.8%)        |         |
| Other                | 5 (1.2%)         | 1 (2.1%)           | 7 (1.4%)        |         |
| **Ethnicity**        |                  |                    |                 |         |
| Hispanic or Latino   | 6 (1.7%)         | 0 (0.0%)           | 6 (1.5%)        |         |
| Not Hispanic or Latino | 353 (98.3%)  | 41 (100.0%)       | 394 (98.5%)     |         |
| **Housing Tenure**   |                  |                    |                 |         |
| Rent                 | 28 (6.5%)        | 3 (6.3%)           | 32 (6.6%)       |         |
| Own                  | 380 (88.0%)      | 40 (83.3%)         | 423 (87.4%)     |         |
| **Current marital status** | 1                 |                    |                 | 0.9402  |
| Married              | 204 (47.2%)      | 25 (51.0%)         | 229 (47.5%)     |         |
| Widowed              | 128 (29.6%)      | 13 (27.1%)         | 141 (29.3%)     |         |
| Divorced             | 71 (16.4%)       | 8 (16.7%)          | 79 (16.5%)      |         |
| Separated            | 2 (0.5%)         | 0 (0.0%)           | 2 (0.4%)        |         |
| Never married        | 18 (4.2%)        | 1 (2.1%)           | 20 (4.1%)       |         |
| **Highest education level** | 0.247         |                    |                 |         |
| Less than high school | 9 (2.1%)        | 1 (2.1%)           | 10 (2.1%)       |         |
| High school graduate or GED | 106 (24.5%)  | 8 (16.7%)          | 114 (23.2%)     |         |
| Some college or an associate degree | 158 (36.6%)  | 14 (29.2%)         | 177 (35.7%)     |         |
| Bachelor's degree    | 88 (20.4%)       | 15 (31.3%)         | 103 (21.3%)     |         |
| Graduate degree      | 58 (13.4%)       | 9 (18.8%)          | 67 (13.8%)      |         |
| **Annual Household Income** | 0.5005       |                    |                 |         |
| $24,999 or less      | 95 (22.0%)       | 13 (27.1%)         | 108 (22.3%)     |         |
| $25,000 - $49,999    | 133 (30.8%)      | 10 (20.8%)         | 143 (29.3%)     |         |
| $50,000 - $99,999    | 103 (23.8%)      | 17 (34.7%)         | 120 (24.8%)     |         |
| $100,000 or above    | 26 (6.0%)        | 3 (6.3%)           | 29 (6.0%)       |         |
| **Any neurodegenerative disease** | 0.0018       |                    |                 |         |
| Parkinson's disease  | 6 (1.4%)         | 4 (8.3%)           | 10 (2.1%)       |         |
| Dementia History     | 5 (1.2%)         | 3 (6.3%)           | 8 (1.7%)        | 0.0367  |
| Other Neurodegenerative disease | 4 (0.9%)    | 3 (6.3%)           | 7 (1.4%)        | 0.0247  |
| History of heart attack | 59 (13.7%)   | 8 (16.7%)          | 67 (13.5%)      | 0.869   |
| History of stroke    | 37 (8.6%)        | 3 (6.3%)           | 40 (8.3%)       | 0.516   |
| History of cancer    | 164 (38.0%)      | 19 (39.6%)         | 183 (37.5%)     | 0.5204  |
| Diabetes             | 79 (18.3%)       | 15 (31.3%)         | 94 (19.6%)      | 0.1182  |
| HL-RBD               | 3 (0.7%)         | 13 (27.1%)         | 16 (3.3%)       | <0.0001 |

4 patients who didn’t answer act out of dream question were also included here.

4. Discussion

We found that 8.8% of our survey population had probable iRBD based upon a positive response to the RBD1Q. The validity of a related instrument, the RBD screening questionnaire (RBDSQ) has been questioned in at least three separate studies. It showed much lower sensitivity and specificity when administered without support of a more detailed sleep history, showed insufficient sensitivity and specificity in de novo PD, and showed poor consistency when administered to the same subjects 2 years apart [16, 17, 18]. While the RBD1Q has shown sensitivity of 93.8% and specificity of 87.2% in academic sleep center populations, its utility in an unselected general population is unclear and there were serious concerns (given the limitations of the RBDSQ) of any single instrument alone to estimate prevalence of RBD in the general population. Our survey design was therefore guided by a recent population-based screening study which (in order to optimize positive predictive value in identifying individuals with prodromal neurodegenerative disease) utilized a strict interpretation of the Inselsbruck RBD In- ventory (which differs from the interpretation proposed in the original validation study by requiring positive responses to at least 4/5 responses) and found that 57 (51%) of 111 individuals with pRBD also had HL-RBD after additional screening with the RBD-I [15]. After in-person screening for other sleep conditions or secondary causes including dementia, 31 underwent PSG and 19 (61.3%) were confirmed to have iRBD. Among these lines, the prevalence of definite iRBD in Sun City, Arizona is estimated to be at least 2/3 of HL-RBD cases: 1.7% overall, 1.6% of men and 1.9% of women. This rate is similar to that reported in recent community based studies using PSG confirmation in Caucasian (mean age 59 +/- 11.1 years, overall RBD prevalence 1.03% of 1977 participants) [15] and Korean populations (mean age of 68.4 +/- 6.2 years, iRBD prevalence 1.34% of 12,784 overall; 2% of men and 1.3% of women) [19]. While individuals enrolled in prospective iRBD studies were predominantly (80-100%) male [3, 4, 5, 10], pRBD prevalence was similar across genders in our study and all prior population prevalence studies that utilized screening instruments without PSG confirmation [9, 11, 13]. This was also true in one of two Caucasian population studies that utilized PSG confirmation [19]. Therefore; the prevalence of RBD in Caucasian women aged 50 and over may be higher than previously thought.

Our study was limited by a relatively low response rate of 16% overall, and respondents were significantly older, less likely to be Hispanic, wealthier and better educated than non-respondents. The overall prevalence rates reported can be viewed as generalizable to older North American retirement populations with similar demographics to our survey sample. With exception of one participant, we were not successful in bringing our survey respondents in for PSG confirmation. This suggests that, even in a retirement community with a presumably higher rate of age-related prodromal synucleinopathy, survey-based research may not be sufficient for the recruitment of iRBD subjects for clinical prevention trials. Newspaper ads utilized in the above noted screening study [15] appear to have been more successful.

An overall iRBD prevalence rate of 1-2% appears useful in guiding feasibility and recruitment strategies for purposes of observational and interventional trials in a population with prodromal synucleinopathy. Given the limitations recently demonstrated with a commonly used screening instrument, the RBDSQ, more specific prevalence estimates would benefit from a detailed sleep history and polysomnogram confirmation. Survey-based research does not appear to be an adequate strategy for recruitment of individuals with iRBD into clinical research studies.

Declarations

Author contribution statement

D. Shprecher: Conceived and designed the experiments; Wrote the paper.
T. Beach: Conceived and designed the experiments
A. Intorcia, M. Glass, J. Curry, J. Walker, B. Cutler, M. Callan, G. Serrano, L. Sue, K. Davis and A. Garcia: Performed the experiments; Contributed reagents, materials, analysis tools or data.
N. Zhang: Analyzed and interpreted the data.
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Competing interest statement

D. Shprecher received research support from the Arizona Alzheimer's Consortium, Abbvie, Acadia, Axovant, Biogen, Eli Lilly, Neurocrine, Michael J Fox Foundation, NIH, Nuvelution and Teva; consultant fees from Abbvie, Teva, Lundbeck, Merz and Neurocrine; speaker fees from Acadia, Lundbeck, Sunovion, Teva and US World Meds. N. Zhang receives research support from the Arizona Alzheimer's Consortium, Mayo Clinic Foundation, and NIH. T. Beach receives grant support from the Arizona Alzheimer's Consortium, Mayo Clinic, National Institutes of Health and MJFF, performs contracted research for Navidea Biopharmaceuticals, Avid Radiopharmaceuticals and Aprinoia Therapeutics, serves as a paid consultant with Genentech, GSK, Roche and Ventana and is an advisory board member for Vivid Genomics.

Additional information

No additional information is available for this paper.

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