Featured Article

Online study partner-reported cognitive decline in the Brain Health Registry

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Abstract

Introduction: Methods for efficiently identifying cognitive decline and Alzheimer’s disease (AD) are a critical unmet need. The goal of this work was to validate novel online study partner (SP)-reported outcomes to identify cognitive decline in older adults.

Methods: In older adults enrolled in the Brain Health Registry, we analyzed associations between SP-reported cognitive decline, measured by the Everyday Cognition Scale, and either (1) participant cognition, assessed by Cogstate Brief Battery or (2) participant-reported diagnosis of mild cognitive impairment or AD.

Results: We found strong associations between SP-reported Everyday Cognition Scale and both Cogstate scores and participant diagnosis. The associations were cognitive domain specific, dependant on participant diagnosis, and were stronger in spouse dyads and those who knew each other longer.

Discussion: Collecting SP-reported data online from a large cohort is feasible. Results support the construct validity of our approach, which has the potential to facilitate clinical AD and aging research.

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Keywords: Alzheimer’s disease; Mild cognitive impairment; Neuropsychological tests; Cognitive neuropsychology in dementia; Study partner-reported outcomes; Informant-reported outcomes; Cognitive decline; Activities of daily living; Online registry; Brain Health Registry

1. Introduction

Methods for efficiently identifying those at risk for and with Alzheimer’s disease (AD) are needed to better understand disease mechanisms, facilitate clinical trial recruitment, and improve cognitive screening in geriatric health care [1]. Older adults with preclinical and prodromal AD are often underdiagnosed and not treatment seeking, which underscores the need for screening strategies that can be deployed widely in a cost-efficient manner [2].

In older adults, decline in cognition and functional abilities are important indicators of incipient dementia. Functional and cognitive decline are associated with AD pathology [3–5] and are predictors of future disease progression [6]. Furthermore, preservation of everyday function is important to patients and their families, and decline is associated with high caregiver burden [7,8]. Cognitive and...
functional decline can be sensitively and reliably measured by asking a collateral source or study partner (SP). SP report is an integral component of many AD clinical studies, and can discriminate between, and predict progression from, cognitively normal status to mild cognitive impairment (MCI) [9–12].

SP report of decline is also reliably associated with magnitude of cognitive impairment determined from neuropsychological assessment [13,14]. The same relationship is not observed as consistently for self-reported cognitive decline, where factors such as depressed mood [15–17] and lack of awareness associated with dementia limits its usefulness [14,18,19]. SP report of impairment is associated moderately with abnormal levels of AD biomarkers, such as positron emission tomography amyloid burden and hippocampal volume [3,20–22]. Thus, SP ratings of functional and cognitive abilities potentially provide a sound basis for early identification of the disease. Furthermore, use of SP report provides the opportunity to identify decline in adults reluctant to seek care themselves, has low influence from cultural or educational backgrounds, and can be applied widely in the community without requiring any formal clinical setting [23,24].

A number of validated SP-reported instruments exist, including the Clinical Dementia Rating Scale [25], a semi-structured interview incorporating self-report and SP report, which has been adopted as the standard benchmark to detect dementia [25,26]. SP report cognitive and functional questionnaires administered in clinic or by phone, including the Everyday Cognition Scale (ECog) [27–29] and shorter screening instruments, have been developed and validated, with some studies also considering their utility in the context of remote assessment [12,13,30,31]. Thus, SP report has great potential for both identifying early dementia and dementia risk, and ultimately improving health care outcomes in older adults.

Despite the enormous growth of internet use among older adults [32], little research has been directed at developing methods for exploiting Web-based instruments for identification of dementia [2,33,34]. Recently, we developed an online SP-rated assessment of cognitive and functional abilities and applied this within the Brain Health Registry (BHR), a global, internet-based registry with over 57,000 participants that aims to facilitate AD and other brain disease research. The BHR Caregiver and Study Partner Portal (CASPP) is a Web-based tool that launched that allows an SP for each BHR participant to separately register and answer questions about the participant online, with data linkage between the SP and participant. In a large cohort of dyads comprising older adult participants in BHR and their SPs, we tested the hypotheses that (1) online SP-reported data collection from a large cohort is feasible, including in participants likely to have MCI and AD; (2) online SP report of participant cognitive decline is significantly associated with objective measures of participant cognition; and (3) online SP report is significantly associated with participant diagnosis.

2. Methods

2.1. Brain Health Registry

BHR is a public Web site and registry. Participants register, sign informed consent, and perform tasks online including questionnaires and neuropsychological tests [35]. Participants in this study came from two sources: (1) they were recruited to join BHR from the general public between April 2014 and February 2018; or (2) they were participants enrolled in the Imaging Dementia-Evidence for Amyloid Scanning study who were invited by email to join BHR between February 2017 and February 2018. All participants from both sources who provided data necessary to perform analyses were included. The CASPP [35–37] within the BHR Web site allows an SP of a BHR participant to separately register, consent, and complete questionnaires (see also Supplementary materials).

2.2. Everyday Cognition Scale

SPs complete the Everyday Cognition-Informant version (SP-ECog) within the CASPP, consisting of 39 items assessing the participant’s capability to perform everyday tasks in comparison to activity levels 10 years prior, including activities that map to cognitive abilities across six domains [27]. The BHR uses an adapted version of the ECog in an online survey form, where the text of all items is identical to the paper version. Alzheimer’s Disease Neuroimaging Initiative (ADNI) ECog-SP version data were collected according to the ADNI protocol and downloaded from the Laboratory of Neuro Imaging ADNI Web site (http://adni.loni.usc.edu/) in October 2017.

2.3. Self-reported diagnosis

Self-reported diagnosis of MCI and AD was obtained from the BHR medical history questionnaire question, “Please indicate whether you currently have or have had any of the following conditions in the past.”

2.4. Cogstate Brief Battery

This is a computerized cognitive assessment battery that has been validated under supervised [38,39] and unsupervised [40–43] conditions in a variety of patient populations. It consists of four cognitive tests using playing card stimuli: (1) detection (detection task to measure processing speed), a measure of psychomotor function and information processing speed that uses a simple reaction time paradigm; (2) identification (identification task to measure attention), a measure of visual attention that uses a choice reaction time paradigm. The primary outcome for
detection task to measure processing speed and identification task to measure attention is reaction time in milliseconds for correct responses normalized using a logarithmic base 10 transformation, with a possible range of 2.00 to 6.00; (3) One Card Learning (OCL), a measure of visual learning and memory that uses a pattern separation paradigm; and (4) One-Back Test (ONB), a measure of working memory that uses an n-back paradigm. The primary outcome variable for OCL and ONB is proportion of correct responses normalized using an arcsine transformation, with a possible range of 0 to 1.57.

2.5. Diagnostic risk group classification

Participants were assigned to one of two likely diagnostic groups based on the following criteria: (1) higher likelihood of being cognitively unimpaired (Likely CU)—Cogstate ONB and OCL scores within one standard deviation (SD) of the age- and education-adjusted mean; no self-reported MCI. Those with self-reported MCI, AD, or dementia were excluded. (2) Higher likelihood of having MCI (Likely MCI)—Cogstate ONB or OCL score greater than 1.5 with standard deviations less than the adjusted mean, self-reported subjective memory concern (SMC), and age older than 60 years. SMC was evaluated by asking participants, “Are you concerned that you have a memory problem?”. Participants with self-reported AD or dementia were excluded from this analysis.

2.6. Statistics and data analysis

We tested the a priori hypotheses that (1) online SP-ECog scores are not significantly different from ADNI ECog scores for CU; (2) online SP-ECog scores are lower (indicating less functional decline) than in ADNI for MCI and AD, as we assumed that BHR participants considered to have MCI/AD are higher functioning compared with ADNI participants in these diagnostic groups; (3) SP-reported ECog is associated with online Cogstate scores, diagnosis of MCI and AD, and diagnostic risk group. Exploratory analyses included the contributions of participant diagnosis and dyad relationship to the previously mentioned associations. Ordinary least squares regression or logistic regression (binomial family) procedures were used. Data for each cognitive test were modeled separately and included SP-ECog, participant age, gender, online participant Geriatric Depression Scale score [44], and education as covariates. Education was parameterized as a three-level factor (less than, equal to, or more than 4 years of college). Geriatric Depression Scale scores omitted response to the question, “Do you feel you have more problems with memory than most?”, because this question is closely related to outcome measures of cognitive status. Model fits were inspected by an analysis of the residuals. We also considered an interaction between SP-ECog and two dyad relationship variables: (1) number of years the dyad has known each other, parameterized as a two-level factor of less than 50 years or greater than 50 years; and (2) whether the dyad comprised spouses.

Estimates, errors, P values, and R² values reported are from multivariable models. Welch’s unpaired t tests were used to determine differences between ADNI and BHR ECog means in each diagnostic group; t tests (difference in means) or χ² tests (differences in proportions) were used to determine differences between participants with and without an SP. Effect sizes (fx) were calculated as Cohen’s d for t tests, or the difference in means divided by the standardized SD (the square root of the average SD between groups) for Welch’s unpaired t tests. For multivariable linear regression models, fx was calculated as the variable estimate divided by the residual error in the model. Effect size, fx, was categorized as small (≤0.2), medium (0.21–0.79), or large (≥0.8) according to Ref. [45]. All analyses were done using R v3.1.1 (www.r-project.org).

3. Results

3.1. Participants and SPs used in this study

Between June 2016 and February 2018, 14,797 BHR participants were asked to identify an SP (see Supplementary material). Of those, 5778 (39%) participants indicated that they had no potential SP, and 8990 (61%) identified a potential SP who was then invited to join the CASPP. Of invited potential SPs, 4463 (45%) enrolled and signed online consent, 4411 (45%) have not yet enrolled, and 116 (1%) declined to participate. Of all enrolled SPs, 3584 have an associated BHR participant age 55 years and older; this cohort was used for the analyses described herein (Table 1). Compared with BHR participants older than 55 years who indicated that they did not have a potential SP, participants with an enrolled SP were slightly older and more educated, with a higher percentage of Caucasians and males. There were significantly more participants with MCI and AD in the group with an SP versus the group without (Table 1).

3.2. SP-reported cognitive decline using the online ECog

We compared SP-ECog scores between the online BHR sample and ECog scores collected in clinic in ADNI. BHR ECog scores were significantly different from ADNI for all diagnostic groups (Table 2). However, for CU and MCI, the effect sizes were less than 0.2. For the AD group, BHR ECog scores were significantly lower, with an effect size of 1.10, indicating less SP report of decline than ADNI scores (Table 2).

3.3. Associations between SP-ECog and cognition

We measured associations between SP-ECog and participant Cogstate scores. In the entire cohort, SP-ECog was
Table 1

| Characteristics of BHR participants with and without study partners | | |
|---|---|---|---|---|---|---|---|---|
| | BHR participants with study partners | | BHR participants without study partners | | | | |
| Total N | 3584 | | 4108 | | | | |
| Demographics | | | | | | | |
| Age, mean ± SD | 66.6 ± 7.0 | | 65.7 ± 7.0 | | * | | |
| Female (%) | 2323 (64.8%) | | 3106 (76.9%) | | * | | |
| Years education (mean ± SD) | 16.7 ± 2.2 | | 16.1 ± 2.2 | | * | | |
| Caucasian (%) | 3283 (91.6%) | | 3602 (87.7%) | | * | | |
| Subjective memory concern | 2041 (57.0%) | | 2273 (55.3%) | | | | |
| Self-report diagnosis | | | | | | | |
| Completed medical history | 3478 | | 3899* | | | | |
| Self-reported diagnosis of MCI | 453 (12.4%) | | 301 (7.7%) | | * | | |
| Self-reported diagnosis of AD | 187 (5.4%) | | 68 (1.7%) | | * | | |
| Dyad relationship | | | | | | | |
| Spouses | 2851 (79.5%) | | N/A | | | | |
| Years known (mean ± SD) | 36.7 ± 14.0 | | N/A | | | | |

Abbreviations: AD, Alzheimer’s disease; BHR, Brain Health Registry; MCI, mild cognitive impairment; SD, standard deviation.

NOTE. Diagnosed MCI and diagnosed AD are based on self-report of diagnosis in a BHR Medical History questionnaire.

Bold values indicate statistical significance of \( P < .001 \).

* \( P < .001 \) compared with participants with study partners.

4. Discussion

The major findings are as follows: (1) it is feasible to collect data online from older adults and their SPs, including older adults likely to have MCI and AD; (2) online SP-reported cognitive decline is comparable to that collected in clinic and is associated with objectively defined participant cognition; (3) the associations are stronger in participants with self-reported SMCs, MCI, and AD than in CU participants; (4) associations are domain specific, depending on the diagnostic group of participants, with the strongest associations found in processing speed and learning; (5) online SP-ECog was associated with self-reported diagnosis of MCI and increased MCI risk; in spouse dyads, SP-ECog was significantly associated with MCI because of lack of awareness about diagnosis [46].

We therefore assigned participants to two diagnostic risk groups based on age, Cogstate scores, and self-reported SMCs. Participants were categorized as more likely to be cognitively unimpaired (Likely CU), or at a higher risk for MCI (Likely MCI) (see Section 2). Of the 2693 participants who provided enough information for classification, 489 (18%) were classified as Likely MCI, 1575 (58%) were classified as Likely CU, and 629 (23%) were excluded because they did not fit the criteria for either classification. Agreement between self-report MCI and Likely MCI classification was 82%; the remaining 18% participants were assigned to the Likely MCI group but did not self-report MCI. SP-ECog was not significantly associated with diagnostic risk group in the whole cohort (Fig. 2B, Table 4). Advanced age (odds ratio [OR] = 1.17), more depressive symptoms (OR = 1.18), and lower education (OR = 3.66) were significantly associated with Likely MCI classification (Table 4). In spouse dyads, there was a significant association between higher (worse) SP-ECog scores and Likely MCI classification (Table 4).

Table 2

| Comparison of ECog scores in ADNI and BHR | | |
|---|---|---|---|---|---|---|---|
| | ADNI | | BHR | | | | |
| Diagnostic group | N | Mean | SD | N | Mean | SD | \( P \) value | Effect size |
| CU | 298 | 1.20 | 0.29 | 2354 | 1.25 | 0.34 | \*0.006 | 0.09 |
| MCI | 376 | 1.69 | 0.65 | 250 | 1.82 | 0.67 | \*0.02 | 0.16 |
| AD | 364 | 3.03 | 0.65 | 65 | 2.22 | 0.44 | \*<0.001 | 1.10 |

Abbreviations: AD, Alzheimer’s disease; ADNI, Alzheimer’s Disease Neuroimaging Initiative; BHR, Brain Health Registry; CU, cognitively unimpaired; ECog, Everyday Cognition Scale; MCI, mild cognitive impairment; SD, standard deviation.

NOTE. Bold values indicate statistical significance of \( P < .001 \).
cognitive aging fields by facilitating clinical trial recruitment and screening, as well as by improving screening of older adults for cognitive problems in various health care settings.

We found significant associations between online SP-ECog and participant online Cogstate scores. This is consistent with previous findings using in-clinic or telephone-based SP report, demonstrating associations between neuropsychological test scores and SP-reported cognitive decline in AD, MCI, and CU [13,14,47]. The supervised version of the Cogstate Brief Battery has been well validated [38,39], and there is accumulating evidence for the reliability, sensitivity to disease state, and validity of the unsupervised version [40–42,48,49], including in participants with MCI and AD [49], and in BHR [43]. Our cohort is large, which could result in statistically significant associations (P < .05) that are not clinically meaningful. Therefore, we mainly evaluated the strength of associations based on fx, and the amount of variance that could be explained by the model (R²) [45]. Online SP-ECog was moderately associated with participant processing speed (fx = 0.44, R² = 0.292) and learning (fx = 0.37, R² = 0.249) in the whole cohort, which included CU, MCI, and AD participants.

Because our cohort is primarily (84%) comprising CU older adults, many of whom have SPs who report no cognitive decline in the participant, we hypothesized that the contributions of impaired participants were driving these associations. In support of this hypothesis, we found no significant associations between SP-ECog and Cogstate scores in a subset of only CU participants. Conversely, we found strong associations in MCI and AD participants. In MCI, the strongest associations were between SP-ECog and participant online Cogstate scores. In support of this hypothesis, we found no significant associations between SP-ECog and Cogstate scores in a subset of only CU participants. Conversely, we found strong associations in MCI and AD participants.

Table 3

| Cogstate subtest | Estimate | Standard Error | P value | Residual error | Effect size | R² | Other significant variables | Significant interactions with SP-ECog |
|------------------|----------|----------------|---------|----------------|-------------|----|-----------------------------|-------------------------------------|
| Whole cohort, n = 2693 | | | | | | | | |
| DET (time) | 0.04 | 0.01 | .003 | 0.09 | 0.44 | 0.292 | Spouse, YK |
| IDN (time) | 0.01 | 0.01 | .562 | 0.07 | 0.08 | 0.255 | Spouse, YK |
| ONB (accuracy) | −0.04 | 0.04 | .235 | 0.25 | 0.17 | 0.245 | Spouse, YK |
| OCL (accuracy) | −0.05 | 0.02 | .010 | 0.14 | 0.37 | 0.249 | Edu |
| CU only, n = 2354 | | | | | | | | |
| DET (time) | 0.00 | 0.01 | .900 | 0.09 | −0.02 | 0.047 | Gender* |
| IDN (time) | 0.00 | 0.01 | .690 | 0.06 | 0.06 | 0.042 | |
| ONB (accuracy) | −0.04 | 0.03 | .207 | 0.20 | 0.20 | 0.034 | |
| OCL (accuracy) | −0.04 | 0.02 | .092 | 0.15 | 0.27 | 0.065 | Edu |
| MCI only, n = 250 | | | | | | | | |
| DET (time) | 0.23 | 0.03 | <.001 | 0.09 | 2.46 | 0.340 | Gender, Edu |
| IDN (time) | 0.05 | 0.03 | .01 | 0.08 | 0.70 | 0.254 | Gender, Edu |
| ONB (accuracy) | 0.12 | 0.09 | .186 | 0.28 | 0.44 | 0.340 | Gender, Edu |
| OCL (accuracy) | −0.02 | 0.05 | .658 | 0.14 | 0.15 | 0.259 | Gender, Edu |
| AD only, n = 65 | | | | | | | | |
| DET (time) | 0.11 | 0.02 | <.001 | 0.07 | 1.62 | 0.519 | Age, gender, Edu, GDS |
| IDN (time) | 0.13 | 0.01 | <.001 | 0.05 | 2.48 | 0.442 | Age, gender, Edu |
| ONB (accuracy) | −0.22 | 0.06 | <.001 | 0.22 | 1.00 | 0.194 | |
| OCL (accuracy) | −0.09 | 0.02 | <.001 | 0.08 | 1.14 | 0.397 | Gender, Edu |
| CU with subjective memory concern, n = 1582 | | | | | | | | |
| DET (time) | 0.01 | 0.02 | .538 | 0.08 | 0.14 | 0.098 | |
| IDN (time) | 0.01 | 0.01 | .218 | 0.05 | 0.28 | 0.139 | Gender* |
| ONB (accuracy) | −0.11 | 0.05 | .020 | 0.20 | 0.53 | 0.076 | |
| OCL (accuracy) | −0.08 | 0.03 | .005 | 0.13 | 0.64 | 0.224 | Edu |

Abbreviations: AD, Alzheimer’s disease; CU, cognitively unimpaired; DET, detection task to measure processing speed; Edu, education level; GDS, Geriatric Depression Scale; IDN, identification task to measure attention; MCI, mild cognitive impairment; OCL, One Card Learning; ONB, One-Back Test; SP-ECog, Study partner-reported Everyday Cognition scale score; Spouse, spouse partners; YK, number of years that the dyad has known each other.

NOTE. The "Other significant variables" column includes all variables with P < .05 and effect size >0.2 in the multivariable models. Significant dyad relationship variables includes those dyad relationship variables with a significant interaction with SP-ECog, P < .05, and effect size >0.20.

Bold values indicate statistical significance of P < .001.

*Females score worse than males.

1Males score worse than females.
agreement with previous in-clinic studies showing that SP-ECog and participant self-reported diagnosis of MCI, in line approach. phone SP report, supporting the construct validity of our on-agree with past studies using traditional, in-clinic or by-memory and executive function[14,50]. Thus these findings strating that SP-ECog, collected in clinic, is associated with ple domains. Our data also support previous studies demon-strating that impairments in MCI are likely to encompass multi-ple factors. Our AD group is relatively small compared with other diagnostic groups, and is likely to be more hetero-geneous than an AD cohort in an in-clinic study. Furthermore, the low burden of SP participation in BHR compared with traditional in-clinic studies may make potential SPs likely to agree to join BHR even if they do not know the associated participant very well and/or do not see them often. If this hypothesis is correct, we should find higher as-sociations between SP-ECog and diagnosis in spouse dyads, which is what we find. Higher (worse) SP-ECog scores are can discriminate between CU and MCI [9,11]. Contrasting findings using in-clinic SP report, online SP-ECog did not significantly predict self-report AD diagnosis, suggesting that online SP-ECog alone is not sufficient to categorize participants into diagnostic groups. This may be because of several factors. Our AD group is relatively small compared with other diagnostic groups, and is likely to be more heterogeneous than an AD cohort in an in-clinic study. Furthermore, the low burden of SP participation in BHR compared with traditional in-clinic studies may make potential SPs likely to agree to join BHR even if they do not know the associated participant very well and/or do not see them often. 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We have not confirmed the clinical diagnosis of BHR participants, which raises concerns about the accuracy of self-report, especially in participants with MCI and dementia [46] who may lack awareness of their diagnosis. Our results identifying Likely MCI participants using Cogstate scores and SMCs support underdiagnosis or a lack of diagnostic awareness of MCI; 18% of participants were classified as Likely MCI, but failed to endorse MCI diagnosis in their medical history questionnaire. On the other hand, we did not find evidence of over-report of MCI diagnosis. No participants who endorsed MCI failed to meet criteria for Likely MCI (Section 3.4.2). This issue can only be fully addressed in a population with BHR data linked to confirmed clinical diagnosis; such data will be available in the near future in cohorts coenrolled in both BHR and in-clinic studies [35].

This study allowed us to uncover important new information about online registry cohorts. SP-reported ECog scores in ADNI and BHR were significantly different across diagnostic groups, but the difference for CU and MCI is unlikely to be meaningful because of low effect size (CU, \( fx = 0.09 \); MCI, \( fx = 0.18 \)). Thus, the data are similar between BHR and ADNI despite important differences between the two cohorts, such as the method of ECog administration and participant selection. For the AD group, BHR had lower (better) ECog scores compared with ADNI. This is not surprising considering the assumed selection bias for less impaired participants in an online registry, in which participants must be functional enough to use a computer and complete tasks online. Another important feature of our registry cohort uncovered in this study is gender bias. The general BHR cohort comprised 73.9% females [35]. Compared with those with an SP, the group without an SP had a significantly higher proportion of females (Table 1). This raises the possibility that online SP-report data will exclude detection of cognitive decline in females, who are at greater risk for developing dementia [33,51]. Although analysis of the contributions of participant and SP gender on SP-report outcomes is outside the scope of the present work, it will be crucial to address such contributions in future studies.

Limitations of our study that affect generalizability include lack of racial/ethnic diversity, high education levels, and restriction to participants who can successfully complete tasks online. SPs of individuals unable or reluctant to volunteer online data are not represented. However, our results suggest that in the future, online SP-ECog could be used to help identify those with cognitive problems, even in the absence of cognitive data from the participant himself/herself. This model requires that an SP be able to initiate registry contact without the participant, a capability that we plan to enable in the near future. Finally, clinical diagnosis of MCI or AD may include SP report of cognitive impairment [52], which could confound the association between SP-ECog and diagnosis.

5. Conclusions

Online SP-ECog is significantly associated with participant cognition and self-reported diagnosis. The associations depend on diagnostic group and dyad relationship. If validated, BHR SP data have many potentially high-impact applications in the aging and AD fields, including using such data alone or in combination with other, remotely collected data for routine screening of older adults in health care and research settings. Because BHR can be accessed remotely by a large number of individuals, it could also be used for longitudinal monitoring in clinical trials, lessening the in-clinic burden of participation on SPs, which is a known barrier to participation [53,54]. These results are a first step to address the feasibility and validity of online SP data in BHR.

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RESEARCH IN CONTEXT

1. Systematic Review. The authors reviewed the literature using PubMed and by personal communication with authors. Past literature demonstrates associations between in-clinic study partner (SP)-reported data and both participant cognition and diagnosis. Remote collection and analysis of SP-reported data from a large Internet-based cohort is novel.

2. Interpretation: Our findings support the feasibility and validity of our approach. They are consistent with past findings using in-clinic data, and also provide novel information about online registry cohorts, including those with mild cognitive impairment and Alzheimer’s disease (AD). Validation of our approach has the potential to facilitate future AD and aging clinical research.

3. Future directions: Future studies will extend these findings by (A) further validating the online approach by linking online data and in-clinic data, including clinical diagnosis; (B) assessing the relative contributions of SP report and additional variables to predicting outcomes; (C) measuring associations between online SP-reported data and additional variables, including AD biomarkers.

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