FEATURED ARTICLE

Characteristics of the Ontario Neurodegenerative Disease Research Initiative cohort

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Abstract

Introduction: Understanding synergies between neurodegenerative and cerebrovascular pathologies that modify dementia presentation represents an important knowledge gap.

Methods: This multi-site, longitudinal, observational cohort study recruited participants across prevalent neurodegenerative diseases and cerebrovascular disease and assessed participants comprehensively across modalities. We describe univariate and multivariate baseline features of the cohort and summarize recruitment, data collection, and curation processes.

Results: We enrolled 520 participants across five neurodegenerative and cerebrovascular diseases. Median age was 69 years, median Montreal Cognitive Assessment score was 25, median independence in activities of daily living was 100% for basic and 93% for instrumental activities. Spousal study partners predominated; participants were often male, White, and more educated. Milder disease stages predominated, yet cohorts reflect clinical presentation.
1 | NARRATIVE

1.1 | Contextual background

Dementia is one of the largest public health crises and is expected to affect almost 75 million people worldwide by 2030.1 It takes a substantial toll on the quality of life of patients and their families, resulting in myriad burdens across social, economic, and health-care systems.

As a result, several large initiatives are focused on advancing our understanding of Alzheimer’s disease (AD) and other causes of dementia.2-8 These include the Alzheimer’s Disease Neuroimaging Initiative2 and Australian Imaging Biomarkers and Lifestyle Study of Aging,3 in which novel findings have furthered our understanding of cognition, brain structure, and the relation to AD development. Such large-scale research initiatives facilitate the acceleration of discovery through broader integration of data and wider collaborations of researchers. Further, many of these initiatives include data-sharing mandates that allow the global community of dementia researchers to explore hypotheses and validate findings by leveraging the constellation of initiatives.

However, most of these initiatives consider only a single disease spectrum (e.g., AD and mild cognitive impairment [MCI]) and there is growing awareness that when dementia occurs after age 65, it often results from multiple, co-existent brain pathologies and mechanisms that may overlap among contributing neurodegenerative (e.g., AD, frontotemporal lobar degeneration, Parkinson’s disease [PD]/Lewy body disorders) and cerebrovascular diseases.9-13 While it is possible to combine data from different studies through the identification of common data elements, this is not optimal as differences in measures and assessments, as well as methodological variations, limit cross-disease comparisons. Moreover, most initiatives collect only clinical, cognitive, neuroimaging, and genomic measures, but cognitive capacity appears to interact with other biological markers, including oculomotor control, retinal changes, gait abnormalities, and balance control.14-17 These markers are usually studied on a much smaller scale and are rarely considered together.

Altogether, research along an integrated and harmonized approach, across both multiple etiologies of dementia and multiple modalities of health assessment, is critical to understanding the causes and markers of neurodegenerative and cerebrovascular diseases, and their relation to cognition.

1.2 | Our approach to the problem

The Ontario Neurodegenerative Disease Research Initiative (ONDRI) is a longitudinal, multi-site, observational cohort study undertaken to enable the exploration of and to extend our knowledge of similarities and differences within and among neurodegenerative conditions, their relationship with cerebrovascular disease, and potential synergistic mechanisms yielding cognitive and motor decline.18 Participants were recruited into five disease groups: (1) AD/MCI, including both amnestic and non-amnestic presentations, and single- or multi-domain amnestic MCI; (2) amyotrophic lateral sclerosis (ALS); (3) frontotemporal dementia spectrum disorders (FTD); including behavioral variant FTD, corticobasal syndrome, progressive supranuclear palsy, and progressive primary aphasia, including agrammatic/nonfluent and semantic variants; (4) PD, with and without cognitive impairment/dementia; or (5) cerebrovascular disease (CVD), with or without cognitive impairment. All participants were assessed with a rigorous set of measurement tasks across seven diverse assessment platforms: clinical, neuropsychology, speech production, eye tracking, gait and balance, neuroimaging, and retinal imaging with spectral domain optical coherence tomography were assessed annually, and genomics was assessed at baseline. Up to three subsequent annual assessments were administered to enable analysis of trajectories of decline across all of the original data-capture platforms. Due to the aggressive nature of ALS, these participants were followed-up at 6-month intervals.

A comprehensive neuropsychological protocol19 was administered to all participants, and included the following tasks: Digit Span,20 Symbol-Digit Modalities Test,21 Judgement of Line Orientation,22 Incomplete Letters,23 Boston Naming Test–15 item,24 Verbal Fluency,25 Verb Naming,26 Semantic Probe,27 Rey Auditory Verbal Learning Test,28 Brief Visuospatial Memory Tests,29 Trail Making Test,30 Stroop,22 Vocabulary, and Matrix Reasoning.31

With the intent of accelerating discovery, ONDRI data were collected to be shared. Consent for sharing the data was provided by participants and their study partners. Controlled data release will be available to the scientific community through the Ontario Brain Institute32 on the Brain-CODE informatics platform33 accessible at www.braincode.ca.
1.3 | Goals of this article

Our primary goal is to describe the baseline clinical and data characteristics of this cohort, recruited to study neurodegenerative and cerebrovascular contributors to dementia. This information serves two audiences: dementia researchers seeking to leverage these in-depth data to identify markers of disease progression, severity, and potential targets for therapy; and researchers seeking to design similar in-depth studies of dementia. To foster discovery, data from this cohort will be shared with the scientific community through a controlled release on Brain-CODE (www.braincode.ca). To this end, we present a case study of ONDRI that can be used to make general recommendations and characteristics required for leveraging these data. This article will appropriately introduce knowledge users to intricacies of these data that must be understood for appropriate interpretation of subsequent baseline and longitudinal analyses. Furthermore, these results will also be useful in the context of comparison to other neurodegenerative cohorts. This cohort of participants—diagnosed with one of multiple neurodegenerative diseases or CVD with a depth of data collected for each—will allow us to advance discoveries of heterogeneous contributors to dementia.

1.4 | Findings, impact, and recommendations

1.4.1 | Recruited cohort

The distribution of age, sex, education, and ethnicity within each disease group are similar to other studies of specific neurodegenerative diseases.2–6,34 ONDRI aimed to enroll participants across a range of disease severities. Participants in earlier or milder stages of disease predominate, facilitating an increased likelihood of continued participation during follow-up visits. Nevertheless, disease groups continue to reflect disease heterogeneity and capture a wide spectrum of clinical presentations: (1) both typical and atypical presentations of AD, as well as single and multi-domain amnestic MCI are represented in the AD/MCI group; (2) both bulbar and limb onset cases are represented in the ALS group; (3) the FTD group includes five disease subtypes; and (4) the PD and CVD groups enrolled both cognitively intact and impaired participants. In addition, observed features that emerged during initial data exploration, including incidental strokes observed in some ALS, FTD, and PD participants (these were identified by a board-certified neuroradiologist and confirmed by board-certified neurologists as unlikely to interfere with disease-specific symptoms and the participants remained in the groups to which they were recruited) and clinical presentations at baseline that led to enrolling a participant in a different cohort from that for which they had been recruited, remain important. Minor variances in clinical characteristics were also induced through protocol amendments. Two analysis approaches to this ONDRI cohort that capitalize on this diversity are indicated. For analyses within disease groups, explicit acknowledgement of heterogeneity through investigation of subgroups could illuminate important differences within standard clinical diagnoses. On the other hand, a disease-agnostic approach that considers ONDRI participants a cohort of individuals with neurodegenerative and/or cerebrovascular disease may identify some features that align well with baseline diagnosis, and other patterns that are more suggestive of mixed disease.

1.4.2 | Impact of inclusion criteria

Inclusion criteria and enrollment strategies played an important role in defining the cohort. Consistent with other studies that enroll study
partners, a majority of ONDRI participants had a spousal study partner, and participants with spousal study partners are more often male, White, and more educated. Previous research has also shown that individuals who identify as non-White are more likely to support non-spousal family members or friends, as was reflected in our cohort. In addition, the geographic location of tertiary clinics from which different disease groups were recruited may have created some unexpected associations between demographics and disease. Specifically, a higher proportion of technical degrees among ALS participants may be attributed to a higher proportion of ALS participants having been recruited from Hamilton, a city known for its large share of the manufacturing industry. This may affect analyses by suggesting such characteristics attributable to geographic region are indicative of a particular disease group. Studies of cognition must consider the interplay between assessment measures and potentially influential demographic characteristics to draw appropriately nuanced conclusions regarding impairment, preservation, or decline.

The AD/MCI group experienced the most difficulty enrolling potential participants, for which two inclusion criteria—disease cohort requirements and the minimum threshold for general cognition—were together responsible for 25 of 45 excluded participants (56%). We have deduced two possible reasons for this phenomenon: (1) our choice to recruit from tertiary clinics, and (2) the use of magnetic resonance imaging (MRI) during screening.

ONDRI recruited individuals through clinicians at tertiary clinics, while individuals with straightforward cognitive impairment are now receiving effective early care through memory clinics at the primary-care level. While treatment for some neurodegenerative diseases such as PD remains at the tertiary level, fewer individuals with typical presentation early in the disease course are available for recruitment through that channel, and future studies of AD and/or MCI might consider recruitment from primary-care clinics.

Moreover, multiple individuals recruited to the AD/MCI group presented with other possible causes for cognitive decline on MRI, including vascular pathologies and markers consistent with traumatic brain injury. Such findings excluded 15 participants from the AD/MCI group and reinforced the importance of neuroimaging for both research studies and standard of practice for patients to receive more appropriate care.

1.4.3 | Considerations for data analysis

More than 80% of participants completed baseline visits within 8 weeks of providing consent to participate. This feat, which required stamina and dedication from participants and their study partners, not only indicates that the protocol was manageable for individuals in early-stage neurodegenerative disease or with CVD, but that the ability to assess participant characteristics across the wide array of assessments is strengthened as symptom progression confounds are minimized. Future research using ONDRI’s longitudinal data will be able to explore whether disease progression is related to attrition and at what stage a protocol such as this becomes too burdensome.

Some participants could not provide data for an entire assessment platform. However, most unobserved data were intermittent across a platform’s measures. Failing to consider the mechanisms leading to a data point not being observed would expose inference to potential bias. Informative missing data codes are therefore embedded in all ONDRI data sets to assist researchers in determining appropriate accommodation of missing values that support generalizable conclusions.

ONDRI data underwent extensive cleaning and quality control pipelines to identify and correct data entry or processing errors, and document anomalies, thereby increasing its integrity and consequently reducing the risk of incorrect conclusions. While such protocols can be time consuming, they allow for more nuanced analyses sensitive to idiosyncrasies in the cohort, in addition to more accurate results due to correction of erroneously recorded data.

1.4.4 | Conclusion and next steps

Our work provides an overview of the baseline characteristics of the recruited ONDRI cohort, and acts as a launching point for myriad studies on the multiple etiologies of dementia. Because of the breadth of neurodegenerative diseases included and the depth of harmonized phenotype characterization, the ONDRI data present a distinct opportunity to catalyze advances in dementia, improving diagnosis, prognosis, care, and outcomes for persons living with neurodegenerative or cerebrovascular diseases. This allows analyses both within disease groups and to take a disease-agnostic approach, which provides an opportunity to identify patterns indicative of mixed disease. A planned characterization of participants based on underlying proteinopathies (e.g., ante mortem plasma phosphorylated [p]-tau181, post mortem immunohistochemical neuropathological diagnosis), degree of neurodegeneration (e.g., plasma neurofilament light chain protein), and markers of neuroinflammation (e.g., plasma glial fibrillary acidic protein), will also expand the capacity to identify individuals with pure versus mixed contributions to cognitive decline. Nevertheless, given the demographic and clinical descriptions presented in this article, plus details regarding recruitment decisions, prevalence of missing data, and time windows for data collection, researchers are well equipped to harness the power of these data to explore the multifaceted features of dementia. Further, with demographic characteristics similar to other studies of neurodegenerative or cerebrovascular disease, these data may be used to validate previous discoveries, just as findings based on these data may be validated with other open datasets.

Finally, a majority of participants were in milder stages of disease severity at baseline. Annual follow-up visits have enabled studies of disease progression. Describing the features of individuals who continued is necessary to further characterize the cohort. Studying attrition will also provide guidance regarding feasibility of such a comprehensive study protocol designed around individuals with neurodegenerative or cerebrovascular disease.
**General Inclusion:**
- Self-rated speaking and understanding of English at 7 or more on two LEAP-Q questions
- Minimum grade 8 education
- Minimum MoCA total score of 18 (14 for atypical AD & FTD)
- Reliable study partner who:
  - Regularly interacts with participant
  - Well informed about cognition, communication, mood, and daily functioning of participant
- Geographic accessibility to ONDRI site
- Able to walk (with or without assistive aids)
  - Exception: individuals recruited to the ALS cohort with lower-limb involvement will be included in ONDRI but exempt from gait and balance assessments
- At least one natural lens (Toronto sites only)

**General Exclusion:**
- Serious underlying disease (other than diseases in ONDRI) that could interfere with the participant’s ability to engage in the study for 3 years
- Enrolled in a disease modifying therapeutic trial (recent enrollment is permitted for ALS or FTD)
- Poorly controlled diabetes or clinical diagnosis of serious eye disease (e.g., glaucoma, age-related wet macular degeneration; Toronto, London, and Ottawa sites only)

**Platform-specific Inclusion:**

**Neuropsychology:**
- Sufficient vision (minimum 20/70 acuity in one eye) and hearing (detect 25 dB HL signal bilaterally at multiple Hz, with or without personal amplification device) to complete battery
- Complete at least 75% of the battery

**Eye Tracking:**
- Able to track stimuli on a computer screen and complete calibration within 30 minutes
  - Exception: Individuals with disease pathology that directly affects oculomotor systems will be included in ONDRI but exempt from the platform
- Sit comfortably for a period of about 45 minutes
- Complete at least 50% of the assessments

**Genomics:**
- Good venous access for phlebotomy

**Neuroimaging:**
- No contra-indication to MRI
- Tolerable of the MRI environment

**FIGURE 1** General and platform-specific inclusion and exclusion criteria. Any changes from previous publications are underlined. AD, Alzheimer’s disease; ALS, amyotrophic lateral sclerosis; FTD, frontotemporal dementia spectrum disorder; LEAP-Q, Language Experience and Proficiency Questionnaire; MoCA, Montreal Cognitive Assessment; MRI, magnetic resonance imaging; ONDRI, Ontario Neurodegenerative Disease Research Initiative

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2 STUDY DESIGN AND RESULTS

2.1 Recruitment and enrolment

Between July 2014 and March 2017, 630 individuals were recruited consecutively and screened through tertiary clinics at 14 academic health science centers in six cities across Ontario, Canada. Figure 1 lists general and platform-specific inclusion and exclusion criteria; additional details are published elsewhere. Eligible participants had been previously diagnosed with one of the ONDRI-focused diseases and met consensus diagnostic criteria that were prevailing at the time of enrolment. In addition, MRI scans for all individuals recruited to the AD/MCI group were assessed before enrolment by a research neuroradiologist to confirm absence of significant pathology that
FIGURE 2 Consort diagram for individuals recruited to ONDRI. Solid-lined boxes below recruitment numbers represent counts of participants not enrolled. Dashed-lined box represents the count of participants who did not meet disease-specific inclusion criteria and were instead enrolled in a different cohort from that to which they were recruited. AD/MCI, Alzheimer’s disease and amnestic mild cognitive impairment; ALS, amyotrophic lateral sclerosis; CVD, cerebrovascular disease; FTD, frontotemporal dementia spectrum disorder; ONDRI, Ontario Neurodegenerative Disease Research Initiative; PD, Parkinson’s disease. *Participant originally recruited to FTD cohort. † Participants originally recruited to AD/MCI cohort.

<table>
<thead>
<tr>
<th>Recruited:</th>
<th>Total</th>
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<th>ALS</th>
<th>FTD</th>
<th>PD</th>
<th>CVD</th>
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<th>PD</th>
<th>CVD</th>
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<th>ALS</th>
<th>FTD</th>
<th>PD</th>
<th>CVD</th>
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<tr>
<td></td>
<td>94</td>
<td>45</td>
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<td>15</td>
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<th>Transferred from other cohort:</th>
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<th>AD/MCI</th>
<th>ALS</th>
<th>FTD</th>
<th>PD</th>
<th>CVD</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>9</td>
<td>1*</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>8†</td>
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<table>
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<tr>
<th>Enrolled:</th>
<th>Total</th>
<th>AD/MCI</th>
<th>ALS</th>
<th>FTD</th>
<th>PD</th>
<th>CVD</th>
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<tr>
<td></td>
<td>520</td>
<td>126</td>
<td>40</td>
<td>53</td>
<td>140</td>
<td>161</td>
</tr>
</tbody>
</table>

would suggest a non-AD–related cause of cognitive impairment. For the CVD group, consenting participants were eligible if they had experienced either a covert or overt ischemic stroke. This included people who presented initially with an acute ischemic stroke or who presented as a transient ischemic attack but for whom imaging confirmed either acute or prior covert infarction (cortical and/or subcortical). Individuals with large vessel occlusion infarction causing severe neurological deficits were excluded. Evidence of stroke had to be confirmed by clinical imaging (computed tomography or MRI), and the presenting symptoms had to occur at least 3 months prior to enrolment.

Ultimately, 520 participants (83%) were enrolled in ONDRI across five disease groups (Figure 2). The regional distribution of the 110 recruited participants who withdrew consent or subsequently did not meet inclusion criteria was not significantly different from the regional distribution of the 520 enrolled participants ($X^2 = 3.4, P = 0.63$). Table 1 summarizes the inclusion criteria not met by 94 recruited individuals (15%). At the time of the initial recruitment, nine individuals (1%) who did not meet inclusion criteria for the disease group to which they were recruited based on MRI results were transferred to another group. One of these participants was transferred from the FTD group (behavioral variant) to the AD/MCI group after identification of prominent hippocampal atrophy, with further historical clarification showing evidence of memory decline and behavioral dysregulation as the presenting symptoms. The other eight participants were excluded from the AD/MCI group (two with AD, six with MCI) and transferred to the CVD group based on the severe burden of vascular pathology, either in the form of small vessel disease (lacunar) or cortical stroke, and in conjunction with the clinical history. It was not possible at the time to say with certainty whether their cognitive symptoms were the result of the CVD or due to concomitant AD pathology. However, we are now obtaining amyloid beta and $\tau$-tau181 results on all ONDRI subjects, which will allow us to determine whether AD co-pathology existed.

Table 2 summarizes demographic variables for enrolled participants and their study partners. The study aimed to enroll individuals with clinical characteristics that would maximize the ability to observe disease progression and permit identification of similarities or differences between the various trajectories of aging with neurodegenerative disease, especially with respect to cognition. As a result, disease-specific inclusion criteria targeted individuals in the earlier stages of disease, and clinicians recruiting for the CVD or PD groups were encouraged to
2.2 Multivariate relationships

A multiple correspondence analysis (MCA) identified two components that explain 25.8% of the total variance (17.2% and 8.7% separately). As illustrated in Figure 3A, Component 1 indicates an association between participants not being married, having non-spousal study partners (i.e., friends, adult children, and other relatives), and not living with their study partner. Component 2 shows an association between participants being male, having female study partners, being younger, having younger study partners, higher MoCA, and higher education. Further, Black, South Asian, and other ethnicities are associated with both of these interrelations.

Reflecting these associations, participants clustered into three groups, as illustrated in Figure 3B. The cluster on the right included 127 participants (24%), all of whom were either not married, had a non-spousal study partner, or did not live with their study partner. Most of this group were female (67%) and 24% were of Black, South Asian, or other ethnicity. Of the remaining 393 participants (76% of 520), 386 (98%) were married, had a spousal study partner, and lived with their study partner; 46 (12%) were of Black, South Asian, or other ethnicity. The upper left cluster included 89 participants (17% of 520), of whom 86 (97%) were female and 33 (37%) had attained a bachelor’s degree or higher, while the lower left cluster included 304 participants (58% of 520), of whom 3 (1%) were female and 159 (52%) had attained a bachelor’s degree or higher.

2.3 Assessment collection and quality control

Participants completed each assessment platform annually for up to 3 years. To account for the more rapid decline anticipated with ALS, participants in that group completed clinical, neuropsychological, and eye tracking assessments at 6-month intervals. Additional information pertaining to the assessment platforms is published elsewhere. To ensure meaningful cross-platform comparisons, participants were required to undertake all assessments. Altogether, 436 participants (84%) provided usable data for all platforms except retinal imaging. Including retinal imaging, 231 participants (44%) provided usable data across all assessment platforms. Many participants did not provide usable data for the retinal imaging platform because (1) retinal imaging was not available to participants enrolled in Kingston, Hamilton, or Thunder Bay (n = 59, 11%); (2) collection of retinal imaging data was delayed as a result of additional service agreements required with some sites, excluding 156 participants (30%) from this assessment during the baseline set of visits (they were invited to complete the assessment during subsequent visits); or (3) data were collected but additional pathologies (e.g., suspect glaucoma, optic neuropathies, and maculopaties) were identified in one or both eyes upon assessment (n = 30, 6%).

Study coordinators aimed to administer all baseline assessments within 8 weeks of the participant providing written consent to optimize cross-platform comparisons and to minimize potential symptom-progression confounds. This goal was met for 430 participants (83%), who completed baseline visits with a median time of 6.14 weeks after providing consent. Most cases in which data collection was outside the 8-week window were a result of scheduling conflicts.

Rigorous, assessment-specific quality assurance, data pre-processing, and quality control procedures were developed and executed to ensure data were of the highest possible accuracy.
TABLE 2  Participant and study partner demographics and relations across the ONDRI cohort and by disease group

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total</th>
<th>Cohort AD/MCI</th>
<th>ALS</th>
<th>FTD</th>
<th>PD</th>
<th>CVD</th>
<th>Association</th>
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</thead>
<tbody>
<tr>
<td>n</td>
<td>520</td>
<td>126</td>
<td>40</td>
<td>53</td>
<td>140</td>
<td>161</td>
<td></td>
</tr>
<tr>
<td>Age: median years (range)</td>
<td>69 (40–87)</td>
<td>71 (53–87)</td>
<td>64 (40–77)</td>
<td>69 (49–80)</td>
<td>68 (55–85)</td>
<td>69 (54–85)</td>
<td>$\eta^2 = 0.085$</td>
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<tr>
<td>Female: n (%)</td>
<td>174 (33%)</td>
<td>57 (45%)</td>
<td>16 (40%)</td>
<td>19 (36%)</td>
<td>31 (22%)</td>
<td>51 (32%)</td>
<td>$w = 0.181$</td>
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<tr>
<td>Education: n (%)</td>
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<td></td>
<td></td>
<td>$w = 0.307$</td>
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<tr>
<td>Less than high school</td>
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<td>13 (10%)</td>
<td>5 (12%)</td>
<td>6 (11%)</td>
<td>8 (6%)</td>
<td>26 (16%)</td>
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<tr>
<td>High school</td>
<td>68 (13%)</td>
<td>11 (9%)</td>
<td>2 (5%)</td>
<td>14 (26%)</td>
<td>17 (12%)</td>
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<tr>
<td>Some college (did not graduate)</td>
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<td>17 (13%)</td>
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<td>Associate degree</td>
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<td>10 (25%)</td>
<td>8 (15%)</td>
<td>18 (13%)</td>
<td>22 (14%)</td>
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<td>Bachelor’s degree</td>
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<tr>
<td>Master’s degree</td>
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<td>3 (6%)</td>
<td>29 (21%)</td>
<td>19 (12%)</td>
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<td>Doctoral degree (e.g., PhD)</td>
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<td>Professional school (e.g., MD, JD, DDS)</td>
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<td>6 (5%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>7 (5%)</td>
<td>7 (4%)</td>
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<td>Ethnicitya: n (%)</td>
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<td></td>
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<td>$w = 0.262$</td>
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<tr>
<td>White (European descent)</td>
<td>432 (83%)</td>
<td>106 (84%)</td>
<td>28 (70%)</td>
<td>46 (87%)</td>
<td>117 (84%)</td>
<td>135 (84%)</td>
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<tr>
<td>Black (African or Caribbean descent)</td>
<td>16 (3%)</td>
<td>4 (3%)</td>
<td>1 (2%)</td>
<td>0 (0%)</td>
<td>3 (2%)</td>
<td>8 (5%)</td>
<td></td>
</tr>
<tr>
<td>South Asian</td>
<td>16 (3%)</td>
<td>6 (5%)</td>
<td>2 (5%)</td>
<td>1 (2%)</td>
<td>4 (3%)</td>
<td>3 (2%)</td>
<td></td>
</tr>
<tr>
<td>Multiple</td>
<td>11 (2%)</td>
<td>1 (1%)</td>
<td>0 (0%)</td>
<td>2 (4%)</td>
<td>7 (5%)</td>
<td>1 (1%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>41 (8%)</td>
<td>9 (7%)</td>
<td>7 (18%)</td>
<td>3 (6%)</td>
<td>8 (6%)</td>
<td>14 (9%)</td>
<td></td>
</tr>
<tr>
<td>Do not know or prefer not to answer</td>
<td>4 (1%)</td>
<td>0 (0%)</td>
<td>2 (5%)</td>
<td>1 (2%)</td>
<td>1 (1%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Marital status: n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$w = 0.250$</td>
</tr>
<tr>
<td>Married or domestic partnership</td>
<td>424 (82%)</td>
<td>100 (79%)</td>
<td>31 (78%)</td>
<td>46 (87%)</td>
<td>123 (88%)</td>
<td>124 (77%)</td>
<td></td>
</tr>
<tr>
<td>Separated or divorced</td>
<td>52 (10%)</td>
<td>13 (10%)</td>
<td>6 (15%)</td>
<td>3 (6%)</td>
<td>13 (9%)</td>
<td>17 (11%)</td>
<td></td>
</tr>
<tr>
<td>Widowed</td>
<td>24 (5%)</td>
<td>12 (10%)</td>
<td>0 (0%)</td>
<td>4 (8%)</td>
<td>1 (1%)</td>
<td>7 (4%)</td>
<td></td>
</tr>
<tr>
<td>Never married</td>
<td>20 (4%)</td>
<td>1 (1%)</td>
<td>3 (8%)</td>
<td>0 (0%)</td>
<td>3 (2%)</td>
<td>13 (8%)</td>
<td></td>
</tr>
<tr>
<td>Living arrangement: n (%)</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>$w = 0.189$</td>
</tr>
<tr>
<td>Own home or Apartment</td>
<td>503 (97%)</td>
<td>119 (94%)</td>
<td>40 (100%)</td>
<td>49 (92%)</td>
<td>135 (96%)</td>
<td>160 (99%)</td>
<td></td>
</tr>
<tr>
<td>Retirement home</td>
<td>5 (1%)</td>
<td>3 (2%)</td>
<td>0 (0%)</td>
<td>1 (2%)</td>
<td>1 (1%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Nursing home or long-term care</td>
<td>1 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>1 (2%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>11 (2%)</td>
<td>4 (3%)</td>
<td>0 (0%)</td>
<td>2 (4%)</td>
<td>4 (3%)</td>
<td>1 (1%)</td>
<td></td>
</tr>
<tr>
<td>Region of recruitment: n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$w = 0.596$</td>
</tr>
<tr>
<td>Toronto</td>
<td>296 (57%)</td>
<td>88 (70%)</td>
<td>20 (50%)</td>
<td>28 (53%)</td>
<td>85 (61%)</td>
<td>75 (47%)</td>
<td></td>
</tr>
<tr>
<td>London</td>
<td>85 (16%)</td>
<td>18 (14%)</td>
<td>4 (10%)</td>
<td>20 (38%)</td>
<td>17 (12%)</td>
<td>26 (16%)</td>
<td></td>
</tr>
<tr>
<td>Ottawa</td>
<td>80 (15%)</td>
<td>12 (10%)</td>
<td>0 (0%)</td>
<td>5 (9%)</td>
<td>38 (27%)</td>
<td>25 (16%)</td>
<td></td>
</tr>
<tr>
<td>Hamilton</td>
<td>41 (8%)</td>
<td>0 (0%)</td>
<td>16 (40%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>25 (16%)</td>
<td></td>
</tr>
<tr>
<td>Thunder Bay</td>
<td>10 (2%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>10 (6%)</td>
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</tr>
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</table>

(Continues)
### Table 2 (Continued)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total</th>
<th>AD/MCI</th>
<th>ALS</th>
<th>FTD</th>
<th>PD</th>
<th>CVD</th>
<th>Association</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kingston</td>
<td>8 (2%)</td>
<td>8 (6%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>w = 0.198</td>
</tr>
<tr>
<td>Relationship of study partner to participant: n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spouse or domestic partner</td>
<td>398 (77%)</td>
<td>88 (70%)</td>
<td>30 (75%)</td>
<td>41 (77%)</td>
<td>118 (84%)</td>
<td>121 (75%)</td>
<td>( \eta^2 = 0.019 )</td>
</tr>
<tr>
<td>Child</td>
<td>63 (12%)</td>
<td>25 (20%)</td>
<td>4 (10%)</td>
<td>8 (15%)</td>
<td>9 (6%)</td>
<td>17 (11%)</td>
<td></td>
</tr>
<tr>
<td>Friend</td>
<td>34 (7%)</td>
<td>6 (5%)</td>
<td>3 (8%)</td>
<td>2 (4%)</td>
<td>6 (4%)</td>
<td>17 (11%)</td>
<td></td>
</tr>
<tr>
<td>Other relative</td>
<td>25 (5%)</td>
<td>7 (6%)</td>
<td>3 (8%)</td>
<td>2 (4%)</td>
<td>7 (5%)</td>
<td>6 (4%)</td>
<td></td>
</tr>
<tr>
<td>Study partner age: median years (range)</td>
<td>64 (19–87)</td>
<td>66 (19–85)</td>
<td>60 (26–77)</td>
<td>62 (22–84)</td>
<td>64 (22–85)</td>
<td>65 (22–87)</td>
<td></td>
</tr>
<tr>
<td>Study partners—female: n (%)</td>
<td>389 (75%)</td>
<td>86 (68%)</td>
<td>26 (65%)</td>
<td>41 (77%)</td>
<td>115 (82%)</td>
<td>121 (75%)</td>
<td>w = 0.132</td>
</tr>
<tr>
<td>Study partner education: n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>w = 0.316</td>
</tr>
<tr>
<td>Less than high school</td>
<td>43 (8%)</td>
<td>10 (8%)</td>
<td>5 (12%)</td>
<td>4 (8%)</td>
<td>6 (4%)</td>
<td>18 (11%)</td>
<td></td>
</tr>
<tr>
<td>High school</td>
<td>75 (14%)</td>
<td>14 (11%)</td>
<td>1 (2%)</td>
<td>10 (19%)</td>
<td>18 (13%)</td>
<td>32 (20%)</td>
<td></td>
</tr>
<tr>
<td>Some college (did not graduate)</td>
<td>57 (11%)</td>
<td>14 (11%)</td>
<td>5 (12%)</td>
<td>8 (15%)</td>
<td>15 (11%)</td>
<td>15 (9%)</td>
<td></td>
</tr>
<tr>
<td>Associate degree</td>
<td>92 (18%)</td>
<td>16 (13%)</td>
<td>13 (32%)</td>
<td>13 (25%)</td>
<td>26 (19%)</td>
<td>24 (15%)</td>
<td></td>
</tr>
<tr>
<td>Bachelor’s degree</td>
<td>143 (28%)</td>
<td>37 (29%)</td>
<td>7 (18%)</td>
<td>12 (23%)</td>
<td>44 (31%)</td>
<td>43 (27%)</td>
<td></td>
</tr>
<tr>
<td>Master’s degree</td>
<td>71 (14%)</td>
<td>24 (19%)</td>
<td>7 (18%)</td>
<td>4 (8%)</td>
<td>21 (15%)</td>
<td>15 (9%)</td>
<td></td>
</tr>
<tr>
<td>Doctoral degree</td>
<td>19 (4%)</td>
<td>5 (4%)</td>
<td>0 (0%)</td>
<td>1 (2%)</td>
<td>7 (5%)</td>
<td>6 (4%)</td>
<td></td>
</tr>
<tr>
<td>Professional school</td>
<td>19 (4%)</td>
<td>6 (5%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>3 (2%)</td>
<td>8 (5%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (0%)</td>
<td>0 (0%)</td>
<td>1 (2%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Study partners living with participant: n (%)</td>
<td>419 (81%)</td>
<td>96 (76%)</td>
<td>33 (82%)</td>
<td>41 (77%)</td>
<td>122 (87%)</td>
<td>127 (79%)</td>
<td>w = 0.109</td>
</tr>
<tr>
<td>Study partner time living with participant (if live together = yes): median years (range)</td>
<td>36 (&lt;1–65)</td>
<td>35 (&lt;1–65)</td>
<td>30 (1–55)</td>
<td>40 (4–57)</td>
<td>36 (&lt;1–63)</td>
<td>38 (1–63)</td>
<td>( \eta^2 = 0.021 )</td>
</tr>
<tr>
<td>Study partner time with participant per week (if live together = no): median hours (range)</td>
<td>6 (0.5–112)</td>
<td>8 (1–112)</td>
<td>15 (3–80)</td>
<td>4.5 (1–16)</td>
<td>3.5 (0.5–23)</td>
<td>7.5 (1–108)</td>
<td>( \eta^2 = 0.066 )</td>
</tr>
</tbody>
</table>

Abbreviations: AD/MCI, Alzheimer’s disease and amnestic mild cognitive impairment; ALS, amyotrophic lateral sclerosis; CVD, cerebrovascular disease; FTD, frontotemporal dementia spectrum disorder; ONDRI, Ontario Neurodegenerative Disease Research Initiative; PD, Parkinson’s disease.

*Any category that observed <3% was regrouped into Other.

Followed by an ONDRI-wide data quality evaluation process that identified data patterns and detected incongruous observations, consequently indicating areas of potential error. All data packages were formatted and structured to meet common specifications, facilitating cross-platform merging and third-party sharing.

### 3 Detailed Methods and Results

#### 3.1 Data Management

All data are stored in Brain-CODE, a secure, centralized neuroinformatics system designed for the collection, storage, federation, sharing,
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Cohort</th>
<th>AD/MCI</th>
<th>ALS</th>
<th>FTD</th>
<th>PD</th>
<th>CVD</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>126</td>
<td>40</td>
<td>53</td>
<td></td>
<td>140</td>
<td>161</td>
</tr>
<tr>
<td>Subgroups</td>
<td></td>
<td>AD</td>
<td>MCI</td>
<td>—</td>
<td>bvFTD</td>
<td>PPA-a</td>
</tr>
<tr>
<td>n(%)</td>
<td>41 (33%)</td>
<td>85 (67%)</td>
<td>21 (40%)</td>
<td>8 (15%)</td>
<td>16 (30%)</td>
<td>—</td>
</tr>
<tr>
<td>Age (years)</td>
<td>67 (49–80)</td>
<td>66 (41–86)</td>
<td>62 (38–76)</td>
<td>60 (48–76)</td>
<td>67 (57–72)</td>
<td>63.5 (53–76)</td>
</tr>
<tr>
<td>Years since first symptoms</td>
<td>4 (0–9)</td>
<td>3 (0–20)</td>
<td>2 (1–5)</td>
<td>5 (1–18)</td>
<td>3 (1–4)</td>
<td>4 (1–11)</td>
</tr>
<tr>
<td>MoCA total score</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥26</td>
<td>4 (10%)</td>
<td>20 (24%)</td>
<td>20 (50%)</td>
<td>3 (14%)</td>
<td>0 (0%)</td>
<td>3 (19%)</td>
</tr>
<tr>
<td>&lt;26</td>
<td>37 (90%)</td>
<td>65 (76%)</td>
<td>19 (48%)</td>
<td>18 (86%)</td>
<td>8 (100%)</td>
<td>13 (81%)</td>
</tr>
<tr>
<td>Lawton-Brody ADL scales (% of independence)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basic: median (range)</td>
<td>100 (67–100)[1]</td>
<td>100 (83–100) [10]</td>
<td>92 (33–100)[1]</td>
<td>92 (63–100)</td>
<td>100 (92–100)[1]</td>
<td>79 (33–100)</td>
</tr>
<tr>
<td>Instrumental: median (range)</td>
<td>77 (26–100)[1]</td>
<td>96 (39–100) [12]</td>
<td>84 (17–100)</td>
<td>57 (17–100)</td>
<td>83 (61–100)[1]</td>
<td>53 (4–100)[1]</td>
</tr>
<tr>
<td>NPI-Q:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MDS-UPDRS: Part 3 (/132)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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</table>

(Continues)
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Cohort</th>
<th>AD/MCI</th>
<th>ALS</th>
<th>FTD</th>
<th>PD</th>
<th>CVD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modified Rankin scale: (/6)</td>
<td>median (range) [missing]</td>
<td>2 (0–3) [14]</td>
<td>1 (0–3) [24]</td>
<td>2 (0–4)</td>
<td>2 (1–3) [8]</td>
<td>1 (1–2) [5]</td>
</tr>
<tr>
<td>WHOQOL-BREF: (/20)</td>
<td>Physical: median (range)</td>
<td>17 (13–20)</td>
<td>17 (7–20)</td>
<td>14 (8–19)</td>
<td>18 (9–20)</td>
<td>18 (13–20)</td>
</tr>
<tr>
<td></td>
<td>Psych.: median (range)</td>
<td>17 (11–20)</td>
<td>16 (9–20)</td>
<td>15 (9–20)</td>
<td>16 (8–20)</td>
<td>18 (12–19)</td>
</tr>
<tr>
<td></td>
<td>Social: median (range)</td>
<td>16 (4–20)</td>
<td>16 (9–20)</td>
<td>16 (9–20)</td>
<td>15 (11–20)</td>
<td>16 (15–20)</td>
</tr>
<tr>
<td></td>
<td>Environ.: median (range)</td>
<td>19 (7–20)</td>
<td>19 (13–20)</td>
<td>17 (10–20)</td>
<td>17 (12–20)</td>
<td>19 (18–20)</td>
</tr>
<tr>
<td></td>
<td>[missing (all four domains)]</td>
<td>[1]</td>
<td>[1]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALSFRS- R: (/48)</td>
<td>median (range)</td>
<td>-</td>
<td>-</td>
<td>38 (29–47)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Hoehn &amp; Yahr: (/5)</td>
<td>median (range)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Abbreviations: AD, Alzheimer’s disease; ADL, Activities of Daily Living; ALS, amyotrophic lateral sclerosis; ALSFRS-R, ALS Functional Rating Scale–Revised; bvFTD, behavioral variant FTD; CVD, cerebrovascular disease; Environ., environmental; FTD, frontotemporal dementia spectrum disorder; MCI, amnestic mild cognitive impairment; MDS-UPDRS, Movement Disorder Society revised Unified Parkinson’s Disease Rating Scale; MoCA, Montreal Cognitive Assessment; NPI-Q, Neuropsychiatric Inventory Questionnaire; PD, Parkinson’s disease; PPA-a, progressive primary aphasia–agrammatic variant; PSP, progressive supranuclear palsy; Psych., psychological; SVD, small vessel disease; WHOQOL-BREF, Abbreviated World Health Organization Quality of Life assessment.

Notes: A higher score on the MoCA, Lawton–Brody ADL scales, WHOQOL-BREF, and ALSFRS-R indicates a closer resemblance of normalcy. A higher score on the NPI-Q, MDS-UPDRS, modified Rankin scale, and Hoehn &Yahr indicates a higher severity of measures symptoms.

*Includes only subtypes with more than 5 participants; corticobasal syndrome: n = 3; primary progressive aphasia - semantic variant: n = 5.
*Imaging data partially unavailable for 6 participants; unable to classify.
*Includes 1 participant diagnosed with both bvFTD and PSP subtypes.
*For CVD, considering age at and time since most recent stroke.
*MoCA total scores greater than or equal to 26 are considered cognitively intact; total scores less than 26 are considered cognitively impaired.
*Study partners reported difficulties in IADLs for three MCI participants (IADL = 39, 56, and 57%). For each of these participants, the MCI diagnosis has been confirmed based on the participant’s clinical profile at the time of enrolment. In addition, study partners reported no difficulties in IADLs for three AD participants. Of importance, our IADL measure did not capture changes in work or hobbies, which are complex activities that are often affected first as an individual progresses from MCI to AD.
*All participants were in the on-state with the exception of 6 FTD participants and 11 PD participants who were in the off-state.
and analysis of different types of data using a diverse set of electronic data capture tools including XNAT, REDCap, and LabKey.

### 3.2 Missing datum in analysis of participant characteristics

All data for measures included in the MCA were observed, with the exception of one MoCA score, for which the participant had not completed the visuospatial portion of the assessment due to physical impairment. While taking into consideration the observed performance of this participant in other sections, a sensitivity analysis was performed to assess the change in results given a range of plausible values before selecting the most appropriate with regression imputation.

### 3.3 Time windows

Data collection time windows were calculated based on the date the participant provided written consent and the date on which each
FIGURE 4  Detectable effect size levels at alpha = 0.05 and with power = 0.80: (A) for up to eight variables in a multivariable linear model using R-squared measure of effect size; (B) for up to 25 degrees of freedom in a Chi-square measure of association using \( \eta^2 \) measure of effect size, assuming equal group size (i.e., each category has floor \( \lfloor n / \# \text{ of categories} \rfloor \) participants) and where degrees of freedom are based on the number of categories in each of the two comparative variables (i.e., if one group has \( j \) categories and the other has \( k \) categories, the degrees of freedom are \( (j-1) \times (k-1) \)). Small, medium, and large effects are based on Cohen.59 AD/MCI, Alzheimer’s disease and amnestic mild cognitive impairment; ALS, amyotrophic lateral sclerosis; CVD, cerebrovascular disease; FTD, frontotemporal dementia spectrum disorder; ONDRI, Ontario Neurodegenerative Disease Research Initiative; PD, Parkinson’s disease

assessment platform was completed. If the assessment was completed over multiple days, the latest date was used, except for the clinical platform, which used the date demographics were captured, and the neuropsychology platform, for which the date most assessments were completed was used.

In addition to scheduling conflicts, two data collection decisions also had an impact: (1) MRI scans that did not meet quality control standards for processing were re-acquired, and 8 of the 10 re-acquisitions (80%) were past the 8-week window, and (2) because of the retinal imaging service agreement delays, participants recruited within the 6 months before agreements were in place were asked to complete the retinal imaging assessment at that time, accounting for 14 of the 58 assessments (24%) beyond the 8-week time window.

3.4  Detectable effect sizes

Figure 4 shows minimum detectable effect sizes for the full 520 participants in the ONDRI cohort and for subsamples the size of each of the disease group. Two types of analysis are considered—multivariable linear model (e.g., estimating the relationship between a continuous, numeric measurement and multiple explanatory variables; Figure 4A) and Chi-square measure of association (e.g., estimating the relationship between two variables with response classification of two or more categories; Figure 4B)—considering several numbers of variables or degrees of freedom (determined by number of categories) at alpha = 0.05 and power = 0.80. The figure illustrates that with a cohort of 520 participants, small effects are detectable by a multivariable linear model with two or three variables, and effects up to \( w = 0.2 \) are detectable by a Chi-square measure of association.

Larger subsamples, such as the AD/MCI, PD, and CVD disease groups, are sufficient to detect medium effects for a multivariable linear model, and 2 to 6 degrees of freedom in a Chi-square test of association, depending on the group. Smaller subsamples, such as the ALS and FTD disease groups, are expected to detect large effects in subsamples for four or fewer variables, and three or fewer degrees of freedom.

The \( \eta^2 \) measure reported for analyses of variance is a special case of the multivariable linear model.

3.5  Ethics approval

Research ethics committees at all participating recruitment sites approved the ONDRI research protocol. All participants and study partners provided written and informed consent prior to contribution and in accordance with the Declaration of Helsinki.

3.6  Cognitively normal control cohort

A cognitively normal control cohort with overlapping assessments to ONDRI has also been collected from the Brain-Eye Amyloid Memory study.60 Baseline characteristics of this control cohort will be reported in a separate paper.

3.7  Software

Analyses were performed with R version 3.4.4, including the ExPosition (v2.8.19)61 and ggplot2 (v3.1.0)62 packages.

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CONFLICTS OF INTEREST
MBor is a clinical trial site investigator for Biogen, Janssen, Roche, Eli Lilly, and Alector; speaker for Biogen, Roche, Merck, and Eli Lilly. EF has received personal compensation for serving on a Scientific Advisory Committee for Biogen, Vigil Neuro, and Denali Therapeutics that are developing treatments for neurodegenerative dementias; received research support paid to her institution (UWO) from CIHR and the Weston Foundation to conduct an ongoing study of oxytocin in FTD, from Alzheimer Society of Canada, and the Physicians and Services Incorporated Foundation, the Ministry of Research and Innovation of Ontario for research; and for site participation in clinical trials sponsored by Alector, Biogen, Vigil Neuro, and TauRx. CF receives grant funding Vielight Inc., Hoffman La Roche, Cortexyme, Brain Canada, the Weston Foundation, NIH, and the St. Michaels Hospital Foundation Heather and Eric Donnelly endowment. MF is listed on a patent related to methods and kits for differential diagnosis of Alzheimer’s disease versus frontotemporal dementia using blood biomarkers and receives support from the Saul A. Silverman Family Foundation as a Canada International Scientific Exchange Program and Morris Kertsner Memorial Fund. MJ received grant support from PSSO, MITACS, Paladin Labs, Ipsen Pharmaceuticals, Research Council of Norway, and GE; and has received honoraria from Allergan, Abbvie, Ipsen, Sunovion, Merz, and Paladin. AL has served as an advisor for AbbVie, AFFiRiS, Biogen, BioAdvance, BlueRock, BMS, Denali, Janssen, Jazz, Lilly, Paladin, Retropphin, Roche, Sun Pharma, and UCB; received honoraria from Sun Pharma, AbbVie, and Sunovion; received grants from Brain Canada, Canadian Institutes of Health Research, Edmond J. Safra Philanthropic Foundation, Michael J. Fox Foundation, the Ontario Brain Institute, Parkinson Foundation, Parkinson Canadian, and W. Garfield Weston Foundation; received publishing royalties from Elsevier, Saunders, Wiley-Blackwell, Johns Hopkins Press, and Cambridge University Press. SHP is a consultant for Zywie Bio LLC, working on a disease modifying treatment for Parkinson’s disease. TKR has received research support from Brain Canada, Brain and Behavior Research Foundation, BrightFocus Foundation, Canada Foundation for Innovation, Canada Research Chair, Canadian Institutes of Health Research, Centre for Aging and Brain Health Innovation, National Institutes of Health, Ontario Ministry of Health and Long-Term Care, Ontario Ministry of Research and Innovation, and the Weston Brain Institute; has received in-kind equipment support from Neuronika for an investigator-initiated study, and in-kind research online accounts from Scientific Brain Training Pro, and participated in 2021 in one advisory board meeting for Biogen Canada Inc.; is also an inventor on the United States Provisional Patent No. 17/396,030 that describes cell-based assays and kits for assessing sexoligic receptor activity. SCS is a shareholder and consultant for ADMdx, a medical diagnostics company specializing in neuroimaging of neurodegenerative disorders. SS sits on an advisory board for Biogen for neuroimaging of ARIA. RHS has received research grants from Canadian Institute for Health Research, National Institute of Health, Heart and Stroke Foundation of Canada, Ontario Brain Institute; received salary support for research from Heart and Stroke Foundation Clinician-Scientist Phase II Award, Ontario Brain Institute, Sunnybrook and UofT Department of Medicine, Sandra Black Centre for Brain Resilience, Recovery and Repair. MCT receives grant support from NIH and serves as a scientific advisor to Women’s Brain Project and Brain Injury Canada. LZ has served as an advisor for the following pharma companies: Mitsubishi Tanabe, Biogen, Cytokinetics, and Amylyx. MM reports grant funding from the Ontario Brain Institute relating to this work. MM reports grants from the Canadian Institutes of Health Research, Woman’s Brain Health Initiative, Brain Canada, Weston Brain Institute, and Washington University, outside of this submitted work. MM
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