

Predicting Cognitive Impairment in Cerebrovascular Disease Using Spoken Discourse Production

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Purpose: Dementia due to cerebrovascular disease (CVD) is common. Detecting early cognitive decline in CVD is critical because addressing risk factors may slow or prevent dementia. This study used a multidomain discourse analysis approach to determine the spoken language signature of CVD-related cognitive impairment. **Method:** Spoken language and neuropsychological assessment data were collected prospectively from 157 participants with CVD as part of the Ontario Neurodegenerative Disease Research Initiative, a longitudinal, observational study of neurodegenerative disease. Participants were categorized as impaired ($n = 92$) or cognitively normal for age ($n = 65$) based on neuropsychology criteria. Spoken language samples were transcribed orthographically and annotated for 13 discourse features, across five domains. Discriminant function analyses were used to determine a minimum set of discourse variables, and their estimated weights, for maximizing diagnostic group separation. **Results:** The optimal discriminant function that included 10 of 13 discourse measures correctly classified 78.3% of original cases (69.4% cross-validated cases) with a sensitivity of 77.2% and specificity of 80.0%. **Conclusion:** Spoken discourse appears to be a sensitive measure for detecting cognitive impairment in CVD with measures of productivity, information content, and information efficiency heavily weighted in the final algorithm. **Key words:** *assessment, biomarker, cerebrovascular disease (CVD), cognition, dementia, multilevel discourse analysis, neurodegeneration, spoken discourse, spoken language, vascular cognitive impairment (VCI)*

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Data will be available to researchers for purposes of reproducing the results or replicating the procedures. Available data files are detailed in Supplemental Digital Content file S1 (available at: <http://links.lww.com/TLD/A72>). De-identified data files and orthographic transcripts used in the reported analyses will be released through Brain-CODE (Vaccarino et al., 2018; <https://www.braincode.ca>) beginning fall 2020. Data governance and access requests will be managed by ONDRI and the Ontario Brain Institute. Audio files of spoken discourse samples will not be available to the general scientific community in compliance with data use as consented to by participants. Study analytical software used in the discourse analysis (SALT) is available at www.saltsoftware.com. Stimuli for eliciting spoken discourse and other source materials for the study are available through various published resources (references noted in the article). The reported

CEREBROVASCULAR DISEASE (CVD) is the second most common cause of dementia (Iadecola et al., 2019), next to Alzheimer's disease. Moreover, vascular factors (i.e., white matter disease and cerebrovascular infarcts) can interact with other underlying pathologies (e.g., Alzheimer's disease) in the development of dementia (Breteler, 2000; Luchsinger et al., 2005; Vermeer et al., 2003; Yatsu & Shaltoni, 2004). Although cerebrovascular-related dementia can be caused by isolated infarcts (and also can occur following covert strokes,

study protocol was not preregistered with an independent, institutional registry.

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accumulation of lacunes, and small-vessel disease), the progressive nature of this condition distinguishes it clinically from acute stroke language impairment (e.g., Broca's aphasia). The term "multi-infarct dementia" (MID) first was coined to capture the idea that multiple cerebral infarcts can cause dementia (Hachinski et al., 1974). However, starting in the early- to mid-1970s, the term "vascular dementia" (VaD) emerged and was used to capture both cortical and subcortical CVD-related cognitive impairments. In the early 1990s, the term "vascular cognitive impairment" (VCI) was introduced (Hachinski & Bowler, 1993) and generally accepted (Gorelick et al., 2011) to account for the multiple and insidiously progressing cognitive and social cognition impairments associated with CVD. Importantly, VCI commonly co-occurs with other neurodegenerative pathologies and can unmask or accelerate the expression of cognitive symptoms (e.g., Snowden et al., 1997; Swartz et al., 2008).

Although the exact prevalence of VCI is uncertain, it is thought to comprise 15%–20% of dementia cases in North America and 30% of cases in Europe (Wolters & Ikram, 2019). Although the presence of CVD is an independent risk factor for dementia, the incidence of VCI increases with age, specifically in adults older than 75 years, with the risk of developing VaD doubling every 5.3 years (O'Brien & Thomas, 2015; Peters et al., 2019). Despite the risks associated with increased age, CVD-related dementia has a number of modifiable risk factors such as hypertension, diabetes, smoking, and high cholesterol (Lewis et al., 2006). Thus, identifying individuals most at risk for developing VaD, in its earliest stage, using sensitive and nuanced measures of cognitive change is critical for reducing dementia prevalence and optimizing outcomes (Peters et al., 2019; Schmidt et al., 2000).

Although it is beyond the scope of this article to review exhaustively the neuropsychological profiles of people with CVD-related cognitive decline, the following sections address key literature on neuropsychological

profiles that provide a robust rationale for considering how these impairments potentially manifest in spoken discourse.

VCI and VaD

There are at least six different published criteria for diagnosing VCI (American Psychiatric Association, 2000, 2013; Chui et al., 1992; Román et al., 1993; Sachdev et al., 2014; Skrobot et al., 2018). Of fundamental importance to the current study, they all require measurable cognitive decline that differs from baseline function and confirmation of cerebrovascular disease on neuroimaging (Iadecola et al., 2019; O'Brien & Thomas, 2015). Labeled in the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (American Psychiatric Association, 2013) as "minor" and "major" forms of cognitive impairment, in "minor" VCI, and consistent with mild cognitive impairment (MCI), independence is mostly maintained in activities of daily living (ADL) despite the presence of cognitive deficits (Iadecola et al., 2019). In "major" VCI, the severest form (i.e., otherwise known as VaD), ADL are significantly impaired and cognitive impairments are typically more severe (American Psychiatric Association, 2013; Iadecola et al., 2019).

Deficits in cognitive functions are a hallmark feature of VCI with specific impairments in memory, attention, information processing, and executive function (O'Brien & Thomas, 2015; Sengupta et al., 2019; Zaidi et al., 2020). Executive dysfunction is the most commonly reported cognitive impairment in VCI and often presents as impaired planning abilities, impaired reasoning, difficulty with complex activities, and disorganized thoughts and behaviors (Korczyński et al., 2012; Venkat et al., 2015). Other symptoms include slowed thinking, forgetfulness, disorientation, depression, and anxiety (Venkat et al., 2015). Symptom onset may appear suddenly or develop in a step-like manner following a stroke or the onset of other cerebrovascular disease (Venkat et al., 2015). The cognitive deficits present in VaD are more

variable than those in Alzheimer's dementia (AD), likely resulting from the heterogeneous vascular pathologies that underlie this condition and the complex interactions between vascular disease and other dementia pathologies (O'Brien & Thomas, 2015; Swartz et al., 2008). As a first step toward parsing the vascular contributions to spoken discourse impairments in neurodegeneration, and developing robust cross-disorder neurodegenerative spoken discourse endophenotypes, herein we examine spoken language abilities in a well-characterized clinical CVD cohort.

The existing literature on the language abilities of persons living with VaD are overwhelmingly designed as between or among diagnostic group comparisons of persons with VaD (or MID), AD, and normal controls. Moreover, these studies, with few exceptions, address language within the conceptual framework of neuropsychological or cognitive assessments. Findings regarding language impairments have been mixed. No significant differences were found between those living with VaD versus AD on verbal-semantic and letter fluency performances (Jones et al., 2006), single picture naming on the Boston Naming Test (Lafosse et al., 1997), or verbal working memory performances on the Token Test (e.g., Marterer et al., 1996). In contrast to this literature, other similar studies showed persons living with VaD performed more poorly than those living with AD on verbal fluency (Duff-Canning et al., 2004) and better on the Boston Naming Test (e.g., Barr et al., 1992). In addition, several studies showed that compared with AD, persons with VaD perform more poorly on word recognition (Kontiola et al., 1990) and phrase repetition tasks (e.g., Loewenstein et al., 1991).

These studies collectively highlight the heterogeneity of this dementia phenotype that is magnified, and made more challenging to characterize, by the broad range of diagnostic criteria used to define VCI across research studies (Ma et al., 2015; Skrobot et al., 2017). Problematically, cognitive assessment data do not generally differentiate, in a reliable way, VaD from other clinical dementia types in-

cluding AD, frontotemporal dementia (FTD), or dementia with Lewy bodies (Braaten et al., 2006), underscoring the importance of examining spoken discourse as a potentially novel behavioral diagnostic biomarker of VaD.

SPOKEN DISCOURSE IN VCI and VaD

Targeting the spoken discourse performances of older adults with and without CVD, cognitive impairment, and dementia is well known to reveal the close and complex interplay among cognitive systems and language production processes (e.g., Cannizzaro & Coelho, 2013; Coelho et al., 1995; Frederiksen et al., 1990; Murray, 2000; Pritchard et al., 2018; Roberts & Post, 2018; Wright et al., 2014). Spoken discourse (i.e., language beyond single words and sentences), elicited using picture stimuli, can be a sensitive and specific measure of cognitive change in dementia and neurodegenerative disorders, having shown the ability to identify prodromal disease in AD (e.g., Duong et al., 2003; Fleming & Harris, 2008) and Huntington's disease (Perez et al., 2018); the ability to discriminate early disease states from typical aging in Parkinson's disease (PD; Murray, 2000; Roberts & Post, 2018) and amnesic MCI (Drummond et al., 2015; Mueller et al., 2018); and the ability to predict disease progression in amyotrophic lateral sclerosis (ALS; Roberts-South et al., 2012), Lewy body disease (Ash et al., 2017), FTD (Hardy et al., 2016), and AD (Fleming & Harris, 2008).

To date, very few studies have examined the spoken discourse signatures within CVD-related cognitive impairment. Thus, little is known regarding whether, and how, cognitive impairments in VCI manifest in spoken discourse. Moreover, the existing literature is plagued by small sample sizes (<20 participants), heterogeneous VaD inclusion criteria, and less than optimal characterization of underlying cognitive profiles. In this limited body of literature, Mendez and Ashla-Mendez (1991), using a picture description task, reported that individuals with MID produced fewer words per minute (WPM) and fewer

utterances than individuals with AD (Mendez & Ashla-Mendez, 1991). In a study comparing early-stage VCI with AD, the spoken discourses of both groups differed from controls in the amount and accuracy of information content but did not differ from one another (Vuorinen et al., 2000). Hier et al. (1985) also found that lower productivity distinguished VCI from AD and uniquely reported lower lexical diversity and fewer syntactically complex utterances in the stroke-related dementia group. These studies suggest that language in CVD-related dementia may differ from AD in productivity and from typical aging adults in information content. However, this body of literature offers limited insight into unique spoken discourse signatures that can potentially discriminate, within CVD, people with cognitive impairment who are at an elevated risk of developing VaD from those who are cognitively normal for age.

CURRENT STUDY

The Ontario Neurodegenerative Disease Research Initiative (ONDRI) is a multisite, longitudinal, observational cohort study that was designed to characterize deep endophenotypes in neurodegenerative disorders using a transdisciplinary approach and to elucidate relationships between these endophenotypes and CVD (Farhan et al., 2017). The ONDRI study enrolled participants with CVD as well as four other disease cohorts, including people with AD/MCI, PD, ALS, and FTD (for details, see Farhan et al., 2017; McLaughlin et al., 2020; Sunderland et al., 2020). As part of the ONDRI study, participants completed a rigorous set of measurement and study tasks annually (for up to 3 consecutive years) across seven assessment platforms: clinical, neuropsychology (under which spoken discourse data were collected), eye tracking/oculomotor, gait and balance, neuroimaging, retinal imaging with spectral domain optical coherence tomography, and genomics. Spoken discourse data, one sample from each elicitation method, were collected

at each time point and included narratives generated from single picture descriptions, picture sequence descriptions, extended narratives using a wordless picture book, and procedural discourse.

In the current study, we applied a multidomain discourse analysis approach, using the picture sequence description task from the baseline data collection, to examine spoken language signatures in a large sample of individuals with CVD from the ONDRI study. Specifically, the aims of the current study were to determine the following:

1. Whether information content, syntax, lexical diversity, productivity, or fluency differ as a function of cognitive impairment in a CVD cohort; and
2. Which discourse measures (and relative weightings) when combined predict the presence of cognitive impairment in a well-characterized CVD cohort.

METHODS

Approvals and data access

Participants in the ONDRI cohort provided written consent. The study utilized a central data collection protocol, approved individually by the Human Subjects Research Ethics Boards at 13 participating academic health sciences centers across Ontario, Canada. The study used ONDRI baseline visit data for the CVD cohort including raw audio files (.wav) for spoken discourse samples; analyzed neuroimaging data; clinical assessment measures; as well as item level, summary, and standardized scores for all reported neuropsychological assessments (see Supplemental Digital Content S1, available at: <http://links.lww.com/TLD/A72>, for file names).

Participants

The ONDRI cohort, including all inclusion/exclusion criteria, is detailed in previous publications (Farhan et al., 2017; McLaughlin et al., 2020; Sunderland et al., 2020). Participants with CVD were recruited by clinical stroke neurologists from academic health

sciences centers across Ontario, Canada. Participants in the CVD cohort (a) were 55–85 years of age, (b) self-reported English as their primary language with proficiency in speaking and understanding ratings of 7/10 using the Language Experience and Proficiency Questionnaire (Marian et al., 2007), (c) had Montreal Cognitive Assessment (Nasreddine et al., 2005) scores of 18 or more, (d) had 8 or more years of formal education, and (e) had magnetic resonance imaging (MRI)/computed tomography (CT)-confirmed mild-moderate ischemic stroke event(s) (mRS 0–3) 3 or more months prior to participation (this included individuals with subclinical strokes/covert strokes, clinical presentation of transient ischemic attack with infarcts on imaging, and clinical strokes with imaging confirmation). Participants with nonvascular etiologies, large cortical strokes (more than one-third middle cerebral artery), severe cognitive impairment, or significant aphasia and/or motor speech issues were excluded to minimize primary aphasia and dysarthria/apraxia confounds on neuropsychological testing. Although neuroimaging and clinical evidence of CVD at presentation were required for study inclusion, participants were not required to have detectable lesions on neuroimaging in the chronic injury state (i.e., from 3 months to several years poststroke for many participants).

The ONDRI CVD cohort had 161 participants with documented CVD. Four participants (2.5%) were excluded from the current study because of issues prohibiting analysis of their spoken language recordings (poor audio quality, $n = 1$; administration error, $n = 1$; lost data due to technical issues, $n = 2$), leaving 157 participants in the final sample. Participants possessed adequate vision and hearing (with accommodations) to complete all neuropsychological testing and discourse tasks. Participants (except those with existing, working hearing aids) completed a pure tone audiometric screening at a threshold of 30 dB HL at 1,000, 2,000, and 4,000 Hz bilaterally using previously published screening guidelines (American

Speech-Language-Hearing Association, 2005). Participants who failed the hearing screening were fitted with a personal amplification device for all neuropsychological testing and language sampling procedures. Demographic data for CVD participants ($N = 157$) who were included in the current study are detailed in Table 1.

Procedure

Classification of participants into low versus high cognition groups

Neuropsychological tests were administered using standard procedures and scored using their published instruction manuals (for details, see McLaughlin et al., 2020). Participants with CVD were allocated to either a cognitively impaired group (“low” cognition, $n = 92$) or a cognitively normal for age group (“high” cognition, $n = 65$) based on their performances on the neuropsychology tests and domains in Table 2. We used conservative criteria for determining the presence of cognitive impairment, whereby participants were allocated to the “low” group if they obtained a standardized score that was at least 1.5 standard deviations (SDs) below the normative mean on two tests within a given cognitive domain (Wood et al., 2016; Zaidi et al., 2020). For the Semantic Probe subtest of the Boston Diagnostic Aphasia Exam (Goodglass et al., 2001), normative data were not available, so we used the cutoff score of 55 as determined by Zaidi et al. (2020). The “low” cognition group generally performed more poorly than the “high” cognition group on the neuropsychological battery, with the majority of measures demonstrating medium to large effect size differences, thus confirming that the applied classification criteria distinguished cognitively impaired from cognitively normal for age participants. Participants in the “low” cognition group ranged from mild to moderate severity, with the group distributed between single-domain ($n = 43$) and multidomain profiles ($n = 49$; impaired in two plus domains).

Table 1. Participant demographics

	Low Cognition (N = 92)		High Cognition (N = 65)		Effect size
	Mean (IQR)	Range	Mean (IQR)	Range	
Continuous variable ^a OR					
Categorical variable ^b OR	<i>n</i>	%	<i>n</i>	%	
Ordinal variable ^c	Median (MAD)	Range	Median (MAD)	Range	
Age ^a	69.99 (13.39)	55.22–85.43	68.43 (8.06)	54.95–84.25	0.21 ^a
Education (years) ^a	14.26 (4)	8–20	15.20 (6)	8–20	0.33 ^a
MRS: Total score ^c	1.00 (1.00)	0–3	1.00 (1.00)	0–4	0.42 ^c
Sex (N female) ^d	29	31.52%	21	32.31%	0.01 ^b
<i>Stroke history</i>					
Duration since stroke (years) ^a	1.99 (2.52)	0.18–10.73	2.59 (1.69)	0.25–34.55	0.16 ^a
Stroke location at time of stroke (N by group) ^b					0.20 ^b
Right	24	26.09%	28	43.08%	
Left	55	59.78%	29	44.62%	
Bilateral	8	8.70%	7	10.77%	
Unknown	4	4.35%	1	1.54%	
Circulation involved at time of stroke ^b					0.06 ^b
Anterior	54	58.70%	38	58.46%	
Posterior	23	25.00%	19	29.23%	
Multiple	8	8.70%	4	6.15%	
Unknown	6	6.52%	4	6.15%	
Presence of subclinical stroke ^b					0.14 ^b
Yes	16	17.39%	10	15.38%	
No	72	78.26%	55	84.62%	
Unknown	4	4.35%	0	0.00%	
TOAST classification of presumed stroke etiology ^b					0.09 ^b
Small-artery occlusion (lacune)	28	30.43%	22	33.85%	
Cardioembolic	12	13.04%	12	18.46%	
Large artery atherosclerosis	19	20.65%	15	23.07%	
Stroke of undetermined etiology	23	25.00%	13	20.00%	
Stroke of other determined etiology	3	3.26%	2	3.08%	
<i>Medical history</i>					
Prior history of stroke (N yes) ^b	17	18.48%	9	13.85%	0.06 ^b
Prior history of transient ischemic attack (N yes) ^b	18	19.57%	6	9.23%	0.14 ^b

(continues)

Table 1. Participant demographics (*Continued*)

	Low Cognition (<i>N</i> = 92)		High Cognition (<i>N</i> = 65)		
Prior intracranial hemorrhage (<i>N</i> yes) ^b	0	0.00%	1	1.54%	0.10 ^b
Hypertension ^b	66	71.74%	48	73.85%	0.02 ^b
Coronary artery disease ^b	14	15.22%	11	16.92%	0.02 ^b
Diabetes ^b	24	26.09%	10	15.38%	0.13 ^b
Prior history of smoking (<i>N</i> yes) ^b	50	54.35%	37	56.92%	0.03 ^b
<i>NIHSS</i> ^d					
Language score ^b					0.06 ^b
% no aphasia	82	96.47%	63	98.43%	
% mild to moderate aphasia	3	3.53%	1	1.56%	
Dysarthria score ^b					0.12 ^b
% Normal	82	96.47%	64	100.00%	
% mild to moderate dysarthria	3	3.53%	0	0.00%	
<i>NIHSS</i> total score ^a	0.74 (1)	0–5	0.53 (1)	0–6	0.20 ^a
<i>GAD</i> total ^c	1.00 (1.00)	0–20	1.00 (1.00)	0–11	0.01 ^c
<i>Ethnicity</i> (% by group) ^b					0.19 ^b
White	76	82.61%	58	89.23%	
Black	7	7.61%	1	1.54%	
Asian	7	7.61%	5	7.69%	
Multiple	0	0.00%	1	1.54%	
Other	2	2.22%	0	0.00%	
<i>Handedness</i> (% by group) ^b					0.10 ^b
Right	81	88.04%	58	89.23%	
Left	9	9.78%	7	10.77%	
Ambidextrous	2	2.17%	0	0.00%	

Note. AD/MCI = Alzheimer's dementia/mild cognitive impairment; CVD = cerebrovascular disease; GAD = Generalized Anxiety Disorder scale (Spitzer et al., 2006); IQR = interquartile range; MAD = median absolute deviation; MRS = "Modified Rankin Scale," a rating scale of overall disability level following stroke, where 0 denotes no symptoms and 6 denotes death (Bonita & Beaglehole, 1988); NIHSS = National Institutes of Health Stroke Scale (Ortiz & Sacco, 2014); TOAST classification = Trial of ORG 10172 in Acute Stroke Treatment Classification (Adams et al., 1992). Proportions of missing data are noted in Supplemental Digital Content S3 (available at: <http://links.lww.com/TLD/A72>).

^aFor continuous variables, means, interquartile ranges, and Cohen's *d* effect sizes are provided. Interpretation of Cohen's *d* effect sizes: 0.2 = "small"; 0.5 = "medium"; 0.8 = "large."

^bFor categorical variables, the numbers and percentages of participants and ϕ effect sizes are provided. Interpretation of ϕ effect sizes: 0 is no relationship, 1 is a perfect positive relationship, and -1 is a perfect negative relationship.

^cFor ordinal variables, medians, median absolute deviations, and Cliff's delta effect sizes are provided. Interpretation: 0.11 = "small"; 0.28 = "medium"; 0.43 = "large."

^dNIHSS scores were not available for eight participants who were transferred into the CVD cohort from the AD/MCI cohort. Percentages for NIHSS scores are therefore calculated out of only 149 participants (low cognition: *N* = 85; high cognition: *N* = 64).

Table 2. Participant neuropsychological assessment

Variable ^a	Mean (IQR) Range		Cohen's d^b
	Low Cognition	High Cognition	
Domain: Executive and speed of processing			
SDMT (z-score)	-1.03 (1.21) -3.80 to 1.19	-0.02 (1.20) -1.64 to 2.18	1.13
TMT A (z-score)	-1.39 (2.22) -12.03 to 1.51	0.03 (1.33) -5.46 to 1.5	0.77
TMT B (z-score)	-2.71 (3.57) -19.14 to 1.48	-0.41 (1.30) -6.2 to 1.43	0.76
DKEFS Color-Word: Color naming (scaled score)	6.83 (4.00) 1 to 13	9.78 (2.50) 4 to 14	0.98
DKEFS Color-Word: Word reading (scaled score)	7.85 (4.75) 1 to 14	10.15 (3.00) 3 to 13	0.82
DKEFS Color-Word: Inhibition (scaled score)	7.79 (6.00) 1 to 13	11.15 (3.00) 7 to 14	1.07
DKEFS Color-Word: Switching (scaled score)	7.99 (6.00) 1 to 15	11.33 (2.75) 5 to 14	1.00
DKEFS Verbal Fluency: Letter (scaled score)	8.58 (5.00) 1 to 19	12.32 (5.50) 7 to 19	0.99
DKEFS Verbal Fluency: Category (scaled score)	8.90 (5.00) 1 to 19	12.25 (5.75) 2 to 19	0.95
Domain: Attention			
Digit Span forward (z-score) (Wechsler, 2011)	0.00 (1.44) -2.31 to 2.47	0.26 (0.95) -1.62 to 2.06	0.29
Digit Span backward (z-score) (Wechsler, 2011)	-0.04 (0.69) -2.07 to 3.64	0.38 (1.16) -1.21 to 2.21	0.51
Digit Span total (scaled score)	9.79 (3.25) 5 to 19	11.31 (2.00) 6 to 19	0.61
Domain: Memory			
RAVLT immediate recall A1-A5 trials (z-score)	-0.79 (1.19) -3.43 to 1.99	0.68 (1.63) -1.35 to 3.19	1.34
RAVLT delayed recall A7 trial (z-score)	-0.92 (1.74) -2.93 to 2.92	0.45 (1.10) -2.27 to 2.92	1.20
RAVLT recognition hits (z-score)	-1.44 (3.25) -7.53 to 1.15	0.09 (1.51) -3.46 to 1.15	0.85
BVMTR immediate recall (t-score)	34.16 (14.00) 20 to 66	45.75 (17.00) 26 to 66	1.05
BVMTR delayed recall (t-score)	35.80 (15.75) 20 to 66	49.80 (16.50) 29 to 67	1.24
BVMTR recognition discrimination (percentage of participants scoring below 16th percentile) ^c	52.17%	21.54%	$\phi = -0.314$
Domain: Visuospatial			
WASI-II Matrix Reasoning (t-score)	47.04 (17.00) 25 to 71	55.58 (10.50) 28 to 76	0.82

(continues)

Table 2. Participant neuropsychological assessment (*Continued*)

Variable ^a	Mean (IQR) Range		Cohen's <i>d</i> ^b
	Low Cognition	High Cognition	
Judgment of Line Orientation (split-half, scaled score)	11.30 (6.00) 6 to 17	12.58 (3.50) 5 to 17	0.43
VOSP Incomplete Letters (<i>z</i> -score)	-0.05 (1.37) -3.37 to 0.74	0.25 (0.83) -2.28 to 0.74	0.35
Domain: Language			
BNT 15-item version (<i>z</i> -score)	0.16 (1.00) -4.00 to 1.00	0.67 (1.00) -1.00 to 1.00	0.57
TAWF Verb Naming (<i>z</i> -score)	-0.58 (1.67) -4.92 to 1.40	0.32 (1.05) -2.81 to 1.40	0.63
BDAE-III Semantic Probe (raw score)	58.02 (2.00) 52 to 60	59.00 (1.00) 53 to 60	0.65
WASI-II Vocabulary (split half, <i>t</i> -score)	52.87 (12.00) 26 to 80	62.88 (19.00) 39 to 80	1.00

Note. BDAE-III = Boston Diagnostic Aphasia Examination—Third Edition (Goodglass et al., 2001); BNT = Boston Naming Test (Mack et al., 1992); BVMT-R = Brief Visuospatial Memory Test—Revised; DKEFS = Delis-Kaplan Executive Function System (Delis et al., 2001); RAVLT = Rey Auditory Verbal Learning Test (Strauss et al., 2006); SDMT = Symbol Digit Modalities Test (Smith, 1991); TMT = A & B Trail Making Test (Spreen & Strauss, 1998); TAWF = Test of Adolescent/Adult Word Finding (German, 1990); VOSP = Visual Object and Space Perception Battery (Warrington & James, 1991); WASI-II = Wechsler Abbreviated Scale of Intelligence—Second Edition (Wechsler, 2011).

^aUsing the published values for each test, raw data were converted to age- and education-adjusted standardized scores for group comparisons.

^bInterpretation of Cohen's *d* effect sizes: 0.2 = "small"; 0.5 = "medium"; 0.8 = "large."

^cBecause of the high number of participants performing at ceiling (>16th percentile), the reported percentage of participants below ceiling and used Pearson's Chi-square test and the phi coefficient to compare these values. Interpretation of ϕ effect sizes: 0 is no relationship, 1 is a perfect positive relationship, and -1 is a perfect negative relationship.

Clinical descriptive data

Data extracted from case histories, study questionnaires, and clinical neurology examinations captured electronically in the ONDRI electronic case report forms and reported subsequently in the ONDRI baseline clinical data release were used to describe the CVD cohort. Vascular risk factors (e.g., smoking, diabetes), National Institutes of Health Stroke Scale (NIHSS; Ortiz & Sacco, 2014) scores from the ONDRI screening visit at the time of study enrollment, stroke history (e.g., duration), and the acute ischemic stroke subtype classification made by the neurologist using the Trial of Org 10172 in Acute Stroke Treatment scale (TOAST; Adams et al., 1992) are reported in Table 1. Both groups had a similar distribution of stroke etiology (i.e., TOAST

scores). The majority of participants in both groups (96.5% in the "low" group and 98.4% in the "high" group) showed no evidence of aphasia at study enrollment, as determined by an experienced stroke neurologist, using the NIHSS. It should be noted that NIHSS data were not available for eight participants who were enrolled originally into the AD/MCI cohort based on a clinical diagnosis of AD and who were transferred to the CVD cohort when their ONDRI neuroimaging protocol results revealed evidence of stroke.

Neuroimaging descriptive data

Data from the ONDRI neuroimaging data set were used to quantify lesion size and white matter hyperintensity (WMH) burden for descriptive purposes. Briefly, structural

MRI (3 T) was acquired at 3+ month post-stroke event (with the exception of two participants who were ~2 months post-stroke) and included the following contrasts: T1-weighted, fluid-attenuated inversion recovery (FLAIR), proton density-weighted and T2-weighted, acquired using protocols consistent with the Canadian Dementia Imaging Protocol (Duchesne et al., 2019). Magnetic resonance imaging was evaluated by a neuroradiologist and processed using previously published methods (Ramirez et al., 2020) for quantification of stroke lesions, lacunes, WMHs, ventricular cerebrospinal fluid, and total intracranial volumes. These summary neuroimaging data including stroke location and lesion size are presented in Table 3. Described elsewhere, all neuroimaging data were subjected to quality assurance (QA)/control processes before being released as part of the ONDRI data set (Scott et al., 2020). The “low” cognition group had higher median values for WMH burden and total lacune volume than the “high” cognition group, but all effects were small in magnitude. Although artery circulation involvement patterns were similar between the two groups, the “high” cognition group had a higher proportion of participants with right hemisphere lesions.

Spoken discourse sampling and recording

Spoken language samples were elicited as part of the larger ONDRI Neuropsychology Platform assessment battery using a variety of elicitation tasks. For this analysis, we intentionally restricted our study to language samples elicited using a single task, the “Argument” picture sequence stimuli from Nicholas and Brookshire (1993). This standardized narrative elicitation stimulus is well reported in the aphasia literature and also was used previously for language sampling in neurodegenerative disorders (Murray, 2000; Murray & Lenz, 2001; Roberts & Post, 2018) and in typically aging older adults (Wright et al., 2014). Our decision to use a language sample generated by a single stimulus was motivated both practically and scientifically. First, although both of the Nicholas and Brookshire picture sequence elicitation stimuli (i.e., “Argument” and “Directions”) were included in the ONDRI protocol, they were administered at alternating time points longitudinally to minimize learning effects; hence, only the “Argument” stimuli samples were collected at baseline. Previous research showed that these two picture sequence stimuli elicit equivalent data for measures

Table 3. MRI-derived volumetrics

	Low Cognition		High Cognition		Cohen's d^a
	Median	IQR	Median	IQR	
Total intracranial volume, ml	761.69	801.50	422.88	787.59	0.20
Ventricular cerebrospinal fluid, ml	19.64	38.23	14.63	28.13	0.29
White matter hyperintensities, ml	6.83	13.04	4.64	10.40	0.20
Lacunes, mm ³	161.00	533.00	64.50	327.00	0.32
Stroke lesion volume, ^b ml	7.54	14.93	9.63	15.70	0.26

Note. IQR = interquartile range; MRI = magnetic resonance imaging; ONDRI = Ontario Neurodegenerative Disease Research Initiative. As volumetric measures were not normally distributed, consistent with previous ONDRI publications (Ramirez et al., 2020), only medians and IQRs were reported. In addition, Cohen's d effect sizes are used to assess group differences rather than p values. Data from six participants were not available for this analysis.

^aInterpretation of Cohen's d effect sizes: 0.2 = “small”; 0.5 = “medium”; 0.8 = “large.”

^bReported in $n = 61$ participants with cerebrovascular disease with poststroke cortical lesion volumes greater than 0 (based on parenchymal damage visible on MRI).

similar to those in our proposed discourse model (Roberts, 2014; Roberts & Post, 2018; Wright et al., 2005). Second, we were interested in examining whether a simple picture sequence description task, with high potential for scalability to remote data collection across a broad range of cognitive and motor impairment profiles, was sufficient for discriminating cognitively impaired from cognitively normal for age participants.

The elicitation stimulus for this task contains six black/white pictures (presented on a single page) that depict chronologically ordered events between a husband and a wife who have a disagreement (see Nicholas & Brookshire, 1993, for details). Preceded by the following instructions “I am going to ask you to tell a story. Look at this series of pictures to familiarize yourself with the story,” CVD participants had a 60- to 90-s preview period to review the picture stimulus before being given the following instructions by the examiner: “Now use these pictures to tell me a story in as much detail as you can.” Examiners were allowed to repeat the instructions once if requested by the participant or the participant appeared to not understand the task. There was no maximum time limit for the task. Participants were provided as much time as needed to produce their narrative. Discourse samples were recorded digitally using an AKG 520C head-worn microphone (positioned ~4–6 cm from the mouth opening) connected to a PC laptop via a Scarlett 2i2 USB preamplifier. Audio files were recorded as .wav files in Audacity at a sampling rate of 44,100 Hz (16-bit format).

Transcription, segmentation, and annotation

Researchers (blinded to group allocation) listened to the spoken discourse audio files in Audacity, transcribed the audio recording orthographically, and then segmented the orthographic files consistent with the Systematic Analysis of Language Transcription (SALT Software LLC, 2016) C-unit conventions. In the ONDRI data set, we determine utterance boundaries using primarily syntactic and se-

mantic information, owing to the potential for ambiguous prosody markers in neurodegenerative disorders (e.g., PD). A C-unit was defined as a main clause and its accompanying dependent clauses. Conjoined main clauses were segmented into separate C-units (even when the subject of the second clause was not stated explicitly). For example, the utterance “She stormed out of the house and crashed her car into the tree” was segmented into two utterances, “She stormed out of the house/And [omitted subject] crashed her car into the tree.” In these cases, omitted subjects were not marked as grammatical errors.

All transcribed segmented files were reviewed by a gold standard coder for transcription accuracy (total words and word-by-word transcription accuracy) and segmentation accuracy (number of utterances and utterance boundaries). Once transcription and segmentation accuracies were verified, files were annotated for 13 discourse behaviors that spanned conceptual (e.g., main events) to speech production (e.g., WPM) using a multidomain, linguistic-based discourse analysis approach informed by previous cognitivist theoretical models (Frederiksen et al., 1990; Sherratt, 2007) and experimental studies (e.g., Ash et al., 2017; Marini et al., 2011; Power et al., 2020; Roberts, 2014; Wright & Capilouto, 2012). Discourse behaviors within the applied framework and their definitions are detailed in Table 4. We used a combination of standard and bespoke annotation systems, readable using SALT software Version 18 (Miller & Iglesias, 2018) including standard SALT annotations (SALT Software LLC, 2018a), custom codes (e.g., correct information units [CIUs]), and annotation conventions from the Northwestern Narrative Language Analysis system (Thompson et al., 1995, 2012).

Quality assurance/quality control procedures

Described in detail in McLaughlin et al. (2020), all neuropsychological test data were entered into a central online REDCap database. Audio recordings of spoken

Table 4. Discourse measures descriptions/definitions

Measure	Definition
Productivity	
# Words	Number of full words intelligible in context. Nonword fillers not counted; contractions and common simplifications counted as separate words; proper names, titles, and compound words counted as separate words (Nicholas & Brookshire, 1993)
Words per minute (WPM)	Number of total words ÷ Participant speaking time in minutes (SALT Inc., 2017)
Information content	
Correct information units (CIUs)	Number of words intelligible in context and accurate, relevant, and informative about the picture content (Brookshire & Nicholas, 1994; Nicholas & Brookshire, 1993)
% CIUs	CIUs ÷ # words (Brookshire & Nicholas, 1994; Nicholas & Brookshire, 1993) × 100
CIUs/min	CIUs ÷ Participant speaking time in minutes (Brookshire & Nicholas, 1994; Nicholas & Brookshire, 1993)
% Main events	Proportion of correct narrative main events (Capilouto et al., 2005)
Lexical diversity	
Moving-average type-token ratio (MATTR) ^a	SALT-generated moving-average ratio of different words:total words (SALT Inc., 2017 ^o). Window size = 23 words, based on the number of words in smallest discourse sample (Roberts & Post, 2018)
Syntax	
Mean length of utterance (MLU)	Mean length of utterance in words for intelligible, complete, verbal, task-relevant utterances (SALT Inc., 2017)
% Gram.	C-units ^b without lexical selection or grammar rule violations (Thompson et al., 1995, 2012) ÷ Total intelligible, complete, verbal, task-relevant utterances × 100
Subordination index (SI)	Subordination index composite score; ratio of total number of subject + Predicate clauses:total number of C-units (SALT Software LLC, 2018b)
# of clauses/C-unit ^b	Number of clauses per C-unit (based on the count of main verbs)
Fluency ^a	
Word-level dysfluencies/C-unit	Total number of word, syllable, and sound repetitions plus the total number of initial, middle, and final sound prolongations (SALT Software LLC, 2018a) ÷ Total utterances
# Pauses/C-unit	Number of pauses > 1.5 s ÷ Total utterances
% Maze words/total words	Maze words (i.e., filled pauses, false starts, reformulations, and interjections) ÷ Maze words + nonmaze words ^c

Note. SALT = Systematic Analysis of Language Transcription.

^aFor fluency and MATTR analyses only, SALT-standard word counting rules were applied: Contractions were counted as one word instead of two, and nonword fillers were counted as maze words.

^bC-units differed slightly from SALT coding conventions in that clauses were permitted to have implicit subjects when an otherwise independent main clause was present, e.g., "C He is sitting C and reading the paper."

^cSI differed from # Clauses/C-unit for utterances with infinitive clauses and/or no explicit subject.

discourse samples were stored both in REDCap and on a separate cloud-based, HSREB-compliant server, housed by the High Performance Computing Center in Kingston, Ontario, from which they were accessed securely for the current study. Using methods applied uniformly for all ONDRI data collection platforms, robust QA/quality control (QC) procedures were implemented for all data collection, scoring/preprocessing, and entry processes (see McLaughlin et al., 2020; Scott et al., 2020). In addition, all analyzed/processed data reported in the current study were subjected to an independent multivariate quality evaluation procedure for identifying and investigating potentially erroneous or spurious data points before being included in any statistical analyses (Sunderland et al., 2019).

Research staff involved in the discourse analysis protocol completed additional rigorous trainings that included formal workshops, mentored annotation, and ongoing fidelity checks with targeted retraining as required. Before working with any of the spoken discourse data, research staff were required to meet a minimum accuracy threshold (transcription and annotation) on a discourse training set used in the first author's laboratory (A.R.) that includes discourse samples with varying language and speech intelligibility severities. The threshold for successful training was an intraclass correlation coefficient (ICC) set at .85 times that of the gold standard annotation.

Reliability

Using procedures consistent with other discourse projects in our laboratory (Roberts, 2014; Roberts & Post, 2018), transcription and annotation reliability studies (inter and intra) were conducted on a minimum of 20% of files (randomly selected). Reliability checks were conducted continuously (as transcription and annotation tasks were completed) over the duration of the study in blocks of 40 files. For each block of 40 files, if interrater fidelity for two raters fell below an ICC of .85 for any annotated be-

havior, a review and retraining procedure was triggered that included (a) review and consensus recoding of all variables that had interrater reliability values of less than .85 for all files within a particular reliability assessment block, and (b) targeted retraining to address any systematic annotation errors. This continuous, threshold-based monitoring approach resulted in a different number of files across reliability studies for each discourse variable. Reliability was determined using ICC statistics completed in SPSS V.24 (IBM Corp., n.d.). Reliability statistics for interrater reliability ranged from ICCs of .850 to .999 (with 21.5%–67.7% of files reviewed) and intrarater reliability ranged from ICCs of .924 to 1.0 (with 25.5%–41.1% of files reviewed), with higher ICC values reflecting stronger reliability. Supplemental Digital Content S2 (available at: <http://links.lww.com/TLD/A72>) contains the inter- and intrarater reliability study results by individual discourse variable.

Statistical analyses

Missing data for all variables (descriptive and neuropsychological tests) are presented in Supplemental Digital Content S3 (available at: <http://links.lww.com/TLD/A72>). Statistical analyses were conducted in SPSS V.26 (IBM Corp., n.d.). Discriminant function analysis (DFA) is a multivariate statistical analysis that combines and estimates weights for predictor variables (discourse behavior measures in the current study) in order to maximize the separation of prior specified groups (cognitively impaired “low” vs. cognitively normal for age “high” in the current study). The result is a function and cutoff points that can be used to correctly classify new cases as belonging to either the “low” group or the “high” group. Predictive accuracy can be conveyed as the sensitivity and specificity of the resulting algorithm.

We performed a two-step procedure to determine the minimum set of discourse variables that would maximize separation of the “low” and “high” cognition groups (Huberty & Olejnik, 2006). In Step 1, we entered all

discourse variables (Table 4) into a DFA to determine whether the overall model was significant and to identify potentially redundant variables that could weaken the model stability (i.e., predictor variables with absolute correlation coefficients $>.70$ of which there were none). In Step 2, we reduced the total number of discourse variables in the DFA model by removing all variables that did not differ significantly as a function of group using a multivariate analysis of variance (MANOVA) procedure, with group as the independent variable, and measures in Table 4 as dependent variables ($n = 13$), with age and education as covariates. We intentionally omitted the NIHSS score as a covariate in the final model for two reasons: (1) When included, NIHSS aphasia/dysarthria stroke scores did not change the overall model significance, or the pattern of results, and (2) NIHSS stroke scores for eight participants were missing systematically (owing to a reclassification of clinically diagnosed AD participants to the CVD group following the discovery of infarcts on neuroimaging; see Table 1) and thus including NIHSS score as a covariate resulted in the loss of these participants' data in the analysis. The final MANOVA results resulted in the removal of three discourse variables from the final model. Reducing the number of discourse variables to a minimum set of discriminative features was judged to be important for clinical use in order to reduce the number of discourse analyses inputs required for the discourse function. We subsequently reexamined the discourse DFA model to ensure that the predictive accuracy remained stable (or improved) by reducing discourse variables. For each model, we performed a leave-one-out cross-validation to test the reliability and generalizability of the discriminant function. For the DFA, the prior probability of cognitive impairment was calculated from the percentage of participants with cognitive impairment based on the neuropsychological assessment.

Box's M test for homogeneity of variances was significant ($p < .001$), and Levene's test based on means indicated unequal variances

for total words ($p = .005$), moving-average type-token ratio (MATTR; $p = .048$), and word-level dysfluencies per utterance ($p = .024$). The multivariate effect of each group comparison test was reported as the Pillai's trace statistic. Effect sizes were reported as partial eta square. Univariate outliers with values of more than 3 SD s above/below their group mean (affecting 3.2% of participants) were replaced with that value (i.e., $M \pm 3 \times SD$). This affected 8/2,041 (0.004%) of data points.

RESULTS

The result of the initial DFA model with all 13 discourse variables was significant, Wilks' $\lambda = 0.72$, $\chi^2(13, 157) = 49.29$, $p < .001$. This initial model correctly classified 75.8% of original grouped cases and 70.7% of cross-validated cases following leave-one-out analysis, with a sensitivity of 79.3% and a specificity of 70.8%.

In Step 2 of our analysis, the MANOVA result was significant for group (i.e., "low" vs. "high"), $F(13, 141) = 4.33$, Pillai's trace = 0.26, $p < .001$. Significant differences were found as a function of group for 10 discourse measures: mean length of utterance (MLU), subordination index, mean number of clauses per C-unit, total words, CIUs/min, WPM, MATTR, percentage of maze words, word-level dysfluencies per utterance, and proportion of main events. For all variables, the "low" group was more impaired (i.e., lower values, with the exception of pauses, mazes, and fluency measures where higher scores reflect greater impairment). The MANOVA results with age and education as covariates are reported in Table 5. As a result of this step, we removed the percentage of grammatical C-units, percentage CIUs, and number of pauses per C-unit from the discourse DFA model.

The overall discriminant function result for the final model was again significant, Wilks' $\lambda = 0.73$, $\chi^2(10, 157) = 47.50$, $p < .001$. The revised model correctly classified 78.3% of original grouped cases and 69.4% of

Table 5. Multivariate analysis of variance results

Variable	Descriptive Statistics, Mean (SD) 95% CI [L, U]		<i>df</i>	<i>F</i>	η_p^2
	Low Cognition	High Cognition			
# Words	120.61 (49.63) [110.33, 130.89]	164.17 (67.08) [147.55, 180.79]	1, 155	17.27***	.10
WPM	139.14 (35.46) [131.80, 146.48]	155.33 (32.14) [147.37, 163.30]	1, 155	10.16**	.06
% CIUs	67.5 (13.4) [64.7, 70.3]	72.1 (11.4) [69.2, 74.9]	1, 155	3.04	.02
CIUs/min	93.87 (29.45) [87.77, 99.97]	111.55 (27.03) [104.85, 118.25]	1, 155	14.44***	.09
% Main events	52.5 (22.1) [47.9, 57.1]	63.7 (21.3) [58.5, 69.0]	1, 155	6.83**	.04
MATTR	0.818 (0.048) [0.808, 0.828]	0.842 (0.039) [0.833, 0.852]	1, 155	10.03**	.06
MLU	6.48 (1.50) [6.17, 6.79]	7.22 (1.18) [6.92, 7.51]	1, 155	8.83**	.05
SI	1.03 (0.23) [0.98, 1.08]	1.11 (0.20) [1.06, 1.16]	1, 155	5.10*	.03
# Clauses/C-unit	1.33 (0.26) [1.28, 1.39]	1.45 (0.21) [1.40, 1.51]	1, 155	7.38**	.05
% Gram.	79.1 (17.3) [75.5, 82.7]	81.6 (13.2) [78.3, 84.8]	1, 155	1.27	.01
Word-level dysfluencies/C-unit	0.146 (0.178) [0.109, 0.183]	0.092 (0.114) [0.063, 0.120]	1, 155	5.72*	.04
Maze words/total words	0.058 (0.046) [0.049, 0.068]	0.044 (0.049) [0.032, 0.056]	1, 155	4.82*	.03
# Pauses/C-unit	0.195 (0.232) [0.147, 0.243]	0.141 (0.173) [0.098, 0.184]	1, 155	2.62	.02

Note. CIUs/min = number of correct information units per minute; % CIUs = percentage of correct information units; # Clauses/C-unit = average number of clauses per C-unit; % Gram. = percentage of grammatical C-units; % Main events = percentage of correct main events; MATTR = moving-average type-token ratio; Maze words/total words = proportion of maze words divided by total words; MLU = mean length of utterance (in words); SI = subordination index; # Pauses/C-unit = number of pauses 1.5 s or more per C-unit; Word-level dysfluencies/C-unit = total repetitions (word, syllable, and sound) and prolongations (initial, middle, and final) divided by the number of C-units; # Words = number of full, intelligible words; WPM = words per minute.

^aInterpretation of η_p^2 effect sizes: 0.01 = small; 0.06 = medium; 0.14 = large (Cohen, 1988).

* $p < .05$.

** $p < .01$.

*** $p \leq .001$.

cross-validated cases following leave-one-out analysis. The optimized model's sensitivity was 77.2% and its specificity was 80.0%. The area under the receiver operating characteristic (ROC) curve (AUC) was AUC = 0.821, suggesting excellent classification performance overall (Mandrekar, 2010). For simplicity, the sensitivity/specificity table and ROC curve for

the final model only are presented in Figure 1. Canonical standardized and unstandardized discriminant function coefficients for both the original and final models are presented in Table 6. Comparing the original and final discourse DFA models, the removal of the three nonsignificant discourse variables increased the model's overall accuracy and specificity.

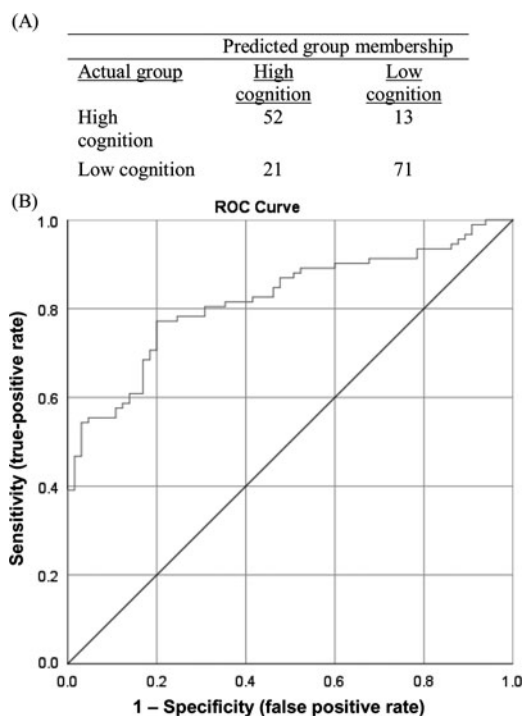


Figure 1. Optimized discriminant function classification performance discriminant function classification results. (A) The ROC curve depicts sensitivity versus specificity trade-offs at each potential cutoff point. The x -axis represents the false-positive rate ($1 - \text{specificity}$ of the discriminant function), and the y -axis represents the true-positive rate (sensitivity of the discriminant function). Curves left of the diagonal reference line, as found in the present study, indicate greater-than-chance (50%) classification accuracy. (B) Discriminant function classification results obtained using the optimal cutoff value for classifying new cases (0.249284). Centroid values, which reflect the mean discriminant scores for each group, were 0.722 for the high cognition group and -0.510 for the low cognition group. ROC = receiver operating characteristic.

DISCUSSION

Our results show that a multidomain discourse analysis approach, conducted on spoken narratives elicited from a standardized picture sequence, is able to discriminate individuals with CVD and cognitive impairment from those who are cognitively

Table 6. Canonical discriminant function coefficients: All variables

Measure	Standardized	Unstandardized
All variables included		
# Words	0.694	0.012
WPM	-1.062	-0.031
% CIUs	-0.683	-5.421
CIUs/min	1.690	0.059
% Main events	0.204	0.937
MATTR	0.319	7.234
MLU	0.254	0.184
SI	0.053	0.246
# Clauses/C-unit	-0.100	-0.414
% Grammatical	-0.067	-0.427
Word-level dysfluencies/C-unit	-0.174	-1.120
Maze words/total words	-0.169	-3.589
# Pauses/C-unit	0.184	0.877
Constant	-	-6.323
Canonical discriminant function coefficients:		
Variables significant in the MANOVA that were included in the final discriminant model		
# Words	0.656	0.011
WPM	-0.366	-0.011
CIUs/min	0.674	0.024
% Main events	0.161	0.739
MATTR	0.299	6.795
MLU	0.280	0.203
SI	0.060	0.278
# Clauses/C-unit	-0.087	-0.362
Word-level dysfluencies/C-unit	-0.203	-1.309
Maze words/total words	-0.133	-2.824
Constant	-	-9.323

Note. CIU = correct information unit; MANOVA = multivariate analysis of variance; MATTR = moving-average type-token ratio; MLU = mean length of utterance; SI = subordination index; WPM = words per minute.

normal for age who also have CVD. The discourse impairments observed in the cognitively impaired group (“low”) appear to be independent of age, education, or aphasia differences between these groups. The sensitivity (77.2%) and specificity (80.0%) values for the final discourse model suggest that a weighted function comprised solely of

spoken language measures correctly classified individuals with cognitive impairment, while minimizing the misclassification of individuals who were cognitively normal for age. The resulting discourse model and optimal cutoff point approaches conventional clinical standards for acceptable sensitivity (>80%) and exceeded conventional thresholds for specificity (>60%) for detecting cognitive impairment poststroke (Stolwyk et al., 2014).

These findings contribute significantly to the existing literature in a number of important ways. First, these data represent the largest, and most comprehensive, published characterization of spoken discourse abilities in a CVD cohort with cognitive impairment, which is important, given that vascular-related dementias are second in prevalence only to Alzheimer's disease pathologies. Second, our findings underscore the value of spoken language for identifying people with CVD who have cognitive impairment and are thus at an increased risk for developing VaD. This is important because spoken language is an ecologically valid, low patient burden assessment method that can potentially augment, or replace, standard neuropsychological measures and cognitive screening protocols for detecting early-stage dementia. Finally, although these results will benefit from further replication studies and also validation in longitudinal data sets, we provide preliminary evidence that the unstandardized coefficients for the final model (Table 6), along with data analyzed from clinical discourse samples, can be used to compute a single "discourse score" for classifying individuals with CVD as either impaired or cognitively normal for age.

In the current study, individuals in the "low" group were more impaired on measures of productivity (words, WPM, C-unit length); information content and efficiency at the lexical (CIUs/min) and event concept level (% main events); lexical diversity (MATTR); syntax complexity (clauses/C-unit, and MLU); and fluency, with an increased percentage of maze words and word-level dysfluencies suggestive of language planning

deficits (Fagan, 1982; Goldman-Eisler, 1972; Levelt, 1983). The standardized coefficient data (Table 6) underscore the importance of efficiency measures (WPM and CIUs/min) in separating the "low" and "high" cognition groups relative to other discourse variables in the classification function.

Although impairments in productivity (Hier et al., 1985; Mendez & Ashla-Mendez, 1991) and information content (Laine et al., 1998; Mendez & Ashla-Mendez, 1991; Vuorinen et al., 2000) have been shown in the previous literature, our results from the "low" cognition group suggest that discourse impairments in those with CVD and cognitive impairment, who are at an elevated risk of developing VaD, are more widespread than previously shown, affecting multiple levels within discourse planning and production. Importantly, these deficits were not observed in participants in the CVD cohort who were cognitively normal for age. In the current study, utterance complexity but not grammatical accuracy also separated the two groups. These findings differ from those of Hier et al. (1985), who reported reduced sentence complexity in participants with advanced stroke-related dementia but not in early-stage participants.

There are some key differences that limit comparing extant literature with our findings. First, whereas we used a picture sequence description task, others have used single picture descriptions such as the "Cookie Theft" stimulus (Hier et al., 1985; Mendez & Ashla-Mendez, 1991; Vuorinen et al., 2000) and conversational interviews (Laine et al., 1998). Single picture stimuli, such as the "Cookie Theft" stimulus, may mask syntax and grammatical impairments, given that speakers can depend on simpler syntax structures to convey the event structure in a single scene than the language formulation demands required to cast narratives that include a series of temporally unfolding events.

Critically, previous studies have used less robust criteria to diagnose cognitive impairment in the context of CVD. Hier et al. (1985) used the presence of cortical

infarcts and a clinical history of “intellectual” decline to diagnose cognitive impairment, whereas others used CT evidence of stroke and the Mini Mental Status Exam (Laine et al., 1998; Mendez & Ashla-Mendez, 1991; Vuorinen et al., 2000), a measure with questionable sensitivity/specificity for detecting cognitive impairment poststroke (Stolwyk et al., 2014). In the current study, we used a conservative neuropsychological-based criteria (impairment in two plus tests within a domain) for separating the CVD cohort into impaired and cognitively normal for age groups, which increases the diagnostic rigor of our participant classification (Stolwyk et al., 2014; Zaidi et al., 2020) and thus confidence that our results present an accurate portrait of VCI spoken language impairment. Although data included in the current study do not allow us to make direct linkages with underlying lesion location or neural connectivity disruptions, this study is an important first step in generating informed hypotheses that can be tested in the larger ONDRI data set. Doing so is important because previous studies have linked specific disruptions of white matter pathways to distinct spoken language profiles in neurodegenerative disorders (e.g., Marcotte et al., 2017) and in poststroke populations (e.g., Alyahya et al., 2020).

Our discourse analysis is remarkable for its comprehensive multidomain approach and methodological rigor (Stark et al., 2020). This investigation underscores the critical importance of multidomain discourse analysis approaches that take an expanded view of discourse abilities informed by cognitive models (Frederiksen et al., 1990; Sherratt, 2007) and thus may be sensitive to nuanced cognitive changes. Although less commonly applied in the discourse literature and in clinical practice, in previous studies such multidomain approaches demonstrated the ability to detect subtle manifestations of cognitive and language impairments in neurodegenerative disorders (e.g., Roberts, 2014; Roberts & Orange, 2013, for review; Ash et al., 2012, 2013, 2017; Murray, 2000) and

in acquired disorders (Cannizzano & Coelho, 2013; Coelho et al., 1995; Marini et al., 2011; Power et al., 2020; Pritchard et al., 2018). A frequently cited limitation of comprehensive discourse analysis approaches is that they are time intensive. Continued research identifying minimal sets of clinically meaningful discourse variables that can discriminate groups, predict disease progression, and measure treatment response is a critical step toward improving the feasibility of discourse as an ecologically valid clinical measure. Moreover, recent and rapidly evolving advances in machine learning for transcription and discourse annotation are moving the field ever closer to clinic-friendly, feasible, and high-fidelity automated solutions (Fraser et al., 2014, 2019; Fromm et al., 2020; Perez et al., 2018). Increasing the feasibility and accuracy of such tools depends critically on robust, rigorously annotated data sets from well-characterized clinical cohorts (Fraser et al., 2019) and as such highlights the importance of the ONDRI study, and foundational spoken language data repositories such as AphasiaBank (MacWhinney et al., 2011), DementiaBank (Becker et al., 1994), and the TalkBank system broadly (<https://childes.talkbank.org/>), that provide open data resources for the development of novel machine learning transcription and clinical assessment tools.

When interpreting these data, several factors should be considered. For one, although the ONDRI neuropsychological assessment protocol was extensive, to reduce participant testing burden, given the expansive nature of the protocol, it did not include a comprehensive aphasia battery. As such, the severity of aphasia when present cannot be quantified or subtyped. That noted, the NIHSS aphasia score did not account for group variance in discourse performance in any significant way and when removed as a covariate did not change our MANOVA results. Moreover, all participants were able to complete a rather rigorous neuropsychological assessment battery, without significant concern, suggesting any aphasia or dysarthria was minimal in severity. Also of note, our CVD cohort

was skewed toward men and represented a narrow cultural/ethnic spectrum. The male skew in our data is not atypical in VCI research (O'Neill et al., 2019), and there is little evidence for sex effects on structured spoken discourse tasks such as those in the current study (Mackenzie, 2000; Roberts & Post, 2018). Notwithstanding this, the discourse model will benefit from further validation in more diverse speaker samples and in a broader range of dialects.

It is important to consider that we used a single elicitation genre (i.e., picture sequence description) and thus our analysis is limited to more structural and linguistic variables. Understanding cross-elicitation task effects is important in spoken language research. Moreover, sampling across elicitation methods with differing cognitive-linguistic demands can reveal meaningful patterns of spoken language impairments (Alyahya et al., 2020; Roberts & Orange, 2013; Roberts-South et al., 2012; Shadden, 1998; Shadden et al., 1991). Notwithstanding this, our task choice is consistent with researchers in neurodegeneration who reported that a single spoken language sample, elicited from a picture stimulus, is sufficient for discriminating those with cognitive and language impairments from cognitively normal aging adults (Ash et al., 2013; Drummond et al., 2015; Duong et al., 2005).

In addition to task effects, the effect of language sample size remains unclear in our data. Our task generated a mean language sample size of 121 words in the "low" group and 160 in the "high" group. Several studies have examined the stability of discourse measures (particularly WPM and CIUs), with the general consensus that larger samples (~300–400 words) collected across multiple samples yield more stable measures in both typical adults and those with aphasia resulting from stroke (e.g., Boyle, 2014; Brookshire & Nicholas, 1994). However, overall, there is a paucity of literature on the reliability and stability of discourse measures broadly across domains and in neurodegenerative diseases specifically. That said, Ash et al. (2013)

reported rigorous and reproducible findings using a single narrative task that produced language samples, similar in length to those in our study, that were comparable with longer narratives elicited using a wordless picture book. Although not fully overlapping, a number of measures reported in the Ash et al. study overlap in construct to those in the current study including markers of speech fluency, utterance length, number of dependent clauses as a measure of syntax complexity, grammaticality, and lexical diversity. On whole, this research underscores (as have other recent publications, e.g., Pritchard et al., 2018; Stark et al., 2020) the importance of considering sample characteristics when using discourse in clinical contexts and highlights the critical need for more methodological research identifying optimal language sample sizes, and tasks, across disorders, as this issue remains far from resolved. Still yet, we acknowledge this as a potential limitation in our work.

CONCLUSIONS

On whole, our work is clinically applicable to neurologists, speech-language pathologists, and neuropsychologists who work with individuals following stroke and those at risk for VaD. These foundational results underscore the value of multidomain discourse analysis approaches and highlight the potential use of spoken language as a biomarker of cognitive impairment in CVD. The hope is that this research will advance machine learning and clinical tools for detecting early cognitive decline. In our future work, we intend to examine spoken discourse endophenotypes in the longitudinal CVD data and extend our work cross-sectionally across cohorts in the ONDRI study. With both academic and industry partners, we are currently leveraging the ONDRI data set, using data-driven approaches, to address questions around optimal discourse sampling and the stability of these measures over time to produce guidance for collecting robust and reproducible discourse data across different

clinical populations, severities, and measures, including the reproducibility of findings from the current study. This is of particular importance in neurodegenerative disorders generally, and for longitudinally studies specifically, where issues of fatigability, disease progression, and behavioral concerns may (1) limit the ability to collect longer duration or multiple discourse samples, and (2) introduce noise that affects test-retest stability

of measures. Importantly, there may be opportunities to optimize dementia detection by combining spoken language analyses with other clinical measures such as select cognitive tests or neuroimaging. It will also be critical, as we progress this research, to establish important linkages to impairments in specific cognitive domains and underlying neural changes in order to advance theories of discourse planning and production.

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