Exploring Effects of Type 2 Diabetes on Cognitive Functioning in Older Adults

Sophie E. Yeung, Ashley L. Fischer, and Roger A. Dixon
University of Alberta

Type 2 diabetes may be associated with exacerbated aging-related declines in cognitive neuropsychological performance. The authors examined whether such effects are systematic (i.e., broadly distributed across domains or domain-specific) or moderated by age (i.e., varying across age within older adults). The authors assembled recent cross-sectional data from the Victoria Longitudinal Study (VLS) Sample 3 (Wave 1; initial n = 570; initial age = 53–90 years). Using a comprehensive, multidimensional spectrum of cognitive neuropsychological tests, the authors examined performance differences by diabetes status (diabetes group vs. healthy controls) and age (young-old vs. old-old). Our results showed that healthy controls significantly outperformed the diabetes group only on markers of executive functioning and speed. Notably, the diabetes-related effects were robust across the two late-life age groups. Future research examining longitudinal changes is recommended.

Keywords: Type 2 diabetes, cognitive aging, executive function, speed

Type 2 diabetes is a chronic metabolic condition characterized by abnormally high blood glucose levels as a result of insufficient usage of insulin. Formerly known as Non-Insulin Dependent Diabetes Mellitus or adult-onset diabetes, its prevalence significantly increases across adulthood, typically affecting individuals over the age of 40 years (Votey & Peters, 2005). Recent estimates on the prevalence of diabetes (Type 1 and Type 2) have indicated diagnosis rates for adults over age 60 at about 12% in Canada (Health Canada, 2002) and 20% in the United States (National Institute of Health, 2005). Approximately 90% of these cases are Type 2. Associated with Type 2 diabetes are increased risk of hypertension, stroke, and cerebrovascular disease (e.g., Awad, Gagnon, & Messier, 2004; Messier, 2005; Reunanen, Kangas, Martikainen, & Klaukka, 2000). These potential comorbidities have been shown to affect neural integrity and cognition, especially when coexistent with diabetes (Hassing, Hofer, et al., 2004). Recent literature has reported a relationship between diabetes and an earlier or accelerated decline in cognition (e.g., Awad et al., 2004; Hassing, Grant, et al., 2004; Hassing et al., 2003), including a twofold increase in the risk of dementia (Nilsson, 2006).

Few studies have examined whether adverse cognitive effects of diabetes are broad or selective across domains, or whether such effects differ across a broad age band of older adults. We explore these issues with a relatively healthy and generally cognitively intact sample of 53–90 year-old adults tested on multiple domains of cognitive neuropsychological performance. Specifically, our database includes multiple indicators of the key domains represented (often separately) in the literature: episodic and semantic memory, neurocognitive speed, executive functioning, fluency, and global cognitive competence. This comprehensive approach is designed to contribute to resolving some of the mixed patterns of results across studies varying in cognitive domains, measures, and age groups represented.

Although the general trend is for diabetes-related deficits in performance, discrepant results are common (Nilsson, 2006). First, verbal episodic memory is typically (but not uniformly) affected in diabetes patients (Arvanitakis, Wilson, Bienias, Evans, & Bennett, 2004; Messier, 2005; Ryan & Geckle, 2000; Wahlson, Nilsson, & Fastbom, 2002), extending well-known patterns of normal aging-related decline (e.g., Dixon et al., 2004). These deficits have been seen predominantly in adults over the age of 70 (Messier, 2005), and for measures of immediate verbal memory (e.g., word list recall; Awad et al., 2004). Notably, Hassing, Grant, et al. (2004) found no diabetes-related cognitive performance deficits at baseline but observed accelerated longitudinal decline in episodic memory (and speed) for the diabetes group. Second, diabetes-related slowing has been observed with a variety of speeded tasks, especially those measuring basic reaction time or perceptual speed (e.g., Arvanitakis, Wilson, & Bennett, 2006; Awad, 2004; Fontbonne, Berr, Ducimetière, & Alpérovitch, 2001; Messier, 2005). However, Messier’s (2005) review indicated that less than half the included studies actually reported diabetes-related slowing. We include indicators of three main domains of neurocognitive speed: reaction time, perceptual speed, and a unique set of semantic speed measures. Third, selected measures of executive functioning have produced diabetes-related performance deficits in some (but not all) studies (Awad et al., 2004; Messier, 2005; Ryan & Geckle, 2000; Stewart & Liolitsa, 1999). Because executive functioning may involve multiple underlying processes or dimensions (de Frias, Dixon, & Strauss, 2006; Miyake, Freidman,
Emerson, Witzki, & Howerton, 2000), it may be especially sus-
cceptible to task-related selection effects in special population re-
search (Nilsson, 2006). Our database taps multiple aspects of
executive functioning (i.e., inhibition, shifting, speed). Fourth,
some studies have focused on general measures of global cognition
with diabetes-related deficits both observed (e.g., Hassing et al.,
2003) and not found (e.g., Arvanitakis, Wilson, & Bennett, 2006;
Fontbonne et al., 2001). We use and report global cognition results
descriptively only.

The exact neuroanatomical or neurochemical effects of Type 2
diabetes on cognitive performance are relatively unknown. One
study suggests that frontal structures may be affected by diabetes
sequelae and may therefore be associated with occasionally ob-
served deficits in episodic memory recall, verbal fluency, and
executive functioning (Wahlin et al., 2002). Additionally, reduced
volumes of the amygdala and the hippocampus in diabetes patients
may underlie deficits associated with learning and memory (den
Heijer et al., 2003). A recent report on MRI abnormalities and

Two additional methodological features should be noted. First,
our diabetes patients report that their cases are relatively mild or
moderate (97.56%), and that their conditions are controlled by oral
medication (39.02%), insulin (7.32%), diet and exercise (24.39%),
or a variety of other combinations (19.53%). Accordingly, this
diabetes group supplements those in the literature comprised of
relatively severe patients from nursing homes or health clinics
(e.g., Arvanitakis et al., 2004). By examining community-dwelling
volunteers to a large-scale project, the present sample may be more
representative of current early or well-controlled Type 2 diabetes
populations in North America. Arguably, for more severe cases,
cognitive deficits may be attributed to disease severity, neurolog-
ical sequelae, or multiple comorbid conditions (Nilsson, 2006).
Second, because previous studies are each characterized by rela-
tively few (and nonoverlapping) cognitive measures, our analyses
are conducted at the level of each measure, but clustered within
cognitive domains. Regarding the first research question, we ex-
pected significant diabetes-related differences in performance on
episodic memory, verbal fluency, and neurocognitive speed, but
not semantic memory. The mixed results in research on executive
functioning in diabetes and normal aging do not support a strong
hypothesis. Regarding age differences, we hypothesized (in the
absence of previous research) that the group differences in cogni-
tive performance will be more pronounced in the old-old adults.

Method

The Victoria Longitudinal Study (VLS) is a multicohort epide-
miological study of biomedical, health, cognitive, and neurocog-
nitive aspects of aging. Three independent samples of initially
healthy older adults are followed at 3-year intervals (see Dixon &
de Frias, 2004).

Participants

The base participants were from the first wave (2002–03) of
VLS Sample 3 (n = 570, age range = 53–90 years; M age = 68.29
years, SD = 8.60). Data from an in-progress second wave are
unavailable. A strict sequential procedure for selection and exclu-
sion of participants in two groups (Type 2 diabetes and control)
was adopted. Inclusion into the diabetes group was based on a
three-step diagnosis flowchart, including required confirmatory
information from all three sequential sources. First, all diabetes
patients self-reported (a) a formal diabetes diagnosis, (b) an adult
onset age (over 31), and (c) treatment or control practices (i.e.,
diet, exercise, oral medication, insulin, or a combination). Second,
the actual objective medications of the diabetes patients were
checked concurrently for the presence of relevant drugs (e.g.,
metformin, glyburide, tolbutamide, glitazide, and pioglitazone
hydrochloride). Third, all surviving diabetes patients were con-
tacted three years after the present testing for confirmation of
self-reported diabetes diagnoses. Although the VLS does not have
access to additional diabetes-confirming medical information (i.e.,
blood glucose level above 6.0mmol/L at baseline, or elevated
HbA1c level), our three-step diagnostic procedure goes beyond
the frequently used and validated self-report classifications (e.g.,
Arvanitakis, Wilson, Li, et al., 2006; Connolly, Unwin, Sherriff,
Bilous, & Kelly, 2000; Kriegsman, Penninx, van Eijk, Boeke, &
Deeg, 1996; McNeely & Boyko, 2004; Midthjell, Holmen, Bjørndal,
ratings of their health on 5-point scales (1 very poor health relative to a perfect state, $F(1, 461) = 34.13, p < .000$, partial $\eta^2 = 0.069$ ($M_D = 2.39, SD_D = 0.86$; $M_C = 1.69, SD_C = 0.71$), and relative to others their own age, $F(1, 461) = 17.33, p < .000$, partial $\eta^2 = 0.036$ ($M_D = 2.00, SD_D = 0.78; M_C = 1.50, SD_C = 0.68$). Given the chronic illness for which they were selected into this study, these perceptions accurately reflect their different overall health status.

We further characterized the groups using VLS physiological measures (see MacDonald, Dixon, Cohen, & Hazlitt, 2004). Body mass index (BMI; kg/m$^2$) was significantly higher in diabetes participants, $F(1, 459) = 29.99, p < .000$, partial $\eta^2 = 0.061$ ($M_D = 30.20, SD_D = 4.65; M_C = 26.46, SD_C = 3.97$). Eight readings of blood pressure (mmHg) were averaged across four testing sessions. Whereas no group differences were observed for diastolic blood pressure ($M_D = 77.35, SD_D = 9.20; M_C = 75.06, SD_C = 8.89$), mean systolic blood pressure in the diabetes group was significantly higher than controls, $F(1, 444) = 14.38, p < .000$, partial $\eta^2 = 0.031$ ($M_D = 134.14, SD_D = 15.27; M_C = 125.21, SD_C = 13.69$). Potential diabetes-related visual acuity complications were assessed using the Close Vision task (Snellen fractions), but no significant differences were observed. Comparisons of audition (using a test of audio acuity, dB) also showed no significant group differences. As noted earlier, we assessed global cognitive competence using the standard 18-item MMSE (Folstein et al., 1975). Scores were generally high and clinically insignificant for both groups. Overall, the diabetes participants were aware of their chronic condition and calibrated their personal health evaluation accordingly, but they were not substantially inferior in other health, sensory, and physiological characteristics. Final demographic and physiological characteristics of the age (YO, 53–70 years; old-old, OO, 71–90 years) X diabetes status (diabetes and controls) groups are reported in Table 1.

Measures

**Episodic memory.** First, the VLS word list recall task consisted of the immediate free recall of two standardized lists of 30 words, each including six words from each of five taxonomic categories (e.g., Dixon et al., 2004; Hultsch, Hertzog, Dixon, & Small, 1998). The score was the average of the number of words recalled from the two lists. Second, the Rey Auditory Verbal Learning Test (RAVLT; see Vakil & Blachstein, 1993) required that a word list (15 nouns; List A) was read to the participant, followed by free recall, in each of five trials (Trial A1-A5). Next, for Trial B, an interference list of 15 different nouns was followed by free recall. Next, the words from List A (Trial A6) were recalled. Raw scores from Trial B (acquisition) and Trial A6 (retention) were used. Third, we administered six standardized structurally equivalent story memory tests (with approximately 300 words and 60 propositions within 24 sentences), used in the VLS (e.g., Dixon, Hertzog, Friesen, & Hultsch, 1993; Dixon et al., 2004). Average gist recall was computed and converted to proportions.

**Semantic memory.** First, the vocabulary test consisted of 54 multiple-choice questions from the Educational Testing Service kit of factor-referenced cognitive tests (Ekstrom, French, Harman, & Dermen, 1976). The score was the total number of correct items. Second, fact recall was measured with two different 40-item tests of general information (e.g., from history, arts, sports) derived
from a normed battery (Nelson & Narens, 1980). The two scores were averaged and converted to a percentage of correct (see Hultsch et al., 1998).

Verbal fluency. The VLS fluency tests have three standard parts (Hultsch et al., 1998), including subtests of opposites, figures of speech, and similarities. Participants used a limited time to write as many correct words as possible. Raw scores for each subtest were recorded.

Executive functioning. Four tests of executive functioning have been validated, normed, and analyzed in the VLS and elsewhere (see Bielak, Mansueti, Strauss, & Dixon, 2006; de Frías et al., 2006). First, for the Hayling sentence completion test, initiation speed and response inhibition were tested (Burgess & Shallice, 1997). In two sections requiring speeded responses, participants were read 15 sentences, each with the last word missing. Whereas the goal of the first section was to respond with a word that swiftly completed the sentence, the goal of the second section was to suppress an initial response by providing a word disconnected to the sentence. Recorded were response latencies (ms) and overall standard scores based on correct responses from the two sections. Second, the Brixton spatial anticipation test measured abstraction of logical rules (Andrés & Van der Linden, 2000). Each page of a 56-page booklet contained two rows of five circles, with one of the 10 circles filled in blue. Participants selected which circle they anticipated would be filled on the next page based on the pattern they deduced. A standard score out of 10 (ranging from 1 = impaired to 10 = very superior) was derived. Third, for the three-part Stroop test, participants were required to inhibit their automatic verbal responses in reading printed words and instead name the color in which each word was printed. A standard interference index calculated the difference in response latency between Part A (name the color of the printed dots) and Part C (read the color name when printed in incongruent ink), divided by the initial response latency in Part A alone ([Part C – Part A]/Part A). Fourth, the Color Trails 2 (CT-2) task measured response inhibition without the influence of language. Numbers from 1–25 were randomly arranged twice on a page, once in pink-colored and once in yellow-colored circles. Participants were instructed to connect the numbers from 1–25 in proper sequence, during which they must alternate from one color to the next. The time to complete the task was measured in seconds.

Neurocognitive speed. Five standard speed tests have been used in previous VLS research in aging and special populations (e.g., Dixon et al., 2007; Hultsch et al., 1998). Four were computerized tests presented using a 386 IBM-compatible computer that controlled stimulus timing and presentation. Participants responded by pressing designated keys on a response console, and performance was recorded in milliseconds (ms). Two of these were semantic speed tests (lexical decision, sentence verification) and two were reaction time tests. The fifth test measured perceptual speed (digit symbol substitution). First, for lexical decision, participants read a string of five to seven letters and indicated whether the letters produced an English word (e.g., Dixon et al., 2007; Hultsch et al., 1998). Four were computerized tests presented using a 386 IBM-compatible computer that controlled stimulus timing and presentation. Participants responded by pressing designated keys on a response console, and performance was recorded in milliseconds (ms). Two of these were semantic speed tests (lexical decision, sentence verification) and two were reaction time tests. The fifth test measured perceptual speed (digit symbol substitution). First, for lexical decision, participants read a string of five to seven letters and indicated whether the letters produced an English word (e.g., Dixon et al., 2007; Hultsch et al., 1998).
to which participants pressed a key. Ten practice trials were followed by 50 test trials. Ten trials were presented at a time, with randomly alternating intervals separating the warning and signal stimuli (500, 625, 750, 875, and 1000 ms). Each interval was presented five times across the trials. The score was the average latency of the 50 trials. Fourth, for the choice reaction time (CRT4) test, a 2 × 2 grid corresponding with the key arrangement on a response console was presented. Each block had 10 trials, wherein the participant attended to four plus signs, one of which transformed into a square, to which the matching key was pressed. Following 10 practice trials, the average latency across 20 test trials was calculated. Fifth, the Wechsler Adult Intelligence Scale-Revised Digit Symbol Substitution task (DSS; Wechsler, 1991) has been used widely to measure perceptual speed (Hassing, Grant, et al., 2004; MacDonald, Hultsch, Strauss, & Dixon, 2003). In a 90-s period, participants used a coding key of nine numbers paired with specific symbols to fill rows of empty numbered test boxes. The score was the number of correctly transcribed items.

Procedure and Analyses

VLS protocol requires that all measures are administered in the same sequence to all participants. For each wave, actual testing occurs across four sessions about one week apart (for participant comfort and testing efficiency). Detailed VLS procedural information has been previously documented (Dixon & de Frias, 2004; Hultsch et al., 1998). In order to optimize comparison with previous reports of specific cognitive effects, a series of two-way univariate analyses of covariance (ANCOVA) was conducted. The covariate was systolic blood pressure, given (a) observed group differences as noted above, and (b) recent research showing effects of hypertension on diabetes-cognition relationships (Hassing, Hofer, et al., 2004). Diabetes status (diabetes or control) and age group (YO or OO) were the fixed factors, with each cognitive measure as the dependent variable. Regarding statistical significance, to partially adjust for multiple ANCOVAs, we focused on alpha levels of p ≤ .01. For limited archival, exploratory, and comparative purposes, we also note statistical trends up to p ≤ .05 (Nilsson, 2006). Analyses were conducted using SPSS Version 15.0 statistical software.

Results

See Table 2 for basic age and diabetes status group results. No significant interaction effects were found, indicating that the cognitive effects of Type 2 diabetes are not moderated by late-life age differences. Significant main effects are described below, emphasizing the diabetes status factor.

Episodic memory. In contrast to several previous findings, no significant differences were observed between diabetes and control groups for episodic memory measures. However, a significant main effect of age was observed, with older adults showing worse performance on measures such as the Hopkins Verbal Learning Test (HVLT) and the California Verbal Learning Test (CVLT).

Table 2
Mean Cognitive Performance for Main Effects of Diabetes Status and Age Group

<table>
<thead>
<tr>
<th>Cognitive measure</th>
<th>Diabetes status group</th>
<th>Age group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diabetes n = 41</td>
<td>Controls n = 424</td>
</tr>
<tr>
<td>Global cognition</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMSE</td>
<td>28.75 (1.08)</td>
<td>28.87 (1.04)</td>
</tr>
<tr>
<td>Episodic memory</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Word recall</td>
<td>16.01 (5.37)</td>
<td>17.63 (4.32)</td>
</tr>
<tr>
<td>RAVLT acquisition</td>
<td>5.70 (2.26)</td>
<td>6.31 (4.46)</td>
</tr>
<tr>
<td>RAVLT retention</td>
<td>9.93 (3.42)</td>
<td>10.25 (4.92)</td>
</tr>
<tr>
<td>Story memory</td>
<td>35.27 (9.72)</td>
<td>39.10 (10.21)</td>
</tr>
<tr>
<td>Semantic memory</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vocabulary</td>
<td>41.70 (6.48)</td>
<td>42.45 (6.62)</td>
</tr>
<tr>
<td>Fact recall</td>
<td>50.25 (16.52)</td>
<td>51.43 (15.36)</td>
</tr>
<tr>
<td>Verbal fluency</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opposites</td>
<td>12.98 (5.20)</td>
<td>13.66 (4.49)</td>
</tr>
<tr>
<td>Figures of speech</td>
<td>9.33 (3.12)</td>
<td>9.81 (3.16)</td>
</tr>
<tr>
<td>Similarities</td>
<td>14.70 (6.22)</td>
<td>15.79 (6.04)</td>
</tr>
<tr>
<td>Executive functioning</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hayling</td>
<td>5.16 (1.44)</td>
<td>5.84 (1.21)</td>
</tr>
<tr>
<td>Brixton</td>
<td>4.43 (1.88)</td>
<td>5.11 (2.12)</td>
</tr>
<tr>
<td>Color Trails 2 (s)</td>
<td>106.09 (36.05)</td>
<td>91.08 (29.10)</td>
</tr>
<tr>
<td>Stroop Test</td>
<td>1.39 (0.88)</td>
<td>1.17 (0.61)</td>
</tr>
<tr>
<td>Semantic speed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lexical dec. (ms)</td>
<td>1550.26 (606.68)</td>
<td>1315.34 (494.66)</td>
</tr>
<tr>
<td>S.V. (%) error</td>
<td>5.25 (4.48)</td>
<td>3.99 (3.25)</td>
</tr>
<tr>
<td>S.V. (ms)</td>
<td>4074.65 (1017.75)</td>
<td>3451.27 (1207.54)</td>
</tr>
<tr>
<td>Reaction time</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SRT (ms)</td>
<td>370.59 (76.80)</td>
<td>343.90 (79.06)</td>
</tr>
<tr>
<td>CRT4 (ms)</td>
<td>951.34 (168.56)</td>
<td>886.14 (171.53)</td>
</tr>
<tr>
<td>Perceptual speed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSS raw score</td>
<td>46.25 (12.42)</td>
<td>50.43 (10.84)</td>
</tr>
</tbody>
</table>

Note. Means and standard deviations are presented as M (SD). SRT, CRT4, Lexical dec., S.V., and DSS represent simple reaction time, choice reaction time, lexical decision, sentence verification, and Digit Symbol Substitution, respectively. Actual ms vary across cognitive tasks due to missing data. All ps are for main group effects.
groups on any outcome measure of episodic memory. However, in concordance with normal aging patterns, YO groups performed significantly better than OO groups on two episodic measures, including word list recall, $F(1, 443) = 18.32, p < .000$, partial $\eta^2 = 0.040$, and story memory recall, $F(1, 443) = 11.49, p < .001$, partial $\eta^2 = 0.025$, with a trend for RAVLT retention, $F(1, 443) = 4.69, p < .031$, partial $\eta^2 = 0.010$.

**Semantic memory.** No significant group differences were observed on either measure.

**Verbal fluency.** No significant diabetes-related group differences were observed.

**Executive functioning.** The control group performed significantly better than the diabetes group on the Hayling task, $F(1, 434) = 8.86, p < .003$, partial $\eta^2 = 0.020$, with a trend for Color Trails 2, $F(1, 440) = 6.26, p < .013$, partial $\eta^2 = 0.014$. No diabetes-related group differences were evident on the Brixton or the Stroop test. Significant age group differences were observed for all four measures of executive functioning, including the Hayling, $F(1, 434) = 9.32, p < .002$, partial $\eta^2 = 0.021$; Color Trails 2, $F(1, 440) = 21.73, p < .000$, partial $\eta^2 = 0.047$; and the Brixton, $F(1, 438) = 7.98, p < .005$, partial $\eta^2 = 0.018$.

**Semantic speed.** Healthy controls performed significantly faster than participants with diabetes on the sentence verification task, $F(1, 442) = 7.17, p < .008$, partial $\eta^2 = 0.016$, with a trend for a lower error rate, $F(1, 442) = 4.32, p < .038$, partial $\eta^2 = 0.010$. Healthy controls also displayed a trend for faster performance on the lexical-decision task, $F(1, 442) = 5.96, p < .015$, partial $\eta^2 = 0.013$. Regarding age, the YO group tended to outperform the OO group on the lexical-decision task, $F(1, 442) = 4.83, p < .029$, partial $\eta^2 = 0.011$, and the percent error, $F(1, 442) = 3.98, p < .047$, partial $\eta^2 = 0.009$, and latency measure, $F(1, 442) = 4.25, p < .040$, partial $\eta^2 = 0.010$, of the sentence verification task.

**Reaction time.** There were no observed diabetes group differences on SRT or CRT4. As expected, YO participants were faster than OO participants on both the SRT, $F(1, 440) = 12.11, p < .001$, partial $\eta^2 = 0.027$, and CRT4, $F(1, 440) = 47.25, p < .000$, partial $\eta^2 = 0.097$.

**Perceptual speed.** No significant diabetes-related effect was observed between the diabetes group and the healthy controls on the DSS task. YO participants performed significantly faster than OO participants, $F(1, 442) = 30.42, p < .000$, partial $\eta^2 = 0.064$.

**Discussion**

A growing literature has examined the extent and depth of potential cognitive effects of Type 2 diabetes in older adults. We contribute to this literature by examining simultaneously a broad range of cognitive neuropsychological measures as performed by both YO and OO healthy controls and relatively mild diabetes patients. Our findings revealed significant group differences within select domains, most consistently in speed-intensive measures of executive functioning and semantic speed. As suggested by Nilsson (2006), not all aspects of cognition may be equally or coincidentally affected by Type 2 diabetes, at least in relatively mild-to-moderate cases.

Two results are briefly noted and not further discussed. First, performance on global cognition (i.e., MMSE) for both groups was high and virtually identical. We excluded low performers from a relatively well-educated volunteer sample and reported MMSE results for descriptive purposes only. Second, previous studies have employed older adults from different and mixed age bands (e.g., under age 70, Fontbonne et al., 2001; over age 70, Hassing, Grant, et al., 2004). Examining whether systematically sampling along the age index would affect diabetes-related cognitive effects, we found commonly observed late-life cross-sectional age effects but no interactions of age group with diabetes status. Diabetes-related cognitive effects may be generally constant across age, at least for the current ranges of duration and severity.

Regarding the executive functioning results, two measures produced significant performance differences in favor of the controls: that is, the Hayling (involving speed and inhibition) and Color Trails 2 (involving speed and shifting). In addition, the group means were nonsignificant but in the same direction for the other two executive tests: that is, the Brixton (involving rule attainment and planning) and Stroop interference index (involving inhibition of responses). The fact that executive functioning tests are associated with inconsistent patterns of diabetes-related deficits (Messer, 2005) is not unexpected given the broad and sometimes multidimensional nature of the construct and the variable tasks used to measure associated processes in different populations (e.g., de Frias et al., 2006; Zhang, Han, Verhaeghen, & Nilsson, 2007). Because studies on diabetes and aging may produce executive functioning results that are in part a function of the tests used, a theoretically convergent pattern has been elusive. The present results contribute to potential consolidation of the executive functioning deficit associated with milder forms of diabetes in that the tasks for which we found group differences required a contribution of speed. Conceivably, simpler tasks measuring less speed-intensive aspects may be less sensitive to milder diabetes-related effects. Some of the inconsistency in the literature may be due to the fact that multiple aspects of executive functioning are differentially represented in neuropsychological test batteries and perhaps even applied unsystematically across age and disease severity continua. The notion that earlier effects may be observed in tasks requiring rapid performance of executive-demanding processes may be tested in future research using samples of broader clinical severity and with longitudinal follow-ups. Such deficits may cascade throughout the executive functioning domain as diabetes progresses and the rates of aging- and disease-related structural changes in the brain accelerate (Manschot et al., 2006).

The results were selective also within the neurocognitive speed domain. Of the three sets of speed measures, no group performance differences were found for either traditional reaction time (SRT and CRT4) or perceptual speed tasks (e.g., Cosway, Strachan, Dougall, Frier, & Dreary, 2001; Fontbonne et al., 2001; Hassing, Grant, et al., 2004). Instead, the diabetes group performed most prominently and significantly slower than the control group on the sentence verification task, with a consistent trend for lexical decision. Perhaps tasks requiring quick and precise processing of new verbal information may be sensitive markers for detecting cognitive deficits in relatively milder diabetes patients (Arvani-takis, Wilson, & Bennett, 2006; Nilsson, Fastbom, & Wahlin, 2002), a conclusion not available without the presence of semantic speed tasks (as well as the Hayling). Normal aging-related slowing of performance is well known, and accelerated (or inconsistent) slowing may signal early cognitive impairment or Alzheimer’s disease (Dixon et al., 2007; Rapp & Reischies, 2005).
clinical and longitudinal research may test the possibility that speed-intensive tasks involving semantic operations may be differentially sensitive markers in older diabetes patients. However, given the novelty of semantic speed assessments in diabetes literature, replication studies would be useful.

Two conspicuous null findings require brief comment, as they are relevant to previous literature and complement the two observed deficits described above. First, although verbal episodic memory tends to be more frequently impaired in both healthy older adults (e.g., Dixon et al., 2004) and older diabetes patients (see Nilsson, 2006), we observed no significant diabetes-related differences for any of our three verbal episodic tasks. The provisional importance of this null result is weakened by the informal observation that the group means are generally in the expected direction (see Table 2). This implies both methodological (e.g., role of covariates, statistical power) and clinical directions for future research. We were able to check one of these issues, namely, the role of a comorbidity covariate. Post hoc ANOVAs (without systolic BP as covariate) revealed a tendency for two memory tasks (and the two additional speeded tasks) to produce trends \( (p \leq .05) \) in the expected direction. Therefore, active diabetes-related comorbidities (e.g., hypertension) may be a contributing factor to whether domain-specific cognitive deficits are observed (Saxby, Harrington, McKeith, Wesnes, & Ford, 2003; Hassing, Hofer, et al., 2004; Waldstein, 1995). Future clinical research may examine whether episodic memory deficits are not leading indicators of early diabetes-related cognitive effects, but markers of further progression of the disease and expanded neurological involvement.

A second set of null findings merits brief comment. In contrast to some previous research (see Nilsson, 2006), we did not find significant group differences in performance on any measure of verbal fluency. As with executive functioning, the fluency tests used in various studies differ considerably in procedure and cognitive demands. For example, whereas our measures required relatively abstract thinking in finding opposites, figures of speech, and similarities between words, the fluency tasks used by Wahlin et al. (2002) required more basic letter-word fluency. Future research comparing more levels of complexity and demand in fluency could be helpful in delineating the extent of the deficit, its relationship to severity of the disease, and the possibility of some early preserved fluency skill. Similarly, expected null findings for semantic memory were observed for the typical vocabulary measure and this pattern was extended to include the previously untested fact memory task. Broadening the range of diabetes severity, exploring further comorbidities, and conducting longitudinal follow-ups will begin to clarify the timing of and extent to which fluency and semantic memory may be affected by diabetes (Arvanitakis et al., 2004; Hassing, Grant, et al., 2004).

Overall, our interpretation has emphasized three important themes: (a) classification and diagnosis clarity (e.g., disease identification and severity, comorbidities, exclusionary criteria), (b) possible temporal ordering of diabetes-related cognitive neuropsychological outcomes as the disease progresses, and (c) potential theoretical and clinical value of comprehensive cross-sectional and follow-up longitudinal assessments. If executive resources and speed may be most prominently compromised relatively early in Type 2 diabetes, confirmatory and complementary evidence should be observed across studies with various combinations of the elements of the three themes. Among the strengths of this study is the unusually broad age range of older adults, with which we confirmed that aging-related diabetes effects may be invariant across young-old and old-old age groups. Second, we accessed VLS Sample 3 archives for self-report and objective diagnostic information, background and comorbid health indicators, and an extensive battery of cognitive neuropsychological domains. Third, with the broad cognitive neuropsychological battery, we were able to detect a profile of robust effects in select domains, most notably executive functioning and speed. Given the current comprehensive cross-sectional baseline, future longitudinal research—with the VLS and other studies—can examine potentially differential decline patterns. Fourth, we covaried systolic blood pressure in our analyses, as there is evidence to suggest that elevated blood pressure increases cognitive decline independent of diabetes (Elia, D’Agostino, Elia, & Wolf, 1995; Waldstein, 2003). The importance of considering hypertensive effects is highlighted, as it may differentially contribute to cognitive decline and inflate the differences attributed to diabetes.

A first limitation reflects several unmodifiable characteristics of our sample: It is volunteer-based, from a smaller urban population in Canada, predominantly Caucasian, relatively well-educated, initially selected on global cognitive intactness, and with generally available health care. Thus, results are not necessarily representative of the entire Canadian or western population, but they may generalize to a large and growing population of relatively healthy aging preboomers and boomer populations. Future studies of greater diversity are encouraged. Second, although provisional diagnoses of Type 2 diabetes were based on a combination of commonly used self-report, follow-ups, and objective medication data, more precise biological information (e.g., HbA1c levels, Fasting Blood Glucose levels) is currently unavailable in the VLS. Conceivably, some nondiagnosed cases may be present in the control group, but their unlikely presence would have rendered a more conservative test of the hypotheses. Third, although well characterized, a larger diabetes group would have been preferable. We noted earlier, however, that our diabetes group \( (n = 41) \) is well within the range of comparable neuropsychological studies (with \( n \)s of 20–41). Moreover, as a proportion of the VLS parent sample, it is similar to Canadian population expectations.

Overall, this study contributes to the literature with a comprehensive neuropsychological battery and a broad age range with which to explore deficits associated with relatively mild Type 2 diabetes in older adults. The results both qualify and extend those of previous reports, particularly (but differentially) in the domains of speed, executive functioning, and episodic memory. Given the modern western lifestyle, associated health risks, and growing populations of older adults, Type 2 diabetes will likely increase as a common aging-related challenge to neurobiological and cognitive health. Future studies examining longitudinal trends in neuropsychological sequelae of diabetes will help determine whether different patterns of cognitive decline occur across both health condition (diabetes group vs. healthy controls) and neuropsychological domain (executive functioning, cognitive speed, episodic memory).

References


