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Effects of Hypertension and Diabetes on Sentence Comprehension in Aging

Dalia Cahana-Amitay,[1,2] Martin L. Albert,[1,2] Emmanuel A. Ojo,[1,2] Jesse Sayers,[1,2] Mira Goral,[1,3,4] Loraine K. Obler,[1,2,3] and Avron Spiro III[2,5,6]

[1]Department of Neurology, School of Medicine, Boston University, MA.
[2]Veterans Affairs Boston Healthcare System, Boston, MA.
[3]The Graduate Center, City University of New York.
[4]Lehman College, City University of New York.
[5]Department of Epidemiology, School of Public Health, Boston University, MA and
[6]Department of Psychiatry, School of Medicine, Boston University, MA.

Objectives. To assess the impact of hypertension and diabetes mellitus on sentence comprehension in older adults.

Method. Two hundred and ninety-five adults aged 55 to 84 (52% men) participated in this study. Self-report mail survey combined with medical evaluations were used to determine eligibility. Multiple sources were used to determine whether hypertension and diabetes were present or absent and controlled or uncontrolled. Sentence comprehension was evaluated with two tasks: embedded sentences (ES) and sentences with multiple negatives (MN). Outcome measures were percent accuracy and mean reaction time of correct responses on each task.

Results. Regression models adjusted for age, gender, and education showed that the presence of hypertension impaired comprehension on the multiple negatives task ($p < .01$), whereas the presence of diabetes impaired the comprehension of embedded sentences ($p < .05$). Uncontrolled diabetes significantly impaired accurate comprehension of sentences with multiple negatives ($p < .05$). No significant patterns were found for reaction time.

Discussion. The presence of hypertension and diabetes adversely affected sentence comprehension, but the relative contribution of each was different. These findings support the researchers' earlier speculations on the neurobiological mechanisms underlying the effects of hypertension and diabetes on language and cognition in aging. Uncontrolled disease status demonstrated more complicated age-related effects on sentence processing, highlighting the clinical importance for cognitive aging of identifying and managing vascular risk factors.

Key Words: Cognition—Diabetes—Health—Hypertension—Language—Sentence comprehension.

THIS study addresses the impact of health factors, such as the presence of cardiovascular and cerebrovascular risk factors, on language function in cognitive aging, contributing to the ongoing debate in aging research concerning the interplay among cognitive outcomes, physiological changes, and biological factors currently explored (Alwin & Hofer, 2011; Small, Dixon, & McArdle, 2011; Spiro & Brady, 2011). The researchers focus on the specific effects of hypertension and diabetes on age-related language decline, following an earlier study in which they demonstrated that hypertension, but not diabetes, contributes to *word-finding difficulties* in aging (Albert et al., 2009). The present study wishes to extend this discussion to the effects of these diseases on age-related difficulties in *sentence comprehension*.

Difficulties comprehending spoken sentences are common among older adults and can be seen in conditions that stress the sentence-comprehension system (Wingfield, Peelle, & Grossman, 2003). Such conditions include speech presented in noisy conditions (Obler, Nicholas, Albert, & Woodward, 1985; Schneider, Daneman, Murphy, & See, 2000) and/or speech comprising syntactically complex structures (Caplan, Dede, Waters, Michaud, & Tripodis, 2011; Goral et al., 2011). However, the challenges healthy older adults experience in processing spoken language have yet to be linked to their health status. The present study is designed to fill this gap and it offers some speculations about the neurobiological mechanisms potentially underlying these specific age-related changes.

Hypertension and diabetes, alone or together, adversely affect multiple cognitive domains, including, but not limited to, cognitive speed, mental flexibility, and memory (for recent reviews, see van den Berg, Kloppenborg, Kessels, Kappelle, & Biessels, 2009; Waldstein, Wendell, & Katzel, 2010). Hypertension in older adults has been linked to attention problems (Madden & Blumenthal, 1998), impaired learning and memory (Elias et al., 1997), visuospatial deficits (Elias, Robbins, Elias, & Streeten, 1998), and slowing of verbal fluency and other executive dysfunction (Alves de Moraes, Szklo, Knopman, & Sato, 2002; Elias et al., 1997; Waldstein et al., 1996). Some studies, however, show that low blood pressure can also adversely affect cognitive performance, suggesting a U-shaped relation between blood pressure and cognition in older adults (Bohannon, Fillenbaum, Pieper, Hanlon,

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Blazer, 2002; Glynn et al., 1999; Hebert et al., 2004; Waldstein, Giggey, Thayer, & Zonderman, 2005).

The impact of diabetes on cognition among older adults also covers a wide range of domains affected to different degrees, especially in individuals with mild to moderate diabetes mellitus (DM; Yeung, Fischer, & Dixon, 2009). Age of onset and duration of disease also affect the specific manifestation of cognitive decline (Dey, Misra, Desai, Mahapatra, & Padma, 1997). Changes reported include impaired verbal episodic and semantic memory (Arvanitakis, Wilson, Bienias, Evans, & Bennett, 2004; Nilsson, Fastbom, & Wahlin, 2002), executive functioning (Awad, Gagnon, & Messier, 2004; Messier, 2005; Ryan & Geckle, 2000;Stewart & Liolitsa, 1999; Yeung et al., 2009), fluency (McFall, Geall, Fischer, Dolcos, & Dixon, 2010), cognitive speed (Arvanitakis, Wilson, Bienias, Evans, & Bennett, 2004; Awad et al., 2004; Fontbonne, Berr, Ducimetière, & Alpérovitch, 2001), and global cognitive competence (Arvanitakis, Wilson, Bienias, Evans, & Bennett, 2004; Fontbonne et al., 2001; Hassing et al., 2003).

The benefits of controlling blood pressure and DM for cognitive performance among older adults are less well understood (for discussion, see Spiro & Brady, 2011). However, some potential long-term cognitive gains for controlled hypertensive individuals have been recognized (Waldstein & Katzel, 2001). These include, for example, improved performance on working memory tasks (Muldoon et al., 2002) and less risk of developing cognitive impairment with age (Murray et al., 2002). Even less is known about the effects of controlled DM on cognition because there are virtually no data to shed light on the question (Evans & Sastre, 2009). The complicated picture of health effects (hypertension [HTN] and/or DM) on cognition in older adults results, in part, from several methodological differences, such as study design, measures used to assess performance, as well as population sampling (van den Berg et al., 2009; van den Berg, Reijmer, & Biessels, 2009).

In spite of the rich literature exploring the health effects on cognitive aging, observations about the specific effects of vascular risk factors such as HTN and type II DM on *language* function among older adults remain scarce. This gap is attributable, in part, to the measures used in studies examining health effects on cognition, which often do not include tests specifically developed to assess language performance in healthy elderly persons. In many cases, the measures selected include standardized measures such as the Boston Diagnostic Aphasia Examination (BDAE), designed for persons with language impairment, and may be insufficiently sensitive to detect changes due to normal aging (for related comments, see Kessles & Brands, 2009; van den Berg et al., 2009).

Even in the few studies that use standardized verbal measures, the reported effects of disease are discussed only in relation to measures of lexical retrieval. For example, Waldstein et al. (2005) examined the relationship between blood pressure and a broad range of cognitive measures that included a test of confrontation naming–the Boston Naming Test (BNT). They found that both high and low diastolic blood pressures were associated with reduced executive functions and confrontation naming among less-educated people; yet, only older adults with higher blood pressure performed worse on the BNT, over time, compared to those with lower BP. In another study, Kumari & Marmot (2005) compared people with and without DM, as measured by a combination of self-report and oral glucose tolerance tests, in terms of their performance on verbal fluency, vocabulary, and memory tests. Although they found no effects of glucose tolerance on performance, they did discover that duration of disease adversely affected phonemic fluency in men diagnosed 2.5 years prior to testing date, compared to men without DM. In a study exploring the effects of both HTN and DM on selected items for the BNT and the BDAE, Desmond, Tatemichi, Paik, & Stern (1993) found no correlation between either DM or HTN and these verbal measures. These studies thus do not point to unified health effects on age-related lexical retrieval, as they vary in terms of design (e.g., prospective vs. cross-sectional), health measures (e.g., glucose vs. blood pressure), methods of collecting health information (e.g., oral glucose tolerance tests vs. self-reported diagnosis), cognitive measures (e.g., vocabulary test, phonemic fluency, and categorical fluency vs. verbal and nonverbal memory, attention, perceptuomotor speed, executive functions, and confrontation naming), and reported patterns of language decline (no decline vs. impaired confrontation naming and executive functions).

Nonetheless, these studies suggest that abnormality in cardiovascular biomarkers and their behavioral correlates have long-term neurobiological consequences that compromise brain structures in different ways, for example, white matter degeneration, reduction in gray matter volume, scattered small-sized silent infarcts, and changes in cerebral perfusion, increasing the risk of developing cognitive impairment and different forms of dementia over time (see Waldstein et al., 2005, for related comments). Indeed, HTN is known to produce a set of pathological microvascular changes in the brain (Farkas & Luiten, 2001; Patankar et al., 2005), primarily in frontosubcortical circuits (Takashima et al., 2003; Wolfe, Linn, Babikian, Knoefel, & Albert, 1990), leading to frontal executive system cognitive syndromes (Pugh & Lipsitz, 2002). In contrast, DM has been linked to impairments of memory and learning in aging (Messier, 2005) and prodromal Alzheimer's disease (Herholz, 2010), and, in particular, in these clinical conditions, it has been correlated with abnormalities of glucose metabolism in temporoparietal regions (Mosconi et al., 2009). These observations served as a basis for the researchers' idea, first articulated in Albert et al. (2009), that HTN and DM have distinct effects on word-finding deficits among older adults, with HTN affecting lexical retrieval

by producing microvascular changes primarily in frontal white matter systems, whereas DM likely causes neuronal metabolic abnormality in a more distributed fashion.

In this study, the researchers explore this idea further by examining the effects of HTN and DM on sentence comprehension in otherwise healthy adults, which, to the best of their knowledge, has not been previously studied. Their language measures—tests of comprehension of embedded sentences and sentences with multiple negatives (see Method section for further details)—are expressly designed to assess sentence-processing abilities in neurologically intact adults across different ages (Goral et al., 2011), thus offering a unique look at the impact of health factors on language function in aging. The researchers asked two related questions about the effects of HTN and DM on sentence comprehension: (a) Does the *presence* of HTN and/or DM have adverse effects on sentence comprehension in older adults? (b) Is sentence comprehension adversely affected if HTN and/or DM are *uncontrolled*?

From a neuroscience perspective, difficulties comprehending syntactically complex sentences of the type examined here could be associated with age-related changes in those brain areas typically thought to subserve the processing of these sentence structures. For example, the neural circuitry involved in the processing of sentential negation (Bahlmann, Mueller, Makuuchi, & Friederici, 2011) and relative clauses (Wingfield & Grossman, 2006) has been found to involve the left perisylvian language network among healthy adults. Thus, health-related neural changes in the aging brain could potentially lead to impaired comprehension of syntactically complex sentences, involving distinct patterns of brain activation (as currently explored for negation by Hyun et al., 2011). Such difficulties could reflect an exacerbation of a general decline in the ability to interpret syntactically complex sentences found among older adults.

Method

Subjects

Participants were 295 adults aged 55 to 84 who were tested during the period 2004–2008 as part of the Language in the Aging Brain project (Albert et al., 2009; Goral et al., 2011; Goral, Spiro, Albert, Obler, & Connor, 2007; Obler et al., 2010). Potential participants were excluded if they reported a history of neurological or psychiatric disorders, general anesthesia within the previous 6 months, radiation treatment within the previous year, or loss of consciousness for more than 2 hr.

Procedure

Potential participants were mailed a survey inquiring about their demographic information, health status, health behavior, and medication use prior to testing. They were then scheduled for a visit that began with a standardized physical exam, including medical history, physical and neurological assessments, multiple measures of blood pressure, and the collection of a blood sample after a 12-hour (overnight) fast. Those meeting screening criteria based on the questionnaire and physical examination then completed a battery of neuropsychological and language tests administered starting approximately 1 hr after a meal. The battery was administered in two sessions over a 6-week period.

Participants' hearing was assessed using Speech Recognition Threshold (SRT). The starting decibel level for the SRT for each ear was set as 20 dB more than the average for that ear on the pure-tone average test (500 Hz, 1,000 Hz, 2,000 Hz, and 4,000 Hz) rounded up to a multiple of 5. Participants were asked to repeat any words they heard from a recording of a male speaker saying 36 two-syllable words presented in random order in each ear. The participants were read the words in alphabetical order before testing so that all the words would be familiar. The left ear was always tested first. If the participant failed a trial, the next trial was presented 5dB higher. Accuracy of 50% on a given decibel level was considered the threshold.

All participants provided written informed consent. This study was approved by the Institutional Review Boards of the Veterans Affairs Boston Healthcare System and the Boston University Medical Campus.

Measures

Health measures: hypertension (HTN) and type II DM.—HTN and DM were based on three types of information: (a) self-reports of a physician diagnosis, (b) biomarkers of blood pressure and fasting glucose, and (c) self-reports of medication use. High blood pressure (BP) was defined as a mean systolic blood pressure (SBP) greater than 140 mmHg or a mean diastolic blood pressure (DBP) reading greater than 90 mmHg (Chobanian et al., 2003). High glucose level was defined as 126 mg/dL or higher (American Diabetes Association, 2007). Respondents were asked to list all prescription and nonprescription drugs used; these responses were then coded by a registered nurse and those who were taking antihypertensive or antidiabetic drugs were noted. Participants were grouped according to whether these conditions—HTN and DM—were (a) *present* or *absent*, and (b) whether the condition was *normal/controlled* versus *undiagnosed, untreated*, or *uncontrolled* (collectively referred to as *"uncontrolled").* The latter grouping was based on evidence that these conditions are frequently underrecognized in older Americans (see also Albert et al., 2009; Spiro & Brady, 2011).

Disease *presence* was indicated if a person reported either on a mail survey or during the medical examination that they had received a doctor's diagnosis of the condition. Those who did not report a diagnosis in either place were considered *not* to have the disease.

Based on a combination of biomarker values, medication use, and disease presence information, participants were separated into two groups. The "normal/ controlled" group included those (a) who did not report a condition or (b) who reported the condition, were taking medication, and had normal biomarker values. Grouping of "normal" and "controlled" into a single group is consistent with the observation that nonhypertensives and medicated hypertensives show no significant differences in cognitive performance (Vasilopoulos et al., 2012). In addition, in the sample analyzed here, analysis of variance (ANOVA) tests comparing HTN and DM biomarkers in "normal" versus "controlled" groups demonstrated no significant differences between the two.

The "uncontrolled" group included those who were (a) undiagnosed (high biomarker but neither self-report diagnosis nor on medication), (b) untreated (self-reported diagnosis and high biomarker, but no medication), or (c) uncontrolled (with diagnosis, high biomarker, and on medication). For additional details on how these groups were defined, see Albert et al. (2009).

Language measures: sentence comprehension.—Two tasks—Embedded Sentences and Multiple Negatives (see also Goral et al., 2011, for further details)—were used to assess sentence comprehension. As there are no standardized sentence-comprehension tests for normal older adults, these tasks are modeled after tasks described by others (see the following paragraphs). Both tasks contained prerecorded sentences spoken at normal speech rate, administered to participants through headphones at a comfortable listening level. The participant was asked to judge whether each sentence was likely or unlikely by pressing one of two buttons, marked "likely" and "unlikely," on a response box. Accuracy for each sentence was recorded using E-Prime software (Psychology Software Tools, Inc.). Percent accuracy was computed as the number of correct responses divided by the number of properly administered items. In addition, the mean response latency for correct responses was measured.

Embedded sentences (ES). This is a computerized task based on the works of King & Just (1991), Wingfield & Stine-Morrow (2000), and others, where syntactic structure and plausibility are manipulated. In this task, participants listened to 96 syntactically complex sentences. Sentences included 28 object-relative sentences, 28 subject-relative sentences, 28 control sentences, and 4 distractor sentences per sentence type. For the target sentences, the critical information needed in order to establish the referential link between the noun phrase and its corresponding structural position inside the relative clause (subject or object) was provided in the second half of the sentence. The distractors contained the critical information in the first part of the sentence and were introduced to prevent the participants from developing a bias to attending only to the second part of the sentences they heard.

Each sentence described a plausible or an implausible scenario to be judged by the participant as "likely" or "unlikely." Examples of the types of target embedded sentences used are shown in the Supplementary Appendix. The number of propositions is identical in all syntactic and plausibility conditions, and the content words in the two embedded conditions are identical. The content items in the unembedded sentences differ from those in the embedded sentences by one verb phrase. Examples of these sentence types are also shown in the Supplementary Appendix.

Multiple negatives (MN). This is a computerized task based on the works of Sherman (1976) and Obler, Fein, Nicholas, & Albert (1991), where the number of negatives and plausibility are manipulated. This task contained a total of 50 sentences, including 30 target sentences divided into three groups: 10 zero-negative sentences, 10 one-negative sentences, and 10 two-negative sentences. Because the one- and two-negative stimuli were created by inserting one or two negative markers into the zero-negative sentences, the lexical items and number of propositions are identical in all syntactic and plausibility conditions. To adjust for differences in sentence length, 10 eleven-word and 10 twelve-word nonnegative sentences were added, yielding a total of 50 sentences. For each group of sentences, five of the ten sentences were plausible and five implausible. Again, sentences were to be judged as "likely" or "unlikely." Examples of the target sentence types included in the multiple negatives task are given in the Supplementary Appendix.

Statistical Analyses

Analyses were conducted using SAS version 9.3 (SAS Institute, Inc., 2011). Descriptive analyses used *F* tests or chi-square to compare demographics and biomarkers among disease status groups (presence vs. absence; and controlled vs. uncontrolled) for DM and HTN. Regression analysis was used to compare percent accuracy and mean reaction time for correct responses on both ES and MN tasks by disease status groups, adjusting for potential effects of age, education, and gender. The researchers also assessed the interaction effects of age, gender, and education on disease status. They first examined whether the *presence* of HTN and/or DM was related to accuracy and reaction time in sentence processing; they then examined whether having uncontrolled HTN and/or DM was associated with accuracy and reaction time. Post hoc multiple comparisons (using Duncan's multiple-range test) were conducted to examine the groups that differed significantly from one another. Because the researchers found no significant patterns for reaction time, they do not address it any further in the Results section.

Results

Presence Versus Absence of Disease

Table 1 shows the combination of presence/absence for HTN and DM. Over one third of the sample (38.6%) had neither HTN nor DM, and 11.5% had both. HTN was

Table 1. Demographics and Biomarkers by Presence/Absence of Hypertension and Diabetes (n = 295)

Disease presence	1. Neither disease present	2. HTN only present	3. DM only present	4. Both diseases present	F/χ^2	*df*	*p* Value
Demographics							
Percent subjects, %	38.6	45.8	4.1	11.5	—	—	—
Percent women, %	50.9	51.90	25.0	29.4	8.4	3	**0.04**
Age, years	71.6[ab]	73.5[a]	70.8[ab]	68.7[b]	4.4	3, 291	**0.005**
Education, years	15.2	15	14.7	14.6	0.8	3, 284	0.53
Biomarkers							
Systolic blood pressure, mmHg	124.3[a]	129.1[ab]	125.6[ab]	133.1[b]	3.3	3, 284	**0.02**
Diastolic blood pressure, mmHg	68.0	68.2	65.4	72.2	1.9	3, 284	0.12
Glucose, mg/dL	94.3[a]	98.7[a]	139.4[b]	135.1[b]	53.3	3, 290	**<.001**
Glycosylated hemoglobin, %	5.4[a]	5.7[a]	6.7[b]	6.9[b]	26.7	3, 288	**<.001**
Insulin, µIU/mL	6.7[a]	9.0[ab]	12.7[b]	12.2[b]	6.0	3, 211	**<.001**

Note. Within each row, means with the same superscript (e.g., "a") were not significantly different from each other ($p > .05$) by Duncan's multiple range test. HTN = hypertension, DM = diabetes mellitus, χ^2 = chi-square test, *df* = degrees of freedom, µIU = micro international unit.

Table 2. Unstandardized Regression Coefficients (Standard Error) and Model Fit by Task for Presence/Absence of Hypertension and Diabetes

	Unstandardized regression coefficients (standard error)									
Task	Intercept	Age	Female	Education	Both diseases present	DM only present	HTN only present	Neither disease present	*p* Value	R^2
ES	95.23	–0.23 (0.07)**	2.08 (1.06)	0.69 (0.27)**	–0.12 (1.73)	–5.31 (2.65)*	–1.45 (1.13)	Reference	<.001	0.12
MN	97.95	–0.10 (0.06)	1.36 (0.79)	0.18 (0.20)	–3.67 (1.32)**	–3.28 (2.12)	–2.30 (0.84)**	Reference	<.001	0.09

Note. HTN = hypertension, DM = diabetes mellitus, ES = embedded sentences, MN = multiple negatives.
*$p < .05$. **$p < .01$.

Table 3. Predicted Means (Standard Errors) on Sentence-Comprehension Tasks (% Accuracy) by Disease Presence/Absence and Disease Normal-Controlled/Uncontrolled

	1. Neither	2. HTN only	3. DM only	4. Both
Disease presence				
ES task	89.94 (0.83)	88.49 (0.96)	84.64 (2.51)	89.82 (1.51)
MN task	94.27 (0.62)	91.97 (0.56)	90.99 (2.01)	90.60 (1.17)
Disease uncontrolled				
ES task	89.46 (0.64)	88.42 (1.12)	90.32 (1.57)	81.91 (2.52)
MN task	93.54 (0.48)	91.98 (0.84)	90.06 (1.27)	87.81 (2.02)

Notes. ES = embedded sentences, MN = multiple negatives, HTN = hypertension, DM = diabetes mellitus. The labels "Neither", "HTN only", "DM only", and "Both" for "Disease Presence" correspond to the labels used in Tables 1 & 2; for "Disease uncontrolled," they correspond to those used in Tables 4 & 5.

present in 57.3% and DM in 15.5% of the sample. Women were more likely to have neither condition or have HTN only. Age differences were significant; those with both conditions tended to be a bit younger, and those with HTN only were somewhat older. No difference in education was seen among the groups. Persons with both or with HTN only had higher systolic blood pressure; diastolic blood pressure did not differ among the groups. Persons with DM, regardless of presence of HTN, had higher levels of glucose, hemoglobin A1c, and insulin than those with neither condition or with HTN only.

The researchers examined whether performance on the sentence-processing tasks differed among those with either or both of these diseases present, examining percent accuracy on the ES and the MN tasks (see Table 2). In these analyses, the researchers adjusted for age, gender, years of education, and hearing. Because no significant effects of hearing were found on either task, the researchers excluded SRT from further analyses. The final models accounted for 12% and 9% of the variance in ES and MN performance, respectively. For the ES task, performance was negatively related to age and positively related to education. The presence of DM only was significantly associated with worse performance. For the MN task, the three covariates were unrelated to performance, but having HTN or HTN with DM was negatively associated with performance.

Table 3 presents predicted means (adjusted for the covariates) for the sentence-processing tasks by presence/absence of HTN and DM. Based on post hoc (Duncan's) mean comparisons, those with both conditions had marginally greater mean accuracy on ES than those with DM only ($p < .10$), and those with neither condition had greater accuracy than those with HTN only ($p < .05$). For MN, those with neither condition had greater accuracy than those with both conditions or with HTN only ($p < .01$).

Normal or Controlled Versus Uncontrolled Disease

Table 4 shows the combination of persons with HTN and DM who were normal or controlled versus the undiagnosed, untreated, or uncontrolled persons. About two thirds of the sample (65.4%) did not have either disease or had both of them controlled. For 4.2%, both conditions were uncontrolled; 9% had uncontrolled DM only; and 21.4% had uncontrolled HTN only.

There were no differences among these disease groups in gender or age, but the number of years of education was significantly lower in participants in whom both diseases were uncontrolled, compared to those with normal/controlled status or with only DM uncontrolled. Persons with uncontrolled HTN only or with both conditions had higher SBP and DBP. In addition, participants in whom DM or both conditions were uncontrolled had significantly higher glucose and hemoglobin A1c levels. Although all the insulin readings were within normal range, people with uncontrolled DM had significantly higher levels of glucose.

Regression models (shown in Table 5) included age, gender, and education, as well as disease status variables, and these accounted for 14% and 10% of the variance in ES and MN performance, respectively (see Table 3). In ES, higher age and male gender were associated with lower performance. Those with both diseases uncontrolled also had significantly lower performance. In MN, none of the covariates was related to accuracy; those with DM or both diseases uncontrolled had significantly poorer performance.

Table 3 presents predicted means, adjusted for the covariates, by sentence-processing tasks as a function of whether HTN and DM were uncontrolled. For the ES task, those with both diseases uncontrolled were significantly less accurate than those in the other three groups (all $p < .05$). For the MN task, those with both conditions controlled had higher accuracy than those with both or DM uncontrolled ($p < .05$) but did not differ from those with HTN uncontrolled. Those with both uncontrolled were marginally less accurate than those with HTN uncontrolled ($p = .058$).

Discussion

In this study, the researchers asked (a) whether the presence of HTN and/or DM adversely affects sentence comprehension in older adults, and (b) whether HTN and/or DM, when undiagnosed, untreated, and/or uncontrolled, has an adverse effect on sentence comprehension among older adults. The answer to both questions is 'yes', but the relative contribution of each of these health factors to sentence comprehension among older adults is different.

The presence of HTN, with or without DM, impaired the accuracy of comprehension on the MN task. In a study demonstrating the neural underpinnings of language comprehension, Friederici and her colleagues identified neural networks that mediate reversing the truth value of sentences using specific markers of negation (Bahlmann, Mueller, Makuuchi, & Friederici, 2011). These include the left perisylvian language areas. This study demonstrates that this complicated processing of sentences and the comprehension of such sentences is impaired in otherwise-normal aging by the presence of HTN.

The presence of DM, in contrast, impaired the comprehension of embedded sentences with age, suggesting that DM plays a role in the neurobiological mechanisms underlying age-related changes in the comprehension of embedded sentences. Previous studies describe specific neural networks, including the left inferior frontal

Table 4. Demographics and Biomarkers by Normal/Controlled versus Uncontrolled Hypertension and Diabetes ($n = 289$)

Disease uncontrolled	1. Neither disease uncontrolled	2. HTN only uncontrolled	3. DM only uncontrolled	4. Both diseases uncontrolled	F/χ^2	*df*	*p* Value
Demographics							
Percent subjects, %	65.4	21.4	9.0	4.2	—	—	—
Percent female, %	49.2	58.1	34.6	25.0	7.0	3	.074
Age, years	72.4	72.1	69.7	71.5	1.1	3, 285	.36
Education, years	15.3[a]	14.4[ab]	15.2[a]	14.0[b]	4.2	3, 278	**.007**
Biomarkers							
Systolic blood pressure, mmHg	121.0[a]	145.3[b]	125.8[a]	144.3[b]	66.3	3, 284	**<.001**
Diastolic blood pressure, mmHg	66.5[a]	74.2[b]	69.9[ab]	66.9[a]	10.6	3, 284	**<.001**
Glucose, mg/dL	96.4[a]	95.7[a]	138.3[b]	166.2[c]	102.4	3, 284	**<.001**
Glycosylated hemoglobin, %	5.6[a]	5.6[a]	6.6[b]	7.6[c]	24.5	3, 282	**<.001**
Insulin, µIU/mL	8.0[a]	8.7[a]	13.1[b]	7.7[a]	3.4	3, 211	**.02**

Note. Within each row, means with the same superscript (e.g. "a") were not significantly different from each other ($p > .05$) by Duncan's multiple range test. HTN = hypertension, DM = diabetes mellitus, χ^2 = chi-square test, *df* = degrees of freedom.

Table 5. Unstandardized Regression Coefficients (Standard Error) and Model Fit, by Tasks, for Normal/Controlled versus Uncontrolled Disease

	Unstandardized regression coefficients (Standard Error)									
Task	Intercept	Age	Female	Education	Both diseases uncontrolled	DM only uncontrolled	HTN only uncontrolled	Neither disease uncontrolled	*p* Value	R^2
ES	96.29	–0.24 (0.07)**	2.20 (1.06)*	0.62 (0.28)*	–7.53 (2.63)**	0.87 (1.80)	–1.04 (1.30)	Reference	<.001	0.14
MN	97.63	–0.10 (0.05)	1.34 (0.80)	0.18 (0.21)	–5.73 (2.08)**	–3.48 (1.36)*	–1.56 (0.97)	Reference	<.001	0.10

Note. HTN = hypertension, DM = diabetes mellitus, ES = embedded sentences, MN = multiple negatives.
*$p < .05$. **$p < .01$.

gyrus, dedicated to the processing of embedded sentences (Caplan, Stanczak, & Waters, 2008; Friederici, Fiebach, Schlesewsky, Bornkessel, & von Cramon, 2006; Meltzer, McArdle, Schafer, & Braun, 2010) and their vulnerability to age effects (Grossman et al., 2002).

The presence of both diseases did not always result in a more deleterious effect on sentence comprehension among the older adults (presence of both diseases adversely affected only MN accuracy). However, examination of disease presence alone provides only a limited window into the potential effects of disease on sentence comprehension, as not all people in whom disease is present control for it, and even if they do, their medication might fail to work. This limitation might explain the less-consistent effects of disease presence on sentence comprehension, which might be clarified through examination of uncontrolled disease status.

Indeed, the effects of uncontrolled disease status presented a different picture, with DM demonstrating more complicated age-related effects on sentence processing than uncontrolled HTN. Uncontrolled DM, in and of itself, did not impair the interpretation of embedded sentences, unless it was combined with uncontrolled HTN. However, uncontrolled DM significantly impaired accurate interpretation of sentences in the MN task, regardless of the controlled status of HTN.

The differential effects of HTN and DM on sentence comprehension found in this sample (i.e., diabetes impairs comprehension in the ES task, whereas HTN impairs comprehension in the MN task) lend additional support to the authors' earlier speculations on the neurobiological mechanisms underlying the effects of HTN and DM on word-finding in aging (Albert et al., 2009). The authors proposed that HTN affects language in aging by the production of microvascular changes primarily in frontal white matter systems and that diabetes affects language and cognition in aging primarily by metabolic deficiency associated with insulin resistance or impaired glycemic control, influencing neuronal function throughout the brain. Although some researchers have argued that language resists the age-related effects of DM (Awad et al., 2004; Kessles & Brands, 2009), the distributed effects of DM on sentence comprehension found in this study suggest that language is, in fact, a subtle but important component of the cognitive decline experienced with normal aging.

It is possible, for example, that the impaired glycemic control associated with DM may affect the processing of syntactically complex sentences by limiting the integration between frontal systems associated with syntactic processing and posterior systems associated with lexical processing. Evidence for this effect is found in multiple functional MRI studies documenting the integration of anterior and posterior neural networks in the service of language comprehension (Price, 2010). In contrast, impaired frontal white matter systems affect specific cognitive abilities, such as working memory and attention control (e.g., Hedden et al., 2012; Verdelho et al., 2007), required for accurate processing of complex sentences like those the authors used in the MN task. Dissociating the effects of HTN and DM on specific underlying cognitive abilities supporting complex language processing is clearly fertile ground for further research.

One limitation of this study results from how the authors formed the *normal/controlled* versus *uncontrolled* groups. For analyses of these groups, the authors combined as *normal/controlled* those participants with no signs of either disease with those who had one or both of them but whose biomarkers were controlled by medication. From a brain health perspective, the participants within each group may not be comparable to one another, even if both show no signs of these diseases. The authors also combined as *uncontrolled* three groups who had a diagnosis of either or both diseases, had high biomarkers, and were unsuccessfully controlled by medication. This grouping created a disproportionately small subgroup of people showing signs of diabetes (as low as 4% in some of our analyses), limiting to some extent the power of these findings. In addition, for the diagnosed individuals, the authors have no information of when they were diagnosed, how soon after diagnosis they started treatment, or how severe their disease is. All of these issues are known to have effects on cognitive performance (Dey et al., 1997; Yeung et al., 2009). Nonetheless, the results reported here provide compelling testimony of the effects of health status on language in aging adults and emphasize the importance of managing risk factors not only for cognitive aging, as recommended by Spiro & Brady (2011), but also for "language aging."

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Conflict of Interest

All authors verify that they have no financial or personal conflict of interest with this manuscript.

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Dr. D. Cahana-Amitay was responsible for the overall scientific direction of the project, concept and design, analyses, interpretation, and drafting of the manuscript. Dr. M. L. Albert contributed to the overall concept and design of the study, data interpretation, and drafting of the manuscript. E. A. Ojo and J. Sayers were responsible for compiling and analyzing the data and contributed to the drafting of the manuscript. They have read and approved the final

draft of this manuscript. Drs. M. Goral and L. K. Obler have contributed significantly to the design and concept of the overall study and this manuscript. Dr. A. Spiro contributed to the overall concept and the design of the study, statistical analysis of the data, writing of the manuscript, and interpretation of the data. All authors have read the initial drafts, revised them, and approved the final manuscript for publication.

Correspondence

Correspondence should be addressed to Dalia Cahana-Amitay, PhD, Language in the Aging Brain, Veterans Affairs Boston Healthcare System, 150 South Huntington Avenue, Boston, MA 02130. E-mail: dcamitay@bu.edu.

Supplementary Material

Supplementary material can be found at: http://biomedgerontology.oxfordjournals.org/

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