Received: 2 February 2022 | Revised: 10 November 2022 | Accepted: 12 January 2023

DOI: 10.1002/dad2.12400

Alzheimer's & Dementia
Diagnosis, Assessment & Disease Monitoring

RESEARCH ARTICLE

Sensory impairment and algorithmic classification of early cognitive impairment

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Funding information
National Institutes of Health (NIH), Grant/Award Numbers: R01AG061786, U01AG057545, K01AG050699, K01AG054693; Intramural Research Program, National Institute on Aging, NIH

Abstract

INTRODUCTION: Sensory impairment (SI) is linked to cognitive decline, but its association with early cognitive impairment (ECI) is unclear.

METHODS: Sensory functions (vision, hearing, vestibular function, proprioception, and olfaction) were measured between 2012 and 2018 in 414 Baltimore Longitudinal Study of Aging (BLSA) participants (age 74 ± 9 years; 55% women). ECI was defined as 1 standard deviation below age-, sex-, race-, and education-specific mean performance in Card Rotations or California Verbal Learning Test immediate recall. Log binomial models (cross-sectional analysis) and Cox regression models (time-to-event analysis) were used to examine the association between SI and ECI.

RESULTS: Cross-sectionally, participants with ≥3 SI had twice the prevalence of ECI (prevalence ratio = 2.10, $p = 0.02$). Longitudinally, there was no significant association between SI and incident ECI over up to 6 years of follow-up.

DISCUSSION: SI is associated with higher prevalence, but not incident ECI. Future studies with large sample sizes need to further elucidate the relationship between SI and ECI.

KEYWORDS
cognitive impairment, neuropsychological tests, sensory function

Highlights

- Sensory impairment is associated with high prevalence of early cognitive impairment
- Multisensory impairment may pose a strong risk of early changes in cognitive function
- Identifying multisensory impairment may help early detection of dementia

1 | BACKGROUND

Alzheimer's disease (AD) is a highly and increasingly prevalent irreversible neurodegenerative condition that impacts many aspects of daily functioning. As the preclinical phase of AD can take up to 20 years before a dementia diagnosis,[1] early identification of individuals at risk of AD and detection of progression to mild cognitive impairment (MCI) and dementia is critical.

A growing body of evidence suggests that sensory impairments (SI), specifically hearing, vision, and olfaction, are associated with a greater risk of developing cognitive impairment, AD, and all-cause dementia.[2–9] Most studies investigating the relationship between sensory and cognitive function typically consider the association of a single SI (e.g., hearing or vision). A few studies of multiple SI, including hearing, vision, and other senses, have found a graded relationship between the number of SI and the risk of cognitive decline and dementia in older adults.[5–7] These findings suggest that impairment across multiple sensory systems may have a synergistic effect on cognitive function. Few studies have examined the associations of other types of SI, such as proprioception and vestibular function, or the synergetic associations of these as well as other SI with cognitive function. Moreover, previous studies have mainly focused on the associations with dementia diagnoses or the prodromal phase of AD,[5–7] leaving the relationship between SI and pre-clinical AD largely undefined.

Recently, neuropsychological measures have been incorporated into MCI diagnosis and these test-based algorithms have significantly improved the accuracy of MCI classification relative to the conventional Clinical Dementia Rating (CDR) approach.[10] In the Baltimore Longitudinal Study of Aging (BLSA), we developed and compared different algorithms to define early cognitive impairment (ECI) in the preclinical stages of dementia based on neuropsychological tests.[11] Study results indicate that poor performance in a measure of visuospatial ability (Card Rotations) or verbal learning and memory (California Verbal Learning Test [CVLT] immediate recall) significantly predict future progression to MCI and dementia.[11] However, whether SI is associated with this algorithmic classification of ECI remains unknown.

In this study, we investigated individual and joint associations of multiple SI (i.e., hearing, vision, vestibular function, proprioception, and olfaction) with the risk of ECI based on the algorithmic classification. We examined cross-sectional associations between SI and ECI as well as associations between SI and future progression to ECI using time-to-event analysis. We hypothesized that individual and multiple SI are associated with a higher prevalence of ECI and a greater risk of developing ECI during follow-up.

2 | METHODS

The BLSA is a longitudinal cohort study established in 1958 and conducted by the National Institute on Aging Intramural Research Program with the aim to explore the interdependence of aging and disease processes and their mutual impact on physical and cognitive performance. A detailed description of the study design has been previously reported.[12] Briefly, the study continuously recruits community-dwelling volunteers who are free of major chronic conditions and cognitive and functional impairment at the time of enrollment. Participants receive a comprehensive evaluation of overall health, cognitive ability, and physical function every 1-4 years, depending on age (every 4 years for ages <60, every 2 years for ages 60-79, and annually for ages ≥80). In the present study, we selected the most recent BLSA visit with complete sensory data (i.e., hearing, vision, vestibular function, proprioception, and olfaction) for the cross-sectional analysis. Since vestibular function and olfaction were initiated later in the BLSA (2013 and 2015, respectively), for the time-to-event analysis we defined the earliest BLSA visit with complete vision and hearing data as the baseline visit from 2012 to 2018 and participants with ≥2 visits were included in the analysis. For both analyses, we restricted the sample to those aged ≥50 years. Informed consent was obtained from all participants, and the BLSA protocol has been approved by the Institutional Review Board of the Intramural Research Program of the National Institutes of Health.

2.1 | Measurements

2.1.1 | Hearing impairment

Pure-tone audiometric testing was conducted with insert earphones using an Interacoustics AD-629 audiometer in a sound-attenuating booth. A speech-frequency pure-tone average (PTA) of air-conduction thresholds at 0.5, 1, 2, and 4 kHz was calculated for each ear. All thresholds were measured in decibels of hearing level (dB HL). Hearing impairment was defined by the PTA ≥25 dB HL in the better-hearing ear.[13]

2.1.2 | Visual impairment

Visual impairment was defined as having impaired visual function in at least one of the following four visual domains: visual acuity, contrast sensitivity, visual fields, and stereo acuity. Presenting visual acuity was assessed monocularly using the Early Treatment of Diabetic Retinopathy Study (ETDRS) eye chart.[14] Visual acuity impairment was defined as presenting visual acuity worse than 20/40 in the better-seeing eye.[15,16] Contrast sensitivity was measured binocularly using a Pelli–Robson chart with participants' corrective lenses.[17] Contrast sensitivity impairment was defined as the log of the contrast units less than 1.55, based on previous literature.[18] Visual field was measured monocularly using a Humphrey 81-point single intensity (24 dB) full field (60°) test (Humphrey Field Analyzer, Carl Zeiss Meditec, Dublin, CA).[19] Binocular visual fields were calculated from the composite monocular values[19] and impairment was defined as the number of missed points greater than 1 standard deviation (SD) of the population mean out of 96 points.[20] Stereo acuity, measured using the Randot Stereo vision test, assessed the minimum depth differential that the participant could see. Stereo acuity impairment was defined as the minimum depth differential greater than 80 s or arc.[21]

2.1.3 | Vestibular function impairment

Vestibular function impairment was defined as impairment in either saccular function or semicircular canal function. Saccular function was measured using the cervical vestibular-evoked myogenic potential (cVEMP).[22] Semicircular canal function was measured using video head-impulse testing (vHIT) and was determined as vestibulo-ocular reflex (VOR) gain.[22] Impaired saccular function was defined as cVEMP being bilaterally absent. Impaired semicircular canal function was defined as a mean VOR gain <0.7.

2.1.4 | Proprioception impairment

The ankle proprioception threshold test assesses the minimal angular displacement (degrees) required for the participant to perceive passive movement in two directions: plantar flexion and dorsiflexion. A total of four trials were performed at an angular speed of 0.3°/s in the sequence of plantar flexion, dorsiflexion, dorsiflexion, and plantar flexion. Proprioception impairment was defined as the average of the best plantar flexion and dorsiflexion >2.2°.[23]

RESEARCH IN CONTEXT

1. **Systematic Review**: The authors reviewed the literature using traditional sources (e.g., PubMed) and meeting abstracts and presentations. A growing body of evidence suggests that sensory impairment (SI) specifically hearing, vision, and olfaction were associated with a greater risk of cognitive impairment, Alzheimer's disease (AD), and all-cause dementia. One study found that the number of SI across four sensory functions was associated with the risk of dementia in a graded fashion. The relevant citations are appropriately cited.
2. **Interpretation**: This study demonstrated cross-sectional associations between multiple SI and algorithmically defined early cognitive impairment. Identification of SI may help early detection of cognitive decline and dementia.
3. **Future Directions**: Future studies are warranted to (1) examine the combined effects of multiple SI on the development of early cognitive impairment in other larger older cohorts and (2) explore whether treatment for SI can potentially delay the progression of cognitive impairment or prevent the onset of dementia.

2.1.5 | Olfactory impairment

Olfaction was assessed using the 16-item Sniffin' Sticks Odor Identification Test and scored as the number of correctly identified odors ranging from 0 to 16. Two versions of this test were administered randomly at the first visit and then given in alternating order. Olfactory impairment was defined as a score less than the 10th percentile on either of the two test versions.[24,25]

2.1.6 | Algorithmic classification of ECI

The Card Rotations test was used to assess visuospatial ability.[26] The differences between number of correctly and incorrectly classified objects were calculated. Verbal memory was measured using the immediate free recall of the CVLT.[27] Previous findings suggest that visuospatial ability measured by Card Rotations test and CVLT immediate recall showed the earliest changes in cognitive decline during the preclinical stage of AD.[28,29] According to these findings, we developed and compared two ECI classification algorithms based on poor

performance in: (1) Card Rotations or CVLT immediate recall and (2) ≥1 (out of 2) memory or ≥3 (out of 6) non-memory tests.[11] Poor cognitive performance on each test was operationalized as 1 SD below the age-, sex-, race- (white vs. nonwhite individuals), and education-specific means in the BLSA data. Results suggest that the algorithm based on poor performance in Card Rotations or CVLT immediate recall was a strong predictor of future adjudicated diagnosis of MCI and dementia.[11] Thus, this algorithm was used to define ECI in the current study.

2.1.7 | Covariates

Sociodemographic characteristics including age, sex, race, and years of education were collected from a health interview. Self-reported race was categorized into white and non-white. Chronic conditions include diabetes, cardiovascular disease, and hypertension.

2.2 | Statistical analysis

2.2.1 | Cross-sectional analysis

Independent t-tests or chi-squared tests were used to examine differences in sociodemographic characteristics by cognitive impairment status. Individual SI, multiple SI, and number of SI were compared by cognitive impairment status using chi-squared tests or Fisher's exact tests. We further used log-binomial regression models to estimate the prevalence ratios (PRs) and 95% confidence intervals (CIs) by individual and multiple SI. First, the individual SI was compared with those without the specific impairment. Next, participants with two, three, or four combinations of SI were compared with those without the specific combination. We additionally estimated the PRs comparing each individual and multiple SI versus those without any SI. Finally, number of SI was treated as continuous and categorical independent variables in separate models. Model 1 was an unadjusted model and Model 2 was adjusted for age, sex, race, years of education, cardiovascular disease, diabetes, and hypertension.

2.2.2 | Time-to-event analysis

As the earliest visit with complete hearing and vision data was defined as baseline, we had smaller sample sizes for vestibular function and olfaction because these tests were only available at later BLSA visits as noted above. Participants with ECI at baseline (visits at which hearing and vision were first measured) were removed from the analysis. Cox proportional hazards models were used to estimate the hazard ratios (HRs) and 95% confidence intervals (CIs) for risk of developing ECI comparing individual and multiple SI versus those without the specific impairment. We additionally estimated the HRs comparing each individual and multiple SI versus those without any SI. Multivariable models were adjusted for age, sex, and years of education.

All analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC). All statistical tests were two-tailed and the significance level α was set as 0.05.

3 | RESULTS

3.1 | Cross-sectional associations between sensory impairment and ECI

Among 364 participants with both complete sensory and cognitive data in the most recent BLSA visit from 2015 to 2018, 92 (25.3%) had ECI. The mean age was 73.3 (SD = 10.1) years, 203 (55.8%) were women, and nearly two-thirds (62.1%) were white individuals (Table 1). The average number of SI was 1.25 (SD = 1.1). There were no significant differences in age, sex, race, education, chronic conditions, or number of SI by ECI status (Table 1). The distribution of each continuous sensory variable by ECI is shown in Figure S1.

There were significant differences in the proportion of participants with ECI by individual and multiple SI in unadjusted analyses (Table S1). Participants with proprioception impairment were more likely to be classified as having ECI, compared to those without proprioception impairment ($p = 0.032$). For multiple SI, participants with impairments in the following combinations: hearing and proprioception; hearing, vestibular, and proprioception; vision, vestibular, and proprioception; and vision, vestibular, and olfaction were more likely to be classified as having ECI than those without these impairments.

Log-binomial regression models showed similar results as the chi-squared analysis (Figure 1; Table S2). After adjusting for covariates, the associations became stronger. In fully adjusted models, for individual SI, participants with proprioception impairment tended to have a greater risk of having ECI (PR = 1.75; 95% CI: 1.14–2.68; $p = 0.010$; Table S2, Model 2). Participants with any two SI were more likely to have ECI (PR = 1.53; 95% CI: 1.02–2.28; $p = 0.038$). Impairments in hearing and vision, hearing and proprioception, vision and proprioception, vestibular function, and proprioception were associated with a greater prevalence of ECI in the fully adjusted models (PRs = 1.81–2.55; $p < 0.05$). Participants with any three SI had a greater prevalence of ECI (PR = 1.86; 95% CI: 1.15–3.02; $p = 0.011$). Almost all combinations of three SI were associated with a higher prevalence of ECI, except for the following combinations: hearing, vision, and vestibular impairment; hearing, vestibular, and olfactory impairment; vision, proprioception, and olfactory impairment; and vestibular, proprioception, and olfactory impairment. Three combinations of four SI were associated with a greater prevalence of ECI (PRs = 2.43–3.50; $p < 0.05$). There were no substantial changes in results using participants without any SI as the reference group for all models (Table S3). Additionally, using the number of SI as a continuous variable, we found that each additional SI was associated with a 29% greater prevalence of ECI after adjusting for covariates (PR = 1.29; 95% CI: 1.07–1.55; $p = 0.007$). Categorically, participants with ≥3 SI had over double the risk of having ECI (PR = 2.10; 95% CI: 1.14–3.88; $p = 0.017$) than those without any SI after adjusting for demographic and health characteristics.

TABLE 1 Sociodemographic characteristics and algorithmic classification of early cognitive impairment (ECI)[a].

Characteristics	All N = 364	ECI (n = 364) Yes n = 92 (25.3%)	ECI (n = 364) No n = 272 (74.4%)	*p*-Value[a]
Age (years)	73.3 ± 10.1	72.7 ± 10.8	73.5 ± 9.9	0.504
Female	203 (55.8)	54 (58.7)	149 (54.8)	0.513
White race	226 (62.1)	51 (55.4)	175 (64.3)	0.128
Education years	17.6 ± 2.6	17.9 ± 2.7	17.5 ± 2.6	0.251
BMI (kg/m2)	27.5 ± 4.9	27.7 ± 4.9	27.4 ± 4.8	0.644
Cardiovascular disease	28 (7.7)	4 (4.4)	24 (8.8)	0.164
Diabetes	49 (13.5)	15 (16.3)	34 (12.5)	0.355
Hypertension	175 (48.1)	44 (47.8)	131 (48.2)	0.956
Number of sensory impairments	1.25 ± 1.1	1.43 ± 1.3	1.19 ± 1.1	0.071

Note: Chi-squared tests for female, white race, cardiovascular disease, diabetes, and hypertension; independent t-tests for age, education years, and BMI.
Abbreviation: ECI, early cognitive impairment.
[a]ECI was defined as 1 standard deviation below the age-, sex-, race-, and education-adjusted means in Card Rotation test or California Verbal Learning Test immediate recall scores.

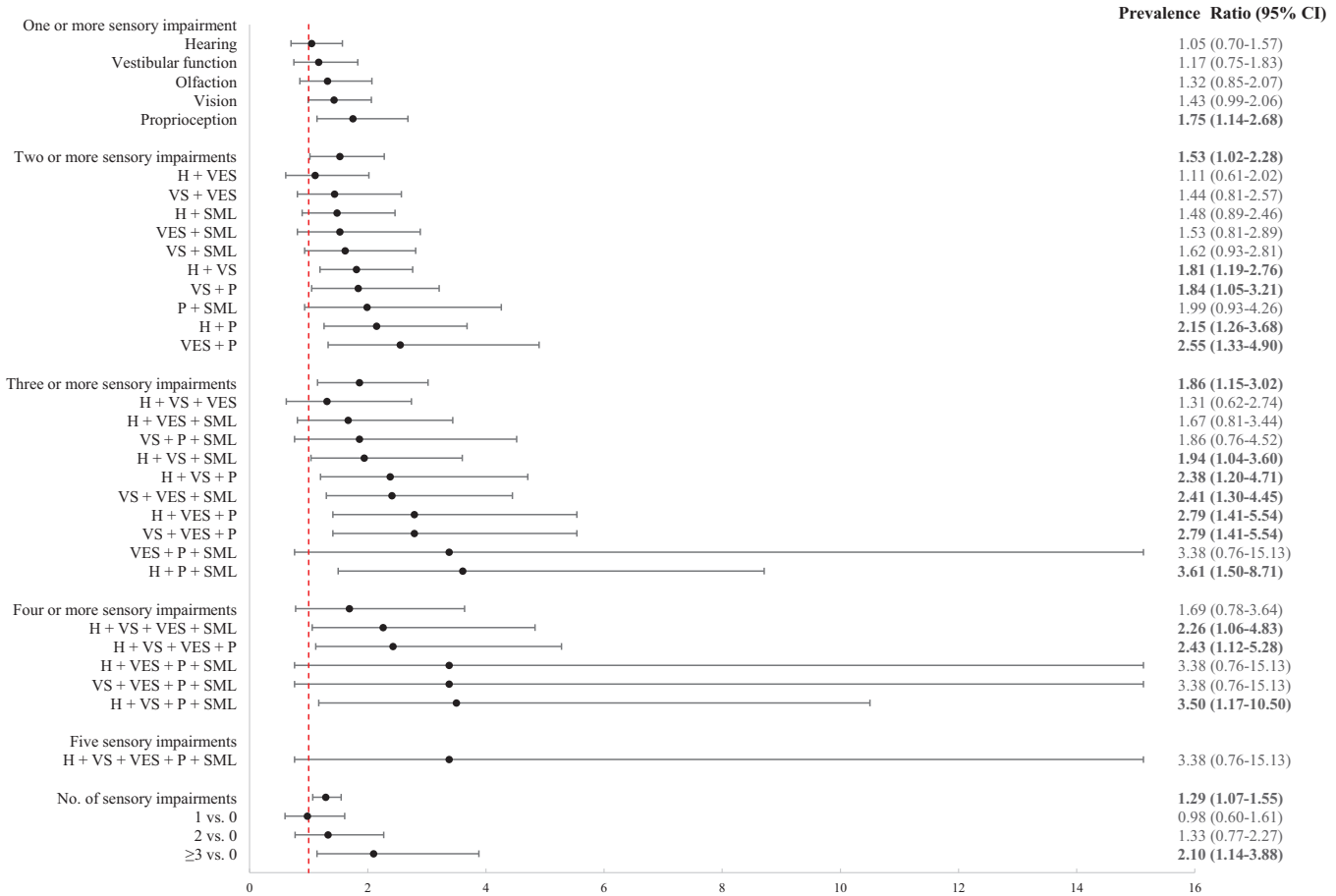

FIGURE 1 Prevalence ratios of algorithmic classification of early cognitive impairment (ECI) by sensory impairments adjusted for age, sex, race, years of education, cardiovascular disease, diabetes, and hypertension. ECI was defined as 1 standard deviation below the age-, sex-, race-, and education-adjusted means in Card Rotation test or California Verbal Learning Test immediate recall scores. CI, confidence interval; H, hearing; P, proprioception; SML, olfaction; VES, vestibular; VS, vision.

3.2 | Baseline sensory impairment and future progression to algorithmic ECI

Among 790 participants with both complete sensory (i.e., hearing and vision) data and cognitive data at baseline, 218 with ECI at baseline were excluded from the analysis. After removing 158 participants with only one BLSA visit, 414 were included in the final analytic sample. The average age at baseline was 74.0 (SD = 8.8) years and 227 (55.0%) were women. Approximately, 70% of the participants were of white race. The average years of education were 17.8 (SD = 2.8). At baseline, 53.1% of the participants had hearing impairment and 33.1% had vision impairment. The percentages of other SI were 30.0%, 10.7%, and 12.1% among 223, 354, and 58 participants with complete vestibular function, proprioception, and olfaction data, respectively. About one-fourth of the participants had no impairment, 40.3% had one impairment, and 32.9% had two or more SI. These participants were followed for an average of 3.4 years after baseline, ranging from 1 to 6 years.

Unadjusted Cox proportional hazards models showed that individual SI or combinations of SIs at baseline were not statistically associated with future progression to ECI (Table 2, Model 1). In terms of the number of SI, we found that compared to those without any SI, participants with 1 or ≥2 SI had double the risk of ECI (HR = 2.00, 95% CI: 1.08–3.71; HR = 1.96, 95% CI: 1.02–3.76, respectively). These associations were attenuated after adjusting for age, sex, and education (Table 2, Model 2). When using those without any SI as the reference group (Table S4), participants with only hearing or vision impairment, or dual impairment had a greater risk of developing ECI over time only in unadjusted models (HRs = 2.00–2.26; $p < 0.03$).

4 | DISCUSSION

This study demonstrated cross-sectional associations between SI and algorithmically defined ECI. In continuous models, each additional SI was associated with a 29% greater risk of having ECI. Furthermore, we found that multiple SI was significantly associated with the prevalence of ECI, where participants with ≥3 SI had double the risk of having ECI. In time-to-event analysis, having one or ≥2 SI was associated with double the risk of developing ECI over the following 4 years, but these associations were diminished after adjusting for demographics. Collectively, these findings suggest that older adults with multisensory impairment may be at higher risk for early changes in cognitive function, facilitating potential early detection of those at greater risk for future cognitive impairment or dementia.

Our study used a novel psychometrically defined ECI as the outcome. This algorithmic classification of ECI captures changes in visuospatial ability and verbal memory, which show early changes during the preclinical phase of AD[28] and predict a future diagnosis of MCI and dementia.[11] Although previous studies have demonstrated a link between multisensory impairment and cognitive impairment, none of these studies have employed the concept of early decline in cognition.[3,5–7] Our approach facilitates the understanding of potential pathways from SI and changes in cognitive function at an early stage when interventions are more likely to be successful. To this end, the associations between SI and ECI may inform future timely and effective interventions that modify sensory loss and delay early cognitive changes, eventually reducing the risk of future AD.

Previous cohort studies found that SIs were strong predictors of cognitive decline and dementia in older adults,[30,5–7,9] including impairment in hearing and vision,[2,5,7,9,30,31] and olfaction.[3,8,32] Yet few studies have investigated other SI such as proprioceptive or vestibular function in relation to cognitive impairment or dementia.[33] Previous cross-sectional work has reported the association between vestibular loss and poorer cognitive function (notably spatial ability) and odds of AD,[34,35] but the potential mechanisms underlying these associations are unclear. To the best of our knowledge, this is the first study to explore the association between proprioception and cognitive impairment. We found that, cross-sectionally, older adults with proprioceptive impairment were more likely to be classified as having ECI than those without impaired proprioception, but no longitudinal association was observed. Other studies with larger longitudinal samples are needed to replicate our findings and further elucidate the relationship between proprioception and cognitive impairment.

The combined association between multiple SI and the risk of dementia has rarely been investigated. Brenowitz et al. found that the number of SI (i.e., vision, hearing, smell, and touch) was associated with the risk of dementia in a graded fashion.[6] Specifically, participants with 1, 2, or ≥3 SI had a significantly greater risk of developing incident dementia over up to 10 years of follow-up.[6] In our study, we observed cross-sectional associations between ≥3 SI and higher prevalence of ECI, but a lack of statistical power to test 3 or more combinations of SI limited our time-to-event analysis. Furthermore, our study builds on this prior study by examining the association between multiple SI and ECI in the preclinical phase, a time window when disease progression may be most modifiable.

Given the robust and consistent findings of the strong association between multiple SI and cognitive impairment in numerous cohort studies, there may be a common etiology between deterioration of sensory and cognitive function.[2] For example, impairments in sensory and cognitive systems may be affected by underlying pathophysiological changes as a consequence of vascular disease, metabolic dysregulation, and/or inflammation.[2] Aging is also a common effect on sensorineural health. Previous studies have found that a high proportion of age-related variance in cognition is shared with vision and hearing.[36,37] Additionally, AD-related pathologic changes, such as beta amyloid (Aβ) deposition, may occur in both sensory and cognitive brain networks.[38] For example, studies have found that the presence of Aβ in the lens and retina may reflect AD progression.[39] Alternatively, it is possible that sensory input loss may directly alter brain structure and function through decreased social engagement and interaction[2] as sensory deprivation has been associated with neuroplastic changes and leads to impairment in cognitive performance.[40] Further studies are needed to examine the combined effects of SI on development of ECI in other older populations.

TABLE 2 Hazard ratios of early cognitive impairment (ECI)[a] by sensory impairment at baseline.

Separate models	No. of participants	No. of events	Survival time (years)	Model 1		Model 2	
				Hazard ratio (95% CI)	*p*-Value	Hazard ratio (95% CI)	*p* value
One or more sensory impairment							
Hearing (N = 414)	220 vs. 194	48 vs. 29	3.3 vs. 3.4	1.51 (0.95-2.39)	0.083	0.97 (0.56-1.67)	0.905
Vision (N = 414)	137 vs. 277	28 vs. 49	3.0 vs. 3.5	1.46 (0.91-2.32)	0.113	1.22 (0.75-1.98)	0.420
Vestibular function (N = 213)	64 vs. 149	8 vs. 30	3.2 vs. 2.9	0.49 (0.21-1.11)	0.088	0.45 (0.20-1.05)	0.064
Proprioception (N = 354)	38 vs. 316	7 vs. 58	3.0 vs. 3.3	1.14 (0.52-2.50)	0.744	1.09 (0.49-2.40)	0.835
Olfaction (N = 58)	7 vs. 51	1 vs. 5	2.3 vs. 2.1	1.33 (0.15-11.45)	0.797	2.61 (0.21-32.65)	0.457
Two or more sensory impairments[b]							
H + VS (N = 414)	83 vs. 331	18 vs. 59	3.0 vs. 3.4	1.44 (0.85-2.45)	0.174	1.02 (0.58-1.79)	0.958
H + VES (N = 213)	36 vs. 177	5 vs. 33	3.2 vs. 3.0	0.60 (0.23-1.60)	0.305	0.51 (0.19-1.42)	0.199
H + P (N = 354)	22 vs. 332	4 vs. 61	3.0 vs. 3.3	1.09 (0.40-3.01)	0.865	0.85 (0.31-2.38)	0.763
H + SML (N = 58)	4 vs. 54	1 vs. 5	2.2 vs. 2.1	3.57 (0.40-32.22)	0.257	6.72 (0.52-87.60)	0.146
VS + VES (N = 213)	19 vs. 194	2 vs. 36	2.8 vs. 3.0	0.61 (0.15-2.57)	0.503	0.60 (0.14-2.55)	0.490
VS + P (N = 354)	12 vs. 342	2 vs. 63	3.0 vs. 3.3	1.07 (0.26-4.39)	0.923	1.04 (0.25-4.28)	0.961
Three or more sensory impairments							
H+VS+VES (N = 213)	12 vs. 201	2 vs. 36	2.6 vs. 3.0	1.08 (0.25-4.61)	0.917	1.06 (0.25-4.56)	0.937
H+VS+PFDF (N = 354)	6 vs. 348	1 vs. 64	2.8 vs. 3.3	1.05 (0.15-7.60)	0.961	0.77 (0.11-5.64)	0.801
No. of sensory impairments (continuous)	–	–	–	1.22 (0.95-1.57)	0.114	0.99 (0.74-1.34)	0.965
No. of sensory impairments (categorical)							
0	111	14	3.7	Ref		Ref	
1	167	37	3.3	2.00 (1.08-3.71)	**0.027**	1.52 (0.78-2.93)	0.216
2 or more	136	26	3.1	1.96 (1.02-3.76)	**0.043**	1.24 (0.59-2.63)	0.570
≥ 2 sensory impairments	136 vs. 278	26 vs. 51	3.1 vs. 3.5	1.25 (0.78-2.00)	0.363	0.89 (0.53-1.49)	0.658
≥ 3 sensory impairments	27 vs. 387	3 vs. 74	2.9 vs. 3.4	0.72 (0.23-2.28)	0.575	0.56 (0.18-1.80)	0.332

Note: Cox proportional hazard model 1: unadjusted model; model 2: adjusted for age, sex, and years of education. The reference group for each model is those without the particular impairment. The bold values indicate statistical significance ($p < 0.05$).

Abbreviations: H, hearing; VS, vision; VES, vestibular; P, proprioception; SML, olfaction; CI, confidence interval.

[a]ECI was defined as 1 standard deviation below the age-, sex-, race-, and education-adjusted means in Card Rotation test or California Verbal Learning Test immediate recall scores.

[b]Combinations H+SML, VES+P, VES+SML, and P+SML were removed from this table due to 0 event among those with sensory impairments.

Importantly, the associations between sensory function and ECI may not be equivalent across the five sensory systems. In addition to the mechanisms noted above, other causal pathways may link hearing and vision impairment to ECI. It is possible that vision and hearing impairment increases cognitive load and may limit the neural resources available to perform cognitively demanding tasks, thus, participants with these impairments may be more likely to be classified as having cognitive impairment. In addition, depression, social isolation, or lack of physical and cognitively stimulating activities, as a result of hearing and vision impairment, may also play a crucial role in cognitive decline.[41–43] Impairments in the other three sensory systems may act as early markers/indicators of cognitive decline instead of upstream causes of ECI.[32,44] Again, the small sample sizes in these sensory systems, especially olfaction, may have limited our statistical power to detect longitudinal associations with ECI.

The strengths of this study include a well-characterized sample, measures of five sensory systems, multiple measures of vision function (i.e., contrast sensitivity, visual field, and stereo acuity in addition to visual acuity), investigations of combined effects of multiple SI, and utilization of a novel algorithmic classification of ECI. Several limitations also need to be considered. First, in the longitudinal analyses, measures of vestibular and olfactory function started later in the BLSA study, which lead to smaller sample size and limited power to detect the associations with future ECI. Future studies with larger sample sizes in these measures are warranted. Second, SI were dichotomized using previously determined clinical cutoffs[45] and severity of impairments was not considered in these analyses. Future studies may investigate the association between different levels of SI and risk of ECI and incorporate severity of impairment into the multisensory variables. Third, we used complete cases for cross-sectional analyses; missing values in sensory function may impact the study results. Hearing and vision impairment may have greater weights in multiple SI in longitudinal analyses due to smaller sample sizes in the other three sensory systems. In addition, the number of measurements varied across sensory domains, each sensory impairment may not have equivalent effects on multiple SI variables.

In conclusion, multiple sensory impairment was significantly associated with higher prevalence of early cognitive impairment cross-sectionally. To this end, the combined effects of impairment in multiple sensory domains may pose a stronger risk of cognitive decline than individual sensory impairment. Identification of SI may thus help early detection of cognitive decline in older adults. Future studies are warranted to examine whether treatment for SI (e.g., vision correction, hearing aid use, etc.) can potentially delay the progression of cognitive impairment or prevent the onset of dementia.

ACKNOWLEDGMENTS

This work was supported by the National Institutes of Health (NIH) grant R01AG061786. Yurun Cai and Jennifer A. Schrack are supported by R01AG061786 and U01AG057545. Alden L. Gross was supported by the NIH K01AG050699. Jennifer A. Deal was supported by NIH grant K01AG054693. This study was also supported in part by the Intramural Research Program, National Institute on Aging, NIH. Nicole M. Armstrong, Qu Tian, Yang An, Eleanor M. Simonsick, Luigi Ferrucci, Susan M. Resnick were all supported by the Intramural Research Program of the National Institute on Aging, NIH.

CONFLICTS OF INTEREST STATEMENT

Frank R. Lin reports being a consultant to Frequency Therapeutics, receiving speaker honoraria from Caption Call, and being the director of a public health research center based at the Johns Hopkins Bloomberg School of Public Health funded in part by Cochlear Ltd. There are no potential conflicts of interest among other authors on the paper. Author disclosures are available in the supporting information.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Cai Y, Schrack JA, Gross AL, et al. Sensory impairment and algorithmic classification of early cognitive impairment. *Alzheimer's Dement*. 2023;15:e12400. https://doi.org/10.1002/dad2.12400