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Elements of Financial/Personal Conflicts	MEF		KJC		CRS		AAP	
	Yes	No	Yes	No	Yes	No	Yes	No
Employment or Affiliation		X		X		X		X
Grants/Funds	X		X		X		X	
Honoraria		X		X		X		X
Speaker Forum		X		X		X		X
Consultant		X		X		X		X
Stocks		X		X		X		X
Royalties		X		X		X		X
Expert Testimony		X		X		X		X
Board Member		X		X		X		X
Patents		X		X		X		X
Personal Relationship		X		X		X		X

Elements of Financial/Personal Conflicts	CMC		BEKK		RK		TST	
	Yes	No	Yes	No	Yes	No	Yes	No
Employment or Affiliation		X		X		X		X
Grants/Funds	X		X		X		X	
Honoraria	X			X		X		X
Speaker Forum		X		X		X		X
Consultant		X		X		X		X
Stocks		X		X		X		X
Royalties		X		X		X		X
Expert Testimony		X		X		X		X
Board Member		X		X		X		X
Patents		X		X		X		X
Personal Relationship		X		X		X		X

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Age-Related Sensory Impairments and Risk of Cognitive Impairment

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Abstract

Background/Objectives—To evaluate the associations of sensory impairments with the 10-year risk of cognitive impairment. Previous work has primarily focused on the relationship between a single sensory system and cognition.

Design—The Epidemiology of Hearing Loss Study (EHLS) is a longitudinal, population-based study of aging in the Beaver Dam, WI community. Baseline examinations were conducted in 1993 and follow-up exams have been conducted every 5 years.

Setting—General community

Participants—EHLS members without cognitive impairment at EHLS-2 (1998–2000). There were 1,884 participants (mean age = 66.7 years) with complete EHLS-2 sensory data and follow-up information.

Measurements—Cognitive impairment was a Mini-Mental State Examination score of < 24 or history of dementia or Alzheimer's disease. Hearing impairment was a pure-tone average of hearing thresholds (0.5, 1, 2 and 4 kHz) of > 25 decibel Hearing Level in either ear. Visual impairment was Pelli-Robson contrast sensitivity of < 1.55 log units in the better eye and olfactory impairment was a San Diego Odor Identification Test score of < 6.

Results—Hearing, visual, and olfactory impairment were independently associated with cognitive impairment risk [Hearing: Hazard Ratio (HR) = 1.90, 95% Confidence Interval (C.I.) =

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1.11, 3.26; Vision: HR = 2.05, 95% C.I. = 1.24, 3.38; Olfaction: HR = 3.92, 95% C.I. = 2.45, 6.26]. However, 85% with hearing impairment, 81% with visual impairment, and 76% with olfactory impairment did not develop cognitive impairment during follow-up.

Conclusion—The relationship between sensory impairment and cognitive impairment was not unique to one sensory system suggesting sensorineural health may be a marker of brain aging. The development of a combined sensorineurocognitive measure may be useful in uncovering mechanisms of healthy brain aging.

Keywords

cognitive impairment; hearing impairment; visual impairment; olfactory impairment; population-based

INTRODUCTION

With aging comes an increase in the incidence of sensory loss and cognitive decline, each having a considerable impact on public health and quality of life.[1–4] In cross-sectional and prospective studies, significant associations of hearing, visual, and olfactory impairment with cognitive decline or impairment, including Alzheimer's disease and all cause dementia, have been observed.[5–16] Among the prospective studies, in a recent investigation in the Baltimore Longitudinal Study of Aging cohort, with a median follow-up of nearly 12 years, an increased risk of incident dementia associated with hearing loss was observed.[14] In a 6-year follow-up investigation in the Maastricht Aging Study, poorer baseline hearing ability and a decline in hearing ability over the 6 years were both related to declining cognitive test scores including tests measuring memory and processing speed.[8] Visual impairment has also been reported to be significantly related to cognitive function. For example, in a study of older individuals with an average age of over 80, the mean Mini-Mental State Examination (MMSE) score was modestly but significantly lower in those with visual acuity impairment.[9] In another study with several thousand women 65 years of age and older, visual impairment (corrected binocular vision worse than 20/40) was related to cognitive decline over a 4 year follow-up.[7]

Prospective investigations of the risk of cognitive decline or impairment associated with olfactory dysfunction have been conducted.[10–12] In the Epidemiology of Hearing Loss Study (EHLS), a significantly elevated risk of developing cognitive impairment over a 5 year follow-up period was observed in those with olfactory impairment at baseline.[11] Olfactory function was also significantly related to the incidence of mild cognitive impairment over a 5 year period in the Rush Memory and Aging Project[10] and with 5-year decline in the MMSE score in the Betula Study.[12]

Previous work has been primarily focused on sensory-specific relationships. Although a few investigations, including early studies, have considered dual impairment,[6,7,9] no longitudinal study has considered the inter-relationship of hearing, visual, and olfactory impairment, and the risk of cognitive impairment or decline. Studying the association between cognition and sensory loss in multiple systems may provide useful information in the consideration of possible mechanisms and interventions. The objective of the present study was to determine

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whether hearing, visual, and olfactory impairment were independently associated with an increased 10 year risk of cognitive impairment. The validity and predictive value of using sensory measures as screening tools for future development of cognitive impairment was evaluated.

METHODS

Study Population

The study population included participants in the EHLS, a population-based, prospective investigation of age-related sensory loss. The EHLS is based in Beaver Dam, Wisconsin and participants in the baseline (1987–1988) Beaver Dam Eye Study were eligible. The baseline EHLS examination was conducted in 1993–1995 and follow-up examinations have been done on a 5-year basis. In the current study, the first 5-year follow-up (EHLS-2, 1998–2000) was used as the baseline with cognitive impairment incidence data coming from the 10-year (EHLS-3, 2003–2005) and 15-year (EHLS-4, 2009–2010) examinations. Additional details of the EHLS and Beaver Dam Eye Study have been reported.[17–19] Institutional Review Board approval by the Health Sciences Institutional Review Board of the University of Wisconsin and informed consent were obtained.

EHLS participants were eligible for inclusion in the current study if they were examined at EHLS-2, had a MMSE[20] score of 24 or greater, had no self- or proxy-reported history of dementia, and were examined again during at least one of the follow-ups. There were 2015 eligible participants and 1884 had complete baseline sensory impairment information. Of these 1884 participants, 258 were examined in EHLS-3 but died before EHLS-4. Among the remaining 1626 participants, 156 (9.6%) participated in EHLS-3 only, and 1470 (90.4%) participated in EHLS-4 (1433 were examined in EHLS-3 and EHLS-4 whereas 37 were examined in EHLS-4 only).

Measurements

Outcomes

Cognitive Impairment: Cognitive impairment was defined as an MMSE score of < 24/30 or a self- or proxy-reported history of dementia or Alzheimer's Disease.[11] The MMSE and Alzheimer's Disease/dementia history were ascertained at all phases included in this report.

Sensory Impairments

Hearing: Examinations included audiometric testing conducted according to the American Speech-Language-Hearing Association guidelines[21] and in compliance with American National Standards Institute (ANSI) standards.[22,23] Clinical audiometers with TDH-50P earphones and ER-3A insert earphones were used in sound-treated booths. Portable audiometers with insert earphones were used for testing in homes or group facilities when the participant was unable to visit the examination office. Pure-tone air-conduction thresholds were obtained at 0.5, 1, 2, 3, 4, 6, and 8 kHz, and bone-conduction thresholds were obtained at 0.5, 2, and 4 kHz. Testing was performed for both ears and masking was done when necessary.[18,19] Hearing impairment was defined as a pure-tone average (PTA) at 0.5, 1, 2, and 4 kHz of > 25 decibel Hearing Level in either ear.[18]

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Vision: Vision was assessed in the Beaver Dam Eye Study examination concurrent with the EHLS study.[24] Contrast sensitivity was measured in both eyes using Pelli-Robson letter charts.[25] The measurement unit was log contrast sensitivity units based on triplet scores and visual impairment as defined as contrast sensitivity < 1.55 log units in the better eye.[26]

Olfaction: Olfactory function was determined using the San Diego Odor Identification Test (SDOIT), a standardized test of the ability to correctly identify 8 common odors.[27] The odorants were presented in a random order and at 45 second intervals. A picture array with illustrations of the 8 odorants and 12 distractors was available during the test to aid in identification and allow for a non-verbal response. After presentation of an odor, participants could respond either verbally or point to the picture of the odorant. If an odor was not identified correctly, participants were told the name of the odor and it was presented a second time later in the test sequence. Olfactory impairment was defined as correctly identifying < 6 odors after 2 trials. This cut point was based on a previous evaluation of scores which found that 95% of the youngest EHLS participants had scores of 6 or better.[27]

Covariates—Covariate information from the current study's baseline (EHLS-2) was used.

Measurements: Blood pressure was measured following the Hypertension Detection and Follow-up Program protocol.[28] Hypertension was defined as systolic blood pressure >=140 mmHg or diastolic blood pressure >= 90 mmHg or a diagnosis of high blood pressure with current anti-hypertensive medication use. Glycosylated hemoglobin was measured using the Gly-Affin assay (Isolab, Inc., Akron OH) and diabetes was defined as Glycosylated hemoglobin > 8% (Hemoglobin A1C >= 6.5%) or a diagnosis of diabetes or suspected diabetes with current treatment. Reflectance spectrophotometry was used to determine cholesterol levels in non-fasting samples and non-high-density (non-HDL) cholesterol (mg/dl) was calculated as total minus HDL. High resolution B-mode carotid artery ultrasound images were obtained with a Biosound AU4 (Indianapolis, IN, USA). A modified Atherosclerosis Risk in Communities protocol[29] was followed to measure the carotid intima-media thickness (IMT) of the near and far walls of the common carotid artery, internal carotid artery and the bifurcation on the left and right sides. The mean of the 12 sites was used in analyses.

High sensitivity C-reactive protein (CRP) and interleukin-6 (IL-6) were measured in non-fasting samples. CRP was measured using a latex particle-enhanced immunoturbidimetric assay kit (Roche Diagnostics, Indianapolis, IN) and a quantitative sandwich enzyme assay technique (QuantiKine High Sensitivity Kit, R&D Systems, Minneapolis, MN) was used to measure IL-6. The interassay coefficient of variation was 4.5% for CRP and 11.7% for IL-6. The CRP and IL-6 values were dichotomized according to highest tertile versus the combined middle and low tertiles of the respective distributions; the cutpoint was 3.53 mg/L for CRP and 2.11 pg/mL for IL-6. A summary variable was created which was a count of the number of inflammatory markers in the highest tertile (range 0–2).

Height and weight were measured and body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters and was categorized as < 26.0, 26.0–29.9, and 30.0+ kg/m^2. A frailty index was obtained by giving a 0–1 score to 4 frailty

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measures and summing.[30] The 4 measures included gait time (time to walk 10 feet at usual pace), the number of attempts to rise from a seated position without using arms, the peak expiratory flow rate using the mini-Wright meter,[24] and handgrip strength in the dominant hand measured with a dynamometer.[24] A score of 1 was assigned if gait time was in the 4th quartile, peak expiratory flow rate was in the 1st quartile, handgrip strength was in the 1st quartile, or the participant could not stand from a seated position in the first attempt.[30]

Self-Reported Information: Interviewer-administered questions gathered information on birthdate, sex, education, occupational history (longest held job), exercise (at least once per week long enough to sweat), smoking status, number of servings of beer, wine or hard liquor consumed during an average week in the past year (converted to grams of ethanol), and history of hypertension, diabetes, recent cold (today or past week), nasal polyps, deviated septum, allergy, head injury, stroke, or epilepsy.

Statistical Methods

All analyses were completed using SAS version 9.4 (SAS Institute, Inc. Cary, NC).

Kaplan-Meier (product-limit) survival analysis produced the 10-year cumulative incidence of cognitive impairment.[31] Cox discrete time proportional hazards analyses were performed to model the relationship between sensory impairment and the incidence of cognitive impairment.[32] Hazard ratios and 95% confidence intervals were calculated from the parameter estimates and standard errors. Covariates previously reported as associated with sensory or cognitive impairment were included in multivariable models.

Sensitivity was calculated as the percentage of the cognitively impaired at follow-up who displayed sensory impairment at baseline (EHLS-2). Specificity was calculated as the percentage of the non-cognitively impaired at follow-up who did not display sensory impairment at baseline. The positive predictive value is the percentage that developed cognitive impairment in those who had baseline sensory impairment whereas the negative predictive value is the percentage that did not develop cognitive impairment in the participants who did not have baseline sensory impairment.

RESULTS

The mean age of the 1884 study subjects was 66.7 years (standard deviation = 8.4 years), 40.9% were male, and 37% had some college or more education (Table 1). Slightly over 10% were current smokers at baseline and less than half exercised long enough to work up a sweat at least once per week. Approximately 56% of the participants had 1 or more sensory impairments (43.9% had hearing impairment, 21.1% had visual impairment, and 17.2% had olfactory impairment). There were 90 participants (4.8%) with all 3 impairments.

The 10-year cumulative incidence of cognitive impairment was 9.9%. Participants with sensory impairment at baseline had higher cognitive impairment incidence rates than those without sensory impairment. The 10-year, unadjusted cumulative incidence of cognitive impairment for subjects with hearing, visual, and olfactory impairment was 17.3%, 23.5%, and 30.0%, respectively (Table 2).

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With adjustment for age, sex, and education, the risk of cognitive impairment was significantly higher among those with baseline hearing impairment [Hazard ratio (HR) = 2.11, 95% Confidence Interval (C.I.) = 1.30, 3.40)], visual impairment (HR = 1.92, 95% C.I. = 1.25, 2.96), or olfactory impairment (HR = 4.18, 95% C.I. = 2.68, 6.51) compared to those without impairment (Table 2). With adjustment for additional covariates, including vascular-related measures, the association between sensory impairment and 10-year risk of cognitive impairment continued to be statistically significant (hearing: HR = 2.09, 95% C.I. = 1.29, 3.39; vision: HR = 1.96, 95% C.I. = 1.25, 3.07; olfaction: HR = 4.04, 95% C.I. = 2.54, 6.43). When the 3 sensory impairments were included in the model simultaneously, each displayed a significant, independent association with cognitive impairment risk. The strength of the associations were similar in the sensory-specific impairment models (Table 2) and the multiple impairment models (Table 3) (Multivariable adjusted: hearing: HR = 1.90, 95% C.I. = 1.11, 3.26; vision: HR = 2.05, 95% C.I. = 1.24, 3.38; olfaction: HR = 3.92, 95% C.I. = 2.45, 6.26).

A sensitivity analysis assessing the impact of cataract surgery on the contrast sensitivity–cognitive impairment relationship was performed. Participants with no cataract surgery history at baseline were selected and results showed the cognitive impairment risk associated with contrast sensitivity impairment in the sub-sample was very similar ($HR_{\text{multivariable adjusted}}$ = 2.14, 95% C.I. = 1.30, 3.52) to that observed in the entire study population. In addition, the relationship between contrast sensitivity in the worse eye and cognitive impairment risk was found to be not significant ($HR_{\text{multivariable adjusted}}$ = 1.46, 95% C.I. = 0.89, 2.40).

The use of sensory measures as screening tools for future cognitive impairment was assessed. Sensitivity ranged from 21.7% for having all 3 sensory impairments to 72.9% for hearing impairment (Table 4). Correspondingly, specificity was low for hearing impairment (59.0%) but very high for the combination of all 3 sensory impairments (96.9%). Positive predictive value was 14.6% for hearing impairment meaning 85.4% of the participants with baseline hearing impairment did not develop cognitive impairment during follow-up. The highest positive predictive value, 40.0%, was associated with having all 3 impairments.

DISCUSSION

Hearing, visual, and olfactory impairment demonstrated significant effects on the 10 year risk of cognitive impairment independent of one another. The results from the joint model suggested that an individual with hearing, visual, and olfactory impairment had a risk of developing cognitive impairment which was 15 times that of an individual without baseline sensory impairment.

These results are consistent with the extensive previous literature reporting that hearing, vision, and olfaction individually are associated with cognition. But the current study extends the research and models the joint effect of the 3 sensory impairments on the risk of cognitive impairment showing that each sensory impairment has an independent effect on the risk of cognitive impairment. The association between sensory impairment and cognitive impairment was not unique to one sensory system.

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The finding of a significant relationship between sensory impairment and cognitive impairment is possibly expected since neurologic functioning is being assessed when sensorineural health is measured as well as when cognitive health is measured. For example, although pure-tone audiometry relies on the functioning of the auditory periphery, it also relies on central auditory processing and decoding of the signals along with some cognitive decision-making in forming a response to the signal. The sensorineural system needs the brain for processing. Audiometric loss may not be indicative of simply peripheral changes; it may also be indicative of auditory system-wide changes. Cognitive processing, judgment and decision-making are also involved in contrast sensitivity and olfaction testing. Therefore, in models using sensory measures to predict cognitive impairment or decline, one contributory explanation for the observed relationships may be that essentially there are measures of neurologic health on both the dependent (outcome) and the independent (predictors) sides of the model.

Alternatively, more than 20 years ago, the common-cause theory was introduced suggesting that one or more underlying factors exist which are contributing to the development of both sensory and cognitive impairment.[6] One such factor or influence may be a generalized aging effect. Previous work has found that a very high proportion of the age-related variance in cognitive measures is shared with sensory measures.[6,33] In the Australian Longitudinal Study of Aging, close to 80% of the age-related variance in cognition was shared with hearing and vision.[33] Sensory declines may be early signs of age-related changes in neurologic functioning, neuropathology or neurodegeneration, before measures of cognitive function show impairment. Sensorineural health may serve as a marker of healthy brain aging.

Another common cause which has been investigated is vascular disease. Many reports have described an association of cardiovascular disease (CVD) and related risk factors with cognitive decline/impairment.[34–38] In addition, cardiovascular-related factors or conditions have also been found to be related to hearing, vision and olfaction function.[18,19,39–47] For example, early ecologic studies suggested an association between CVD and hearing loss and subsequent cross-sectional and prospective studies observed similar findings for CVD, atherosclerotic and microvascular changes, and CVD risk factors.[18,19,39,40,42,44,45] In a recent investigation, a significant association of subclinical atherosclerosis, measured as carotid IMT and plaque, with the 5-year incidence of hearing impairment was reported.[45] Therefore, there is evidence that vascular changes may be associated with both sensory and cognitive health. In the present study, there was only slight attenuation of the estimated risks of cognitive impairment after further adjustment for CVD-related factors and conditions, including a measure of subclinical atherosclerosis. This could mean that strong CVD influences on the sensory-cognitive relationship were not present or that the CVD measures used in the adjustment did not fully represent the shared vascular component, for example, microvascular changes in the brain, so that residual confounding was present.

Sensory and cognitive impairments very likely share more than age and vascular disease as common causes. Sensorineural impairment may be a surrogate for poor health in general and it is highly unlikely that an adequate set of covariates accounting for all facets of poor health can be measured and included in modeling.

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It is important to note that there may also be independent mechanisms involved in specific sensory-cognitive associations. With olfaction the independent process may involve shared neuropathology such as neurofibrillary tangles in areas of the brain involved in olfactory processes.[48] With hearing, it has been suggested that there may be a causal relationship between hearing loss and cognitive decline/impairment involving either increased cognitive load, resource allocation changes, sensory deprivation, and/or social isolation[14] but the evidence is not clear. For example, while some studies have suggested a positive relationship between social engagement and cognitive function,[49] a review of observational studies found that support for a link between social support/network and cognitive decline was low.[50]

Even though the underlying mechanism for the association between sensory and cognitive loss is not clearly understood, there is interest in being able to use sensory measures as screening tools for cognitive impairment risk. This study found the highest sensitivity when using baseline hearing impairment as the screening tool. But the sensitivity was only 72.9% so more than 1 out of 4 of those who developed cognitive impairment were not identified as being at high risk for it. In addition, 41.0% of those who did not develop cognitive impairment were identified as being likely to develop impairment, i.e. false positives. The positive predictive value of baseline hearing impairment was 14.6% which means 85.4% of the participants who had a baseline hearing impairment did not develop cognitive impairment during follow-up. The greatest positive predictive value was associated with having all 3 sensory impairments (40.0%) but even then 60.0% of the participants who had the 3 sensory impairments did not develop cognitive impairment. Interventions for the treatment of sensory loss in a large segment of the older population are reasonable for enriching lives and maintaining good quality of life, but are probably not warranted as a means to prevent cognitive impairment. Sensory impairments, particularly hearing, are highly prevalent in an aged population but cognitive impairment is relatively uncommon. The likelihood of developing cognitive impairment must be considered and not only the elevated relative risk associated with sensory loss.

The strengths of this study included the prospective design, large population, and extensive information related to sensory and cognitive measures and demographic, behavioral, and health factors. Hearing, vision, and olfaction were measured during the same phase by trained and certified examiners using standardized methods. The MMSE, used to define cognitive impairment, was also administered by certified examiners at each phase. The prevalence of the sensory impairments and incidence of cognitive impairment were high enough to provide adequate power to estimate the independent effect of each sensory impairment. More extensive adjustment for potential confounders was possible, particularly for inflammation and vascular-related factors, such as IMT, a measure of subclinical atherosclerosis. Among the limitations of the study is that the outcome of cognitive impairment included a mix of dementias including Alzheimer’s Disease. As a result there are very likely multiple etiologies associated with the one comprehensive outcome of cognitive impairment. Also, in the modeling, it was not possible to consider duration of sensory impairment prior to measurement; EHLS-1 could not serve as the baseline because olfaction and the MMSE were first measured at EHLS-2. Finally, because EHLS-2 served as baseline, only incidents of cognitive impairment occurring within a 10 year follow-up period

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and not those occurring at a later point, could be included in the analyses. The observed results apply only to the 10-year risk of cognitive impairment.

In the current study, the relationship between sensory impairment and cognitive impairment risk was not limited to a single sensory system but rather a significant, independent association of cognitive impairment risk with hearing, vision, and olfaction impairment was observed. These findings suggest that sensory measures may be markers of brain aging. Future studies are needed to extend this work to cognitive change and decline. In addition, efforts should be made to develop a combined measure of sensorineurocognitive function to more fully represent underlying neural health and to help in elucidating related factors and mechanisms of healthy brain aging.

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Table 1

Baseline (EHLS-2) Characteristics of Participants With Complete Sensory Measurement Data

Baseline Characteristic	N or Mean	% or S.D.[1]
Overall	1884	100.0
Demographic		
Age (Mean, S.D.)	66.7	8.4
Male	771	40.9
Education		
< 12 yrs	245	13.0
12 yrs	941	50.0
13–15 yrs	329	17.5
16+ yrs	368	19.5
Behavioral		
Smoking Status		
Never	894	47.5
Former	790	41.9
Current	200	10.6
Alcohol Consumption[2] (Mean, S.D.)	43.3	83.8
Exercise at Least 1x/Wk	838	44.5
Health History		
Body Mass Index (kg/m^2)		
< 25.0	333	17.7
25.0 – 29.9	649	34.6
30.0+	896	47.7
Hypertension	1066	56.6
Diabetes Mellitus	208	11.0
# High Inflammatory Markers		
0	935	51.9
1	545	30.3
2	321	17.8
Stroke	84	4.5
Head Injury	510	27.1
Non-HDL Cholesterol (mg/dL) (Mean, S.D.)	163.0	38.8
Mean Intima-Media Thickness (IMT) (mm) (Mean, S.D.)	0.86	0.22
Frailty Score		
0	1144	62.3
1	440	24.0
2	177	9.6
3	64	3.5
4	11	0.6
Sensory Impairment[3]		
No Impairment	833	44.2

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Baseline Characteristic	N or Mean	% or S.D.[1]
One Impairment	645	34.2
Hearing Only	449	23.8
Vision Only	114	6.0
Olfaction Only	82	4.4
Two Impairments	316	16.8
Hearing & Vision	165	8.8
Hearing & Olfaction	122	6.5
Vision & Olfaction	29	1.5
Three Impairments	90	4.8

[1] S.D. = Standard Deviation

[2] Alcohol consumption measured in grams of ethanol per week

[3] Hearing impairment: Pure-tone average 0.5, 1, 2,4 kHz, either ear > 25decibel Hearing Level; Vision impairment: Contrast sensitivity better eye < 1.55 log units; Olfaction impairment: San Diego Odor Identification Test score < 6 odors

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Table 2

Baseline (EHLS-2) Sensory Impairment and the 10-year Cumulative Incidence of Cognitive Impairment Hazard Ratios, 95% Confidence Intervals

Baseline Sensory Impairment[1]	Unadjusted Cumulative Incidence (%)	Hazard Ratio (95% Confidence Interval)	
		Age-sex-education Adjusted	Multivariable Adjusted[2]
Hearing		2.11 (1.30, 3.40)	2.09 (1.29, 3.39)
Yes	17.3		
No	4.7		
Vision		1.92 (1.25, 2.96)	1.96 (1.25, 3.07)
Yes	23.5		
No	6.7		
Olfaction		4.18 (2.68, 6.51)	4.04 (2.54, 6.43)
Yes	30.0		
No	6.3		

[1] Hearing impairment: Pure-tone average 0.5, 1, 2,4 kHz, either ear > 25decibel Hearing Level; Vision impairment: Contrast sensitivity better eye < 1.55 log units; Olfaction impairment: San Diego Odor Identification Test score < 6 odors

[2] Hearing and vision impairment models adjusted for age, sex, education, smoking status, BMI, exercise, alcohol consumption, hypertension, diabetes mellitus, number of high inflammatory markers, non-HDL cholesterol, mean IMT, and frailty score. Olfaction impairment model adjusted for age, sex, education, smoking status, BMI, exercise, alcohol consumption, hypertension, diabetes mellitus, number of high inflammatory markers, non-HDL cholesterol, mean IMT, frailty score, longest held job, cold or stuffy nose, nasal polyps, deviated septum, allergies, head injury, stroke/TIA, and epilepsy.

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Table 3

Multiple Baseline (EHLS-2) Sensory Impairments and the 10-year Cumulative Incidence of Cognitive Impairment[1] Hazard Ratios, 95% Confidence Intervals

Baseline Sensory Impairment[2]	Hazard Ratio (95% Confidence Interval)	
	Age-sex-education Adjusted	Multivariable Adjusted[3]
Hearing	1.96 (1.16, 3.29)	1.90 (1.11, 3.26)
Vision	1.85 (1.15, 2.97)	2.05 (1.24, 3.38)
Olfaction	4.02 (2.58, 6.28)	3.92 (2.45, 6.26)

[1] Models include hearing, vision, and olfactory impairment

[2] Hearing impairment: Pure-tone average 0.5, 1, 2,4 kHz, either ear > 25decibel Hearing Level; Vision impairment: Contrast sensitivity better eye < 1.55 log units; Olfaction impairment: San Diego Odor Identification Test score < 6 odors

[3] Model adjusted for age, sex, education, smoking status, BMI, exercise, alcohol consumption, hypertension, diabetes mellitus, number of high inflammatory markers, non-HDL cholesterol, mean IMT, frailty score, longest held job, cold or stuffy nose, nasal polyps, deviated septum, allergies, head injury, stroke/TIA, and epilepsy.

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Table 4

Performance Characteristics of Sensory Impairments as Screening Tools For Development of Cognitive Impairment

Sensory Impairment[1]	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)
Hearing	72.9	59.0	14.6	95.7
Vision	46.4	81.3	19.3	94.0
Olfaction	47.6	85.8	24.5	94.4
Hearing, Vision, and Olfaction[2]	21.7	96.9	40.0	92.8

[1]Hearing impairment: Pure-tone average 0.5, 1, 2, 4 kHz, either ear > 25 decibel Hearing Level; Vision impairment: Contrast sensitivity better eye < 1.55 log units; Olfaction impairment: San Diego Odor Identification Test score < 6 odors

[2]All 3 sensory impairments are present