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Incident dementia and faster rates of cognitive decline are associated with worse multisensory function summary scores

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Abstract

Introduction: We created a summary measure of multiple sensory (multisensory) impairment and evaluated its association with dementia.

Methods: We studied 1794 adults aged 70 to 79 who were dementia-free at enrollment and followed for up to 10 years in the Health, Aging, and Body Composition Study. The multisensory function score (0 to 12 points) was based on sample quartiles of objectively measured vision, hearing, smell, and touch summed overall. Risk of incident dementia and cognitive decline (measured by two cognitive tests) associated with the score were assessed in regression models adjusting for demographics and health conditions.

Results: Dementia risk was 2.05 times higher (95% confidence interval [CI] 1.50-2.81) comparing "poor" to "good" multisensory score tertiles and 1.45 times higher comparing the "middle" to "good" tertiles (95% CI 1.09-1.91). Each point worse multisensory function score was associated with faster rates of cognitive decline ($P < .05$).

Conclusions: Worsening multisensory function, even at mild levels, was associated with accelerated cognitive aging.

Keywords

cognition; dementia; epidemiology; multisensory; sensory impairment

1 | BACKGROUND

Sensory function declines with age,[1] and impairments in vision, hearing, and smell are individually associated with increased risk of dementia.[2-9] Sensory impairments often occur together[10,11];however, the majority of prior studies focus on individual sensory impairment. Emerging evidence suggests that multiple deficits in sensory function (eg, multisensory impairment) have a greater impact on health outcomes than a single sensory deficit.[12-15] Few studies have examined combined effects of sensory impairments on dementia risk by incorporating often-unstudied senses such as smell and touch or examined potential mediators or moderators of this association.

In prior work we found that increasing numbers of impairments in vision, hearing, olfaction, and touch were associated with increased risk of dementia.[15] This along with two studies that examined associations of hearing, vision, and olfaction in one model,[4,6] suggests that there are additive effects of multiple impairments in sensory function on dementia. These studies focused only on relatively severe impairments, we hypothesize that there may be larger and more graded effects by incorporating both severity and number of impairments into a multisensory measure. There are no established scores for quantifying multisensory impairment. Additional efforts to examine multisensory impairment along a continuum of severity may help elucidate causes of brain aging and provide a useful approach for future multisensory research.

The mechanism that explains the link between sensory impairments and dementia are not well established[16] but have implications for whether multisensory impairment could be a useful tool to help identify or prevent dementia. Sensory impairments could be due to underlying neurodegeneration[3] or the same disease processes as those affecting cognition, such as cerebrovascular disease.[17-19] Alternatively, sensory impairments, particularly those due to hearing or vision, may accelerate cognitive decline, either directly impacting cognitive load or indirectly through the effects of sensory impairment on other health-related outcomes.[20,21] Potential mediators include poor physical function, disability, reduced physical activity, and psychosocial factors such as poorer quality of life, social isolation, and depression, which are associated with sensory impairments[22-25] and increased risk of cognitive decline.[26] However, hearing and visual impairments in the absence of a true cognitive deficit may lead to false identification of cognitive impairment, which questions the role of a biologic link.[27-29] Few studies have examined whether there is potential mediation in the context of multisensory impairment and risk of dementia.

Building off our prior work,[15] the objectives of this study were to create a combined summary measure of multisensory function and to evaluate the extent to which multisensory impairment along a continuum of severity is associated with higher risk of dementia and faster rates of cognitive decline. We based the multisensory function score on continuous objective measures of hearing, vision, olfaction, and touch (specifically lower extremity peripheral sensory nerve function). We also examined mobility and psychosocial factors as potential mediators of the relationship between multisensory impairment and dementia and we tested for effect modification by sex and race. We studied black and white older adults in the Health, Aging and Body Composition (Health ABC) Study.

2 | METHODS

2.1 | Participants

Health ABC Study is a prospective cohort study of well-functioning 3075 black and white women and men.[30] Participants aged 70 to 79 years of age and living within in selected ZIP codes in Pittsburgh, PA, and Memphis, TN, in 1997-1998, were recruited from a random sample of Medicare-eligible adults. Recruited individuals were enrolled if they were free from life-threatening cancers as well as functional or mobility difficulties, and they had to plan to remain in the study area for at least 3 years. Enrolled participants underwent clinical examinations annually, phone calls every 6 months, and medical records review for major incident health events for up to 16 years. Written informed consent was obtained from each participant. The Health ABC Study was approved by institutional review boards at each site and the study coordinating center.

Our current analysis focused on 1794 participants with non-missing sensory assessments between Health ABC Years 3 and 5 and at least one follow-up assessment. Excluded participants included 276 participants missing one or more sensory assessment in hearing, vision, smell, or touch; 142 participants with prevalent dementia at Year 5; 90 participants without any assessments after Year 5; and 773 participants missing covariate data.

2.2 | Multisensory function

Between Health ABC Study Years 3 and 5 sensory function was assessed once for each domain (hearing, vision, smell, and touch). We created a multisensory function summary score based on sample quartiles for each sensory function test, since there are no established scores for quantifying multisensory impairment or function. We focused on four sensory tests with continuous measurements. Visual function was assessed with the Pelli-Robson contrast sensitivity test in Year 3; participants were tested binocularly with usual corrective lenses per study protocol.[31] Olfaction was measured with the 12-item Cross Cultural Smell Identification Test (B-SIT) in Year 3.[32] Touch was measured with vibration detection threshold (in μm), which was measured at the bottom of the big toe in Year 4. Hearing was based on pure tone average calculated from audiometric thresholds at 0.5, 1, 2, and 4 kHz for the better hearing ear. Audiometric assessments were performed in a sound-treated booth in Year 5 and hearing aids were not allowed per study protocol.

For each individual sensory measure, participants were assigned a score 0 to 3 based on sample quartiles for sensory function (eg, individuals with the best quartile of sensory function were assigned 0, and those with the worst quartile of sensory function were assigned a score of 3). Scores for the individual senses were summed to create a summary score of multisensory function (0 to 12). Participants with a score of 0 would have good sensory function in all senses, whereas those with 12 would have poor sensory function in all senses and those with intermediate scores could have a mix of impairments (eg, poor function in only one or two senses or mild impairments in all senses). For descriptive purposes, participants were further split into "good," "middle," and "poor," and multisensory function score based on sample tertiles.

As a sensitivity analysis we created two other summary scores. First, we created a modified individual sensory quartile-based scores to incorporate established clinical cut-points for impairment (Table S1) by replacing the highest sample cut points with cut-points for impairments that were available for vision,[9] hearing,[5] and touch.[33] Second, we created a score based on percentile rank of participants, first creating percentile rank score for each sensory function and next by summing percentile rank scores and then calculating percentile rank for participants based on the combined sensory function scores.

2.3 | Cognitive decline and dementia

Cognition was measured by the Modified Mini-Mental State Exam (3MS), a test of global cognitive function,[34] and the Digit Symbol Substitution Test (DSST), a measure of cognitive processing speed.[35] The 3MS and DSST were administered in Years 1,3 (3MS only), 5,8,10, and 11. As in other Health ABC studies,[7,36,37] dementia was defined as meeting one or more of the following criteria through study Year 15: (1) documented use of dementia medication; (2) hospitalization with dementia as a primary or secondary diagnosis; or (3) a 3MS score that was 1.5 SD lower than from Health ABC Study baseline mean (race-stratified). Medication use was collected at annual visits. Self-reported hospital admissions were collected every 6 months, and hospital records were reviewed for either a primary or a secondary diagnosis of dementia related to the admission (by International Classification of Diseases [ICD] codes and available chart/exam information). Date of diagnosis was defined as the first date at which the participant met at least one of the above criteria. The majority of dementia cases (about 75%) were based on hospitalizations either alone or in combination with other sources. We excluded participants from this analysis who met criteria for dementia at or before Year 5 (analytic baseline). To estimate longitudinal trends in cognition we used 3MS and DSST data from Year 5 to 11.

2.4 | Covariates

We selected covariates from the analytic baseline (study Year 1-5). Sex, race, educational attainment, marital status, and study site were recorded in Year 1. Age at Year 5 was considered in this analysis. History of health conditions (hypertension, diabetes, cardiovascular disease [myocardial infarction, congestive heart failure, etc], and cerebrovascular disease [stroke, transient ischemic attack]) cumulative up to Year 5 were defined based on a combination of participant interview, medical record review, medications, and baseline laboratory values. Year 5 body mass index (BMI) was calculated as kg/m^2. Participants were also asked about alcohol consumption and smoking. Alcohol consumption was assessed at Year 1 only; heavy alcohol consumption (yes, no) we defined as more than one drink per day. We categorized smoking status at Year 5 as never, current, or former. Apolipoprotein E (*APOE*) genotype was assessed with serum assay; *APOE* ε4 allele status was defined as (1+ ε4 allele vs none).

We also examined several mobility and psychosocial factors as potential mediators, as these factors may be affected by sensory impairment and may help explain how sensory impairments could increase risk for accelerated cognitive decline.[20-25] Measures were obtained from Year 5. Fast-paced gait speed (m/s) was measured with a 20-meter walking timed test, where participants were instructed to "walk as fast as you can." Psychosocial

measures included depressive symptoms and perceived social support. Depressive symptoms were measured with the Center for Epidemiologic Study Depression scale (CESD) short form.[38] Participants ranked their satisfaction of social support from least to most satisfied (0 to 10) in response to the question "How satisfied are you with how often you see or talk to your family and friends?" A separate question on lack of social support also asked, "In the past year, could you have used more emotional support than you received?" (yes, no, unknown/missing).

2.5 | Statistical analyses

We compared participant characteristics by tertile (good, middle, poor) of multisensory function score. Participants were followed from Year 5 (analytic baseline) to dementia diagnosis or the last available date of contact. Multivariable Cox proportional hazard models evaluated the relationship between multisensory function score and time from Year 5 to the first date at which participant met criteria for dementia (proxy for dementia onset); participants who did not develop dementia were censored at last visit, death, or drop out. The primary predictor in all models was multisensory function score as a continuous measurement. We report estimates for a four-point difference, which is equivalent to a 25% difference in score. As a secondary analysis we examined tertiles of multisensory function score (good function as the reference group). We ran three models with increasing adjustment for covariates: Model 1 included adjustment for demographics; Model 2 included adjustment for demographics plus comorbid conditions and health behaviors; and Model 3 included adjustment demographics, comorbid conditions, health behaviors, and possible mediators (fast walking speed, depression, and social support measures). Model 2 was considered the primary model. We hypothesized that inclusion of potential mediators in Model 3 would result in reduced estimates compared to Model 2.

We included interactions between primary predictors and race, sex, and *APOE ε*4 allele to test whether associations differed for subgroups. Participants excluded from the analytic sample differed by demographics and tended to have more health conditions than those included, so we ran a sensitivity analysis to generalize results to the full Health ABC Study sample.[39] We re-ran our primary model using inverse probability weights to account for participants who were not included in the analytic sample. First, we used a logistic regression with demographics and dementia status as predictors of study exclusion; next, weights were calculated as the inverse of predicted values of this regression and included in Model 2. We calculated 95% confidence intervals (Cis) based on 1000 bootstrapped replications.[40] To confirm earlier findings, which suggest linear effects of sensory function on dementia as well as to compare effect sizes, we estimated the association between individual sensory function measures and dementia. Next we evaluated whether associations with the multisensory score were above and beyond effects of any individual impairment on dementia risk. We included olfaction (impairment in which may indicate preclinical Alzheimer's disease[41]) and then all of the individual sensory measures in Model 2 with the multisensory score. Then, to examine alternative operationalizations of the multisensory score, we re-ran Model 2 with the percentile rank and clinical cut-point adjusted multisensory scores.

Finally, we examined longitudinal trends in cognition (from Year 5 to 11) using linear mixed-effects models with random intercepts and slopes by participant. We evaluated the association between multisensory function score and rate of cognitive decline with a time since baseline X multisensory function score interaction. Models were run with the 3MS and DSST as the outcome separately, and also included time (since baseline), $time^2$, demographics, comorbid conditions, and health behaviors. We explored non-linear trends with polynomial splines, which suggested linear and quadratic terms for time were sufficient (test for interaction between the multisensory score and $time^2$ did not improve model fitP (P = .13 for likelihood ratio test). All tests were twosided with α = 0.05; we report 95% CIs. Analyses were conducted in R (version 3.4.1).

3 | RESULTS

Sensory function measures were slightly correlated (range 0.04 to 0.15), smell, and vision, smell and hearing, touch and all other measures were significantly correlated more than expected by chance (Table 1). By definition, the average multisensory function score was 6 (SD: 2) and the distribution of scores in the sample was approximately normal (Figure 1). Participants with the lowest scores tended to have no sensory impairments, whereas those with the highest scores tended to have multiple moderate-severe sensory impairments; intermediate range of scores could either have 1 moderate-severe sensory impairment or multiple mild impairments. Most participants (75%) wore glasses during the vision testing; 13% reported daily use of hearing aids. Compared to those with good multisensory function scores, participants with worse multisensory function scores tended to be older, white, less educated, and were more likely to have comorbidities, poor mobility, and more depressive symptoms (Table 2).

The average length of follow-up was 6.3 years (SD: 3.1). Three hundred twenty-eight participants (18%) developed dementia over follow-up. Worse multisensory function score was associated with higher risk of dementia (Table 3). In models adjusted for demographics and health conditions, participants with a poor multisensory function score were 2.05 times more likely to develop dementia (P< .001) than those with a good score (95% CI 1.50-2.81). Participants with a middle multisensory function score were 1.45 times more likely to develop dementia (P< .001) than those with a good score (95% CI 1.09-1.91). Even a 1-point difference in multisensory function score was significantly associated with risk of dementia: 1-point worse in multisensory function score was associated with a 14% higher (95% CI 8%-21%) risk of dementia and a 4-point worse score was associated with 71% higher risk of dementia (95% CI 38%-211%). Adjustment for health conditions in addition to demographics did not affect points estimates much. Results were essentially unchanged after inclusion of inverse probability weights to account for potential selection bias into the analytic sample (adjusted hazards ratio [aHR] for 1 point of multisensory function score = 1.16,95% CI 1.10-1.23). Alternative calculations of the multisensory score resulted in similar findings; estimated associations were slightly stronger with including clinical cut-points (Table S2).

Individually, worse sensory function was associated, or borderline associated with increased risk of dementia (Table S3). Smell was the most strongly associated (estimated 19% higher

risk of dementia for each 10⁻percentile difference versus 1% to 3% higher risk for vision, hearing, and touch). Worse multisensory scores were still significantly associated with higher risk of dementia even after inclusion of the olfactory scale, although estimates slightly attenuated (hazards ratio [HR] for 4 points: 1.28, 95% CI 1.01-1.62). Estimates were still elevated with inclusion of all sensory measures but less precise (HR for 4 points: 1.40, 95% CI 0.92-2.12).

Estimates were slightly lower (≈3% to 10%) once including potential mediators (mobility and psychosocial measures) (Table 3). This reduction in the estimate for multisensory function score was due primarily to inclusion of fast walking speed, which was strongly associated with multisensory function score ($P < .001$) and risk of dementia (HR for 1 m/s difference = 2.81, 95% CI 1.88-4.21; $P < .001$). When only fast walking speed was included in the adjusted models, the estimated increased risk of dementia for 1-point difference in multisensory function score was 13%, compared to 12% with inclusion of fast walking speed plus psychosocial factors.

Interactions between multisensory function score and race (HR for interaction: 0.97, 95% CI 0.87-1.07; $P = .52$) and *APOEε*4 allele status (HR for interaction: 1.02, 95% CI 0.92-1.12; $P = .76$) were not significant and close to null. The interaction between multisensory function score and sex was not significant ($P = .13$), but suggested that the association between multisensory function score and dementia was slightly reduced in women (HR for interaction: 0.92, 95% CI 0.84-1.02; $P = .13$.

Worsening multisensory function score was associated with significantly lower cognition at analytic baseline as well as faster annual rates of decline in both the 3MS and DSST ($P < .05$), even after adjustment for demographics and health conditions (Table 4). Inclusion of individual sensory measures did not substantially change estimates for 3MS but attenuated estimates for DSST. Figure 2 shows decline in 3MS by good, middle, and poor multisensory function score.

4 | DISCUSSION

We developed a score to quantify multisensory function and evaluated its association with risk of dementia and cognitive decline among black and white older adults. With worsening multisensory function score, the risk of dementia and rate of cognitive decline increased in a dose-response manner. In fully adjusted models, participants with poor multisensory function scores had a 2 times higher risk of dementia compared to those with good scores. Even participants with middle multisensory function scores had almost a 1.5 times higher risk of dementia than those with good scores. Additional adjustment for potential mediators such as mobility and psychosocial factors slightly attenuated estimates; this was primarily due to adjustment for walking speed. These effects were not attributable to effects of any one sensory function measure, in particular; they were above and beyond the association between olfaction and dementia. Together our findings suggest that function in multiple sensory domains can be quantified along a continuum. Even mild/moderate levels of sensory impairments combined across multiple domains (eg, those with middle multisensory function scores) were associated with increased risk of dementia. This study adds further

evidence that individuals with poor sensory function in multiple modalities are a high-risk population that could be targeted prior to dementia onset for intervention.

Impairment in multiple sensory domains is emerging as an important comorbidity associated with dementia in older adults. Few studies have quantified the effects of multisensory impairment on cognitive impairment. A number of studies have found that individual impairments in hearing, vision, and smell are associated with risk of dementia,[2,3,5,7,8,42] and may have independent effects.[4,6] Combined hearing and visual impairment has been associated with added risk compared to one impairment in some,[14,43] but not all, studies.[44] Another study found impairments among five senses (operationalized as global sensory impairment) predicted lower cognitive function, but did not test for graded effects.[25] Our prior work in the Health ABC Study found significant graded effects of increasing number of sensory impairments in these same four domains, but was focused on only relatively severe sensory impairments.[15] These current results are an important extension of this prior work by showing graded associations along a continuum of multisensory function. Those with poor multisensory function seem to be a subgroup at high risk health outcomes including cognitive decline and could be targeted for dementia prevention strategies. Our findings suggest that these effects are above and beyond those which can be attributed to individual sensory domains, including olfaction, which was the mostly strongly associated with dementia on its own. Furthermore, we developed an approach to quantify multisensory function and impairment in a continuous measure. Our findings suggest that a sample-based score could be improved by incorporating clinical cut-points; however, further research is needed to optimize such a measure for dementia risk. Approaches to quantifying and measuring multisensory function could be useful in clinical settings to screen older adults. The utility of incorporating multisensory assessments and summary scores in dementia-prediction models for patients should also be explored in future research.

We find strong evidence for graded or additive association of our multisensory function score on cognitive decline and risk of dementia. However, the mechanisms underlying this association are challenging to assess, and future work will be required to determine which mechanisms are shared across sensory modalities, which may differ, and whether there are any interactions. Sensory impairments, particularly in hearing and vision, may worsen mobility, functional limitations, depression, and social isolation,[22-25] which may subsequently accelerate cognitive decline.[22] In this study, we began to examine some of these factors as potential mediators. Participants with worse multisensory function had worse mobility and were more likely to have depressive symptoms. We did not find substantial differences by social support measures; however, questions assessing social support were limited in scope. Other research suggests that social engagement is linked to visual and hearing impairments.[22] We further examined potential mediation by including measures of mobility and psychosocial factors as covariates in our models; and estimates were slightly attenuated primarily with the inclusion of walking speed. This finding suggests that mobility may be a potential mediator of the relationship between multisensory impairments and dementia. Future work will be needed to determine that mobility represents a true mediator and not just a proxy for a shared cofounder. A combination of general aging processes, inflammation, or subclinical cardiovascular or metabolic disease may be shared causes of sensory impairments, dementia, and walking speed/physical function.[1,17,33,45]

This may explain why we find slight correlations between many of the individual sensory measures; however, future research should explore whether sensory impairments tend to cluster together (as suggested by some work[10,25]) or sensory impairments interact to contribute to dementia.

Most of the association between multisensory function score and dementia was independent of potential mediators as well as potential confounders. Beyond biologic pathways it is also possible that the association between sensory impairments and dementia could be explained by measurement error. Sensory function tests involve cognitive processing and decision-making and cognitive function tests, including the 3MS and DSST involve auditory and visual cues, which can contribute to misclassification of cognitive impairment in those with impairments.[27-29] Additional studies are necessary to determine which pathways link sensory impairments and dementia. However, our findings of a strong graded association that remained even with adjustment for individual sensory impairments as well as potential mediation by mobility, suggest that some biologic pathway(s) link sensory impairments and dementia beyond the effects of normal aging or measurement error.

This study is not without several limitations. Our dementia variable was based on an algorithm and not a clinical diagnosis, and our Cox proportional models assumed participants did improve cognition during follow-up. We may have misclassified some participants compared to a clinical diagnosis, which could have attenuated associations. Function in each sense was measured only once and not all assessments were in the same study year. This could lead to misclassification in our multisensory measure. Sensory function generally declines with age,[1] but some impairments can be corrected (eg, new glasses, cataract surgery).[46] In addition, participants were instructed to wear glasses or contacts during the visual tests but not to wear hearing aids during hearing tests; it is unclear whether this affected results. Any misclassification would likely occur independent of future dementia risk and so estimates would be biased to the null. Our multisensory measure focused only on specific measures for each sensory domain and may have missed other aspects of vision, smell, hearing, or peripheral sensation that are important. Finally, participants were highly selected to be healthy at baseline and were relatively old. Our findings may not be generalizable to mid-life or the general older adult population, although it is possible that these associations may be even more robust in samples with a wider health range. Estimates did not change substantially when we included inverse probability weighting to account for potential selection bias towards healthy participants.

This study also has appreciable strengths including a large biracial cohort of older adults followed for over 10 years. We used a definition of all-cause dementia based on multiple criteria and sources, and we also separately examined associations with rate of cognitive decline in two global cognitive measures. We used multiple objective measures of sensory function including touch, which is understudied. We also summarized and assessed the combined effects of multiple sensory impairments on cognitive decline and risk of dementia. We included sensitivity analyses to account for potential selection bias in the analytic sample, we tested for interactions by sex and race, and we evaluated potential mediators.

We summarized function across multiple sensory domains using objective sensory measurements in vision, touch, smell, and hearing. Worse multisensory function scores were associated with higher risk of dementia and cognitive decline in a cohort of black and white older adults. This study adds to emerging evidence that multisensory impairment, even at mild levels, is associated with accelerated cognitive aging. Associations remained after accounting for comorbid health conditions, but were slightly reduced with adjustment for potential mediators, especially walking speed. Future studies will be needed to confirm mobility as a potential mediator, evaluate other potential explanations, and to determine whether those with multisensory impairments can be identified and targeted for intervention in clinical settings. Multisensory assessments may be a useful important risk stratification tool to identify those at high risk for accelerated cognitive aging and other poor health outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENTS

REFERENCES

1. Gadkaree SK, Sun DQ, Li C, et al. Does sensory function decline independently or concomitantly with age? Data from the Baltimore Longitudinal Study of Aging. J Aging Res. 2016;2016:1865038.. [PubMed: 27774319]

2. Lin FR, Yaffe K, Xia J, et al. Hearing loss and cognitive decline in older adults. JAMA Intern Med. 2013;173(4):293–299. [PubMed: 23337978]

3. Devanand DP, Lee S, Manly J, et al. Olfactory deficits predict cognitive decline and Alzheimer dementia in an urban community. Neurology. 2015;84(2):182–189. [PubMed: 25471394]

4. Fischer ME, Cruickshanks KJ, Schubert CR, et al. Age-related sensory impairments and risk of cognitive impairment. J Am Geriatr Soc. 2016;64(10):1981–1987. [PubMed: 27611845]

5. Deal JA, Betz J, Yaffe K, et al. Hearing impairment and incident dementia and cognitive decline in older adults: the health ABC study. J Gerontol A Biol Sci Med Sci. 2017;72(5):703–709. [PubMed: 27071780]

6. Schubert CR, Cruickshanks KJ, Fischer ME, et al. Sensory impairments and cognitive function in middle-aged adults. J Gerontol A Biol Sci Med Sci. 2017;72(8):1087–1090. [PubMed: 28535277]

7. Yaffe K, Freimer D, Chen H, et al. Olfaction and risk of dementia in a biracial cohort of older adults. Neurology. 2017;88(5):456–462. [PubMed: 28039314]

8. Ward ME, Gelfand JM, Lui L-Y, et al. Reduced contrast sensitivity among older women is associated with increased risk of cognitive impairment. Ann Neurol. 2018;83(4):730–738. [PubMed: 29518257]

9. Swenor BK, Wang J, Varadaraj V, et al. Vision impairment and cognitive outcomes in older adults: the health ABC study. J Gerontol A Biol Sci Med Sci. 2019;74(9):1454–1460. [PubMed: 30358809]

10. Correia C, Lopez KJ, Wroblewski KE, et al. Global sensory impairment in older adults in the United States. J Am Geriatr Soc. 2016;64(2):306–313. [PubMed: 26889840]

11. Swenor BK, Ramulu PY, Willis JR, Friedman D, Lin FR. The prevalence of concurrent hearing and vision impairment in the United States. JAMA Intern Med. 2013;173(4):312–313. [PubMed: 23338042]

12. Gopinath B, Schneider J, McMahon CM, Burlutsky G, Leeder SR, Mitchell P. Dual sensory impairment in older adults increases the risk of mortality: a population-based study. PloS One. 2013;8(3):e55054. [PubMed: 23469161]

13. Schubert CR, Fischer ME, Pinto AA, et al. Sensory impairments and risk of mortality in older adults. J Gerontol A Biol Sci Med Sci. 2017;72(5):710–715. [PubMed: 26946102]

14. Lin MY, Gutierrez PR, Stone KL, et al. Vision impairment and combined vision and hearing impairment predict cognitive and functional decline in older women. J Am Geriatr Soc. 2004;52(12):1996–2002. [PubMed: 15571533]

15. Brenowitz WD, Kaup AR, Lin FR, Yaffe K. Multiple sensory impairment is associated with increased risk of dementia among black and white older adults. J Gerontol Ser A. 2019;74(6):890–896.

16. Whitson HE, Cronin-Golomb A, Cruickshanks KJ, et al. American Geriatrics Society and National Institute on Aging Bench-to-Bedside Conference: sensory impairment and cognitive decline in older adults. J Am Geriatr Soc. 2018;66(11):2052–2058. [PubMed: 30248173]

17. Fischer ME, Schubert CR, Nondahl DM, et al. Subclinical atherosclerosis and increased risk of hearing impairment. Atherosclerosis. 2015;238(2):344–349. [PubMed: 25555266]

18. Mitchell P, Gopinath B, McMahon CM, et al. Relationship of type 2 diabetes to the prevalence, incidence and progression of age-related hearing loss. Diabet Med. 2009;26(5):483–488. [PubMed: 19646187]

19. Haan M, Espeland MA, Klein BE, et al. Cognitive function and retinal and ischemic brain changes: the Women's Health Initiative. Neurology. 2012;78(13):942–949. [PubMed: 22422889]

20. Davis A, McMahon CM, Pichora-Fuller KM, et al. Aging and hearing health: the life-course approach. Gerontologist. 2016;56:S256–S267. [PubMed: 26994265]

21. Lin FR, Albert M. Hearing loss and dementia–who's listening?. Aging Ment Health. 2014;18(6):671–673. [PubMed: 24875093]

22. Fischer ME, Cruickshanks KJ, Klein BEK, Klein R, Schubert CR, Wiley TL. Multiple sensory impairment and quality of life. Ophthalmic Epidemiol. 2009;16(6):346–353. [PubMed: 19995199]

23. Kiely KM, Anstey KJ, Luszcz MA. Dual sensory loss and depressive symptoms: the importance of hearing, daily functioning, and activity engagement. Front Hum Neurosci. 2013;7:837. [PubMed: 24379769]

24. Keidser G, Seeto M. The influence of social interaction and physical health on the association between hearing and depression with age and gender. Trends Hear. 2017;21:2331216517706395. [PubMed: 28752806]

25. Pinto JM, Wroblewski KE, Huisingh-Scheetz M, et al. Global sensory impairment predicts morbidity and mortality in older U.S. adults. J Am Geriatr Soc. 2017;65(12):2587–2595. [PubMed: 28942611]

26. Hughes TF, Ganguli M. Modifiable midlife risk factors for late-life cognitive impairment and dementia. Curr Psychiatry Rev. 2009;5(2):73–92. [PubMed: 19946443]

27. Cronin-Golomb A, Gilmore GC, Neargarder S, Morrison SR, Laudate TM. Enhanced stimulus strength improves visual cognition in aging and Alzheimer's disease. Cortex. 2007;43(7):952–966. [PubMed: 17941352]

28. Toner CK, Reese BE, Neargarder S, Riedel TM, Gilmore GC, Cronin-Golomb A. Vision-fair neuropsychological assessment in normal aging, Parkinson's disease and Alzheimer's disease. Psychol Aging. 2012;27(3):785–790. [PubMed: 22201330]

29. Jorgensen LE, Palmer CV, Pratt S, Erickson KI, Moncrieff D. The effect of decreased audibility on MMSE performance: a measure commonly used for diagnosing dementia. J Am Acad Audiol. 2016;27(4):311–323. [PubMed: 27115241]

30. Harris TB, Visser M, Everhart J, et al. Waist circumference and sagittal diameter reflect total body fat better than visceral fat in older men and women. The health, aging and body composition study. Ann N Y Acad Sci. 2000;904:462–473. [PubMed: 10865790]

31. Pelli DG, Robson JG, Wilkins AJ. The design of a new letter chart for measuring contrast sensitivity. Clin Vis Sci. 1988;2(3):187–199.

32. Doty RL, Marcus A, Lee WW. Development of the 12-item Cross-Cultural Smell Identification Test (CC-SIT). The Laryngoscope. 1996;106(3 Pt 1):353–356. [PubMed: 8614203]

33. Ward RE, Boudreau RM, Caserotti P, et al. Sensory and motor peripheral nerve function and incident mobility disability. J Am Geriatr Soc. 2014;62(12):2273–2279. [PubMed: 25482096]

34. Teng EL, Chui HC.The Modified Mini-Mental State (3MS) examination. J Clin Psychiatry. 1987;48(8):314–318. [PubMed: 3611032]

35. Wechsler D. Wechsler Memory Scale-Revised Manual. San Antonio, TX: The Psychological Corporation; 1987.

36. Brenowitz WD, Kaup AR, Lin FR, Yaffe K. Multiple sensory impairment is associated with increased risk of dementia among black and white older adults. J Gerontol Ser A. 2019;74(6):890–896.

37. Hong CH, Falvey C, Harris TB, et al. Anemia and risk of dementia in older adults: findings from the Health ABC study. Neurology. 2013;81(6):528–533. [PubMed: 23902706]

38. Andresen EM, Malmgren JA, Carter WB, Patrick DL. Screening for depression in well older adults: evaluation of a short form of the CESD (Center for Epidemiologic Studies Depression Scale). Am J Prev Med. 1994;10(2):77–84. [PubMed: 8037935]

39. Hernán MA, Hernández-Díaz S, Robins JM. A structural approach to selection bias. Epidemiol Camb Mass. 2004;15(5):615–625.

40. Efron B,Tibshirani R. An Introduction to the Bootstrap. New York: Chapman & Hall; 1994.

41. Albers MW, Gilmore GC, Kaye J, et al. At the interface of sensory and motor dysfunctions and Alzheimer's disease. Alzheimers Dement J Alzheimers Assoc. 2015;11(1):70–98.

42. Davies HR, Cadar D, Herbert A, Orrell M, Steptoe A. Hearing impairment and incident dementia: findings from the English Longitudinal Study of Ageing. J Am Geriatr Soc. 2017;65(9):2074–2081. [PubMed: 28734053]

43. Yamada Y, Denkinger MD, Onder G, et al. Dual sensory impairment and cognitive decline: the results from the Shelter study. J Gerontol A Biol SciMed Sci. 2016;71(1):117–123.

44. Hong T, Mitchell P, Burlutsky G, Liew G, Wang JJ. Visual impairment, hearing loss and cognitive function in an older population: longitudinal findings from the Blue Mountains Eye Study. PloS One. 2016;11(1):e0147646. [PubMed: 26808979]

45. Tranah GJ, Yaffe K, Katzman SM, et al. Mitochondrial DNA heteroplasmy associations with neurosensory and mobility function in elderly adults. J Gerontol A Biol Sci Med Sci. 2015;70(11):1418–1424. [PubMed: 26328603]

46. Freeman EE, Egleston BL, West SK, Bandeen-Roche K, Rubin G. Visual acuity change and mortality in older adults. Invest Ophthalmol Vis Sci. 2005;46(11):4040–4045. [PubMed: 16249478]

RESEARCH IN CONTEXT

1. Systematic review: Sensory impairments are individually associated with dementia, but few studies have examined associations with multiple sensory (multisensory) impairments or potential mediators. Furthermore, there is no standardized approach to summarize multisensory impairment along a continuum of severity.

2. Interpretation: These findings highlight that poor function in multiple senses, even at mild levels, predicts accelerated cognitive aging. We show that a novel summary score for quantifying multisensory function and impairment was associated with incident dementia and faster global cognitive decline. Associations were even for mild differences in multisensory function. Secondary analyses suggest that mobility may mediate this association.

3. Future directions: This study provides an approach for studying multisensory impairment in the context of dementia. Future research should explore other potential mechanisms that may explain this relationship to understand whether interventions on those with multisensory impairment could help prevent or delay dementia.

Multisensory Function Score
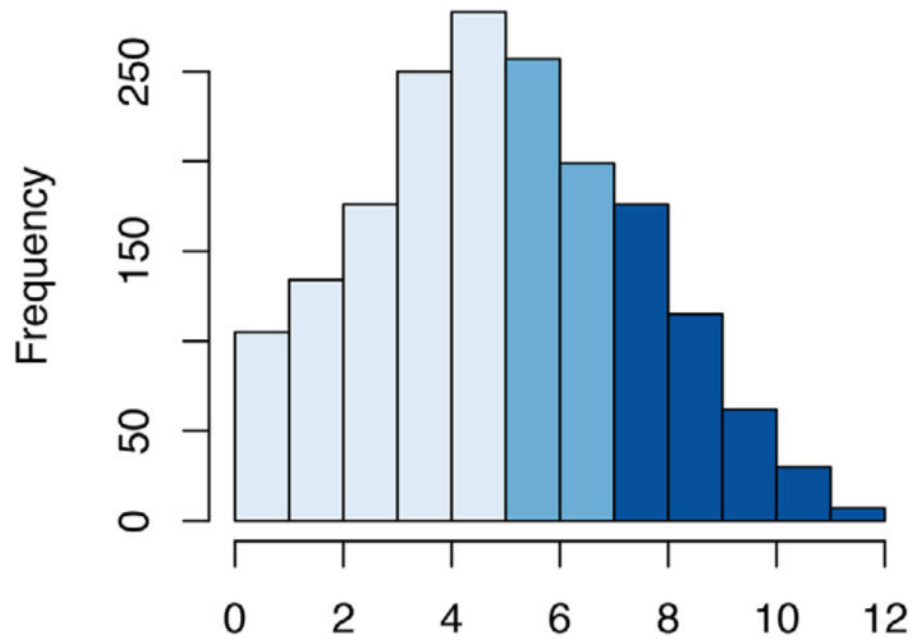
FIGURE 1.
Distribution of multisensory function scores. Colors show tertile of multisensory function score from light (good) to dark (poor)
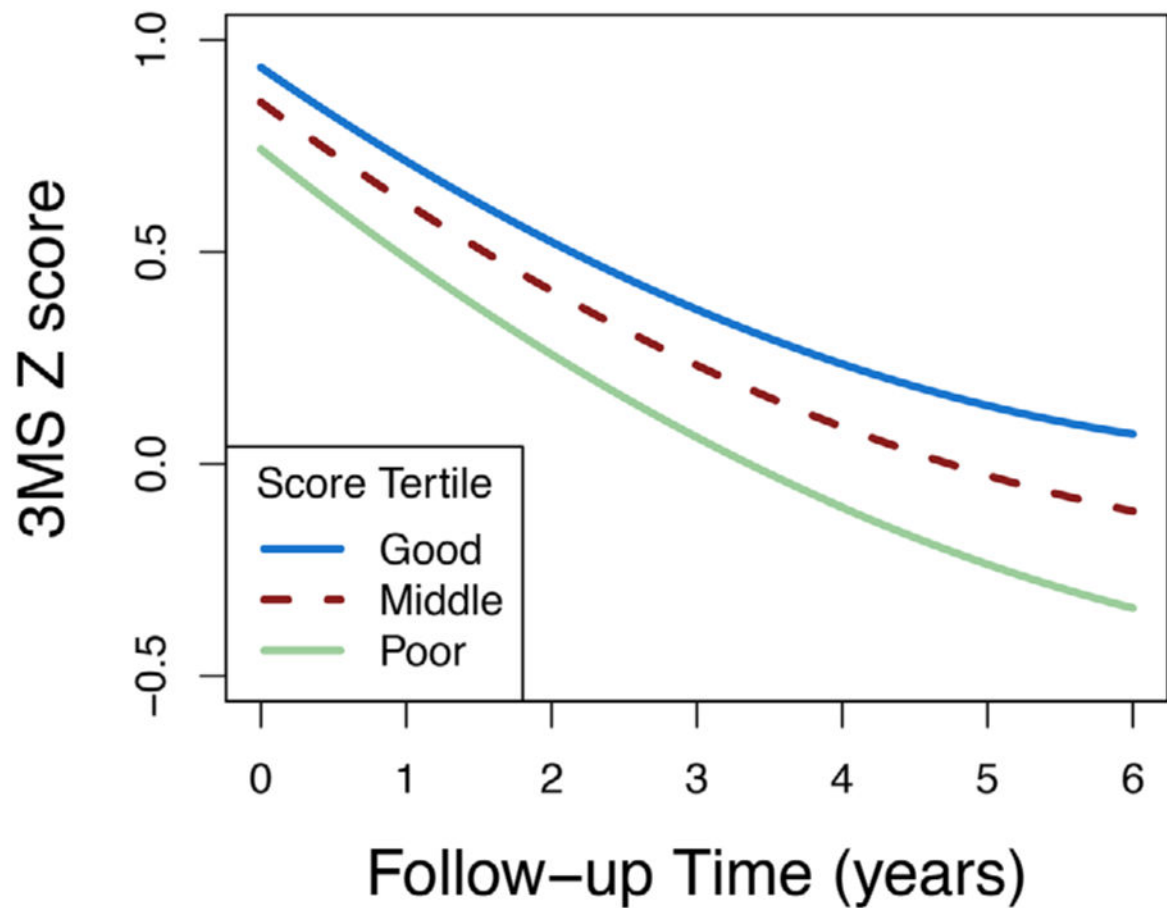
FIGURE 2.
Worse multisensory function score tertiles show graded associations with estimated trajectories of Modified Mini Mental Status Examination across follow-up. Trajectories were based on predicted values for linear mixed-effects models with multisensory score tertile X time interaction, time since baseline, and $time^2$ as primary predictors. Models were additionally adjusted for age at baseline, race, sex, education, hypertension, diabetes, cardiovascular disease, cerebrovascular disease, smoking status, and alcohol use

TABLE 1

Correlation matrix for continuous measures of vision (contrast sensitivity), hearing (pure tone average), smell (olfactory score), and touch (vibration threshold)

	Vision	Hearing	Smell	Touch
Vision	1.00			
Hearing	0.04	1.00		
Smell	0.09[***]	0.09[***]	1.00	
Touch	0.06[**]	0.15[***]	0.08[***]	1.00

[*]
< 0.05.

[**]
< 0.01.

[***]
< 0.001.

TABLE 2

Baseline demographic and clinical characteristics by multisensory function score tertiles

	Good	Middle	Poor	P
N	780	515	499	
	n(%) unless otherwise specified			
Age (years), mean (SD)	76.6 (2.6)	77.6 (2.8)	78.5 (3.0)	<.001
Female	502 (64.4)	251 (48.7)	176 (35.3)	<.001
Black	295 (37.8)	159 (30.9)	163 (32.7)	.023
Completed high-school	663 (85.0)	411 (79.8)	360 (72.1)	<.001
Body mass index (kg/m^2), mean (SD)	27.4 (4.6)	27.3 (4.7)	27.0 (4.5)	.306
Hypertension	628 (80.5)	427 (82.9)	419 (84.0)	.252
Cardiovascular disease	139 (17.8)	114 (22.1)	109 (21.8)	.092
Diabetes	132 (16.9)	104 (20.2)	139 (27.9)	<.001
Stroke/TIA	113 (14.5)	84 (16.3)	88 (17.6)	.308
APOE- e4[a]	216 (29.3)	116 (23.7)	128 (27.4)	.098
Current smoker	46 (5.9)	28 (5.4)	34 (6.8)	.642
Alcohol use (>1 drink/day)	58 (7.4)	44 (8.5)	42 (8.4)	.720
Fast walking speed (m/s), mean (SD)	1.6 (0.3)	1.5 (0.4)	1.4 (0.3)	<.001
Depressive symptoms, mean (SD),	4.6 (4.0)	4.8 (4.0)	5.1 (4.5)	.110
Social support satisfaction, mean (SD)	8.5 (1.7)	8.3 (1.8)	8.4 (1.9)	.199
Lacking social support	211 (27.1)	129 (25.0)	129 (25.9)	.714

TABLE 3

Risk of dementia is associated with worse multisensory scores for both continuous multisensory score (1-point difference shown) and tertiles of multisensory score

Multisensory function score	Demographic adjusted[a] HR (95% CI)	Demographic plus health conditions[b] HR (95% CI)	Multivariable plus mediators[c] HR (95% CI)
4-Point difference	1.70 (1.38,2.08)	1.71 (1.38, 2.11)	1.52 (1.23,1.87)
Tertile			
Good	1.00 (reference)	1.00 (reference)	1.00 (reference)
Middle	1.50 (1.13,1.97)	1.45 (1.09,1.91)	1.33 (1.00,1.77)
Poor	2.07 (1.52,2.83)	2.05 (1.50, 2.81)	1.72 (1.25,2.36)

[a] Model adjusted for age, race, sex, and education.

[b] Demographic adjusted model plus hypertension, diabetes, cardiovascular disease, cerebrovascular disease, smoking status, alcohol use, and physical activity.

[c] Demographic and health conditions model plus fast gait speed, depressive symptoms, satisfaction with social support, lack of social support.

TABLE 4

Continuous multisensory score (4-point difference shown) is associated with baseline cognitive level and faster annual rate of decline on Modified Mini Mental Status Examination and Digit Symbol Substitution Test

Cognitive test	N participants	N observations	Baseline cognitive level β (95% CI)	Annual rate of decline β (95% CI)
3MS	1013	3738	−0.12 (−0.22, −0.02)	−0.02 (−0.03, −0.01)
DSST	1011	3700	−0.09 (−0.20, 0.01)	−0.02 (−0.03, −0.01)

3MS, Modified Mini Mental Status Examination; DSST, Digit Symbol Substitution Test.

[a] Models adjusted for age, race, sex, education, hypertension, diabetes, cardiovascular disease, cerebrovascular disease, smoking status, and alcohol use.