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RESEARCH ARTICLE

Midlife sensory and motor functions improve long-term predictions of cognitive decline and incidence of cognitive impairment

Carla R. Schubert MS[1] | **A. Alex Pinto MS**[2] | **Adam J. Paulsen MS**[1] | **Richard J. Chappell PhD**[2,3] | **Yanjun Chen MD**[4] | **Corinne D. Engelman MSPH, PhD**[1] | **Luigi Ferrucci MD, PhD**[5] | **Laura M. Hancock PhD**[6] | **Sterling C. Johnson PhD**[7,8] | **Natascha Merten PhD, MS**[1,7,8]

[1]Department of Population Health Sciences, School of Medicine and Public Health, University of Wisconsin-Madison, Madison, Wisconsin, USA

[2]Department of Biostatistics and Medical Informatics, School of Medicine and Public Health, University of Wisconsin-Madison, Madison, Wisconsin, USA

[3]Department of Statistics, School of Computer, Data & Information Sciences, University of Wisconsin-Madison, Madison, Wisconsin, USA

[4]Department of Ophthalmology and Visual Sciences, School of Medicine and Public Health, University of Wisconsin-Madison, Madison, Wisconsin, USA

[5]Longitudinal Study Section, Intramural Research Program, National Institute on Aging, NIH, Gaithersburg, Maryland, USA

[6]Neurological Institute, Section of Neuropsychology, Cleveland Clinic, Cleveland, Ohio, USA

[7]Division of Geriatrics and Gerontology, Department of Medicine, School of Medicine and Public Health, University of Wisconsin-Madison, Madison, Wisconsin, USA

[8]Wisconsin Alzheimer's Disease Research Center, School of Medicine and Public Health, University of Wisconsin-Madison, Madison, Wisconsin, USA

Correspondence
Natascha Merten, PhD, MS, Department of Population Health Sciences and Department of Medicine, Division of Geriatrics and Gerontology, University of Wisconsin, WARF Office Building, 610 Walnut St, Madison, WI-53726, USA.
Email: natascha.merten@wisc.edu

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Abstract

INTRODUCTION: We aimed to assess whether midlife sensory and motor functions improve risk prediction of 10-year cognitive decline and impairment when added to risk prediction models using the Cardiovascular Risk Factors, Aging, and Incidence of Dementia Score (CAIDE) and Framingham Risk Score (FRS).

METHODS: Longitudinal data of $N = 1529$ (mean age 49 years; 54% women) Beaver Dam Offspring Study (BOSS) participants from baseline, 5 and 10-year follow-up were included. We tested whether including baseline sensory (hearing, vision, olfactory) impairment and motor function improves CAIDE or FRS risk predictions of 10-year cognitive decline or cognitive impairment incidence using logistic regressions.

RESULTS: Adding sensory and motor measures to CAIDE-only and FRS-only models significantly improved areas under the curve for cognitive decline and impairment models.

DISCUSSION: Including midlife sensory and motor function improved risk predictions of long-term cognitive decline and impairment in middle-aged to older adults. Sensory and motor assessments could contribute to cost-effective and non-invasive screening

tools that identify high-risk individuals earlier to target intervention and prevention strategies.

KEYWORDS
CAIDE, cardiovascular, cognitive decline, cognitive impairment, cohort study, dementia, early detection, Framingham Risk Score, grip strength, grooved pegboard, hearing, longitudinal, motor, olfaction, vision

Highlights

- Sensory and motor measures improve risk prediction models of cognitive decline.
- Sensory and motor measures improve risk prediction models of cognitive impairment.
- Prediction improvements were strongest in midlife (adults < 55 years of age).
- Sensory and motor changes may help identify high-risk individuals early.

1 | INTRODUCTION

Alzheimer's disease and related dementias (ADRD) are a public health concern given their high prevalence in older adults.[1,2] Alzheimer's disease (AD) has a decades-long preclinical stage, with first pathologic changes as early as in midlife.[3] Early identification of people at higher risk of dementia may allow time to initiate lifestyle changes, or future early prevention or intervention methods to prevent ADRD or slow disease progression.

Various risk factors for ADRD have been studied previously. Aside from widely acknowledged sex differences[2,4–6] and education effects,[7–9] particularly cardiovascular factors, such as smoking,[9–11] overweight and obesity,[10,12,13], physical inactivity,[10,11,14,15] diabetes,[9,11,16] hypertension,[9,16] and high cholesterol have been studied.[16] Based on this knowledge, researchers have developed different risk scores for dementia prediction. Two well-established risk scores based on cardiovascular risk factors are the Cardiovascular Risk Factors, Aging, and Incidence of Dementia Score (CAIDE) and the Framingham Risk Score (FRS).[17] The CAIDE was developed using data from the Cardiovascular Risk Factor, Aging and Dementia Study, a population-based study of participants in midlife, with the objective to predict 20-year risk of dementia based on factors associated with risk for cardiovascular disease.[17,18] The FRS, was developed using data from the Framingham Heart Study and Framingham Offspring Study, which are longitudinal, community-based cohort studies on heart disease. The original purpose of the FRS was to assess risk of cardiovascular disease and cardiovascular disease events. More recently, it also has been shown to be useful for risk predictions of cognition and dementia.[19,20]

These prediction models do not perfectly predict dementia onset[17,20] and including additional, easy to assess risk factors could help explain more variance and, thus, improve the risk prediction. Sensory and motor declines also occur in aging adults and have been previously associated with the development of cognitive impairment and decline, making them potential candidates for improving risk prediction.[11,21–26] Importantly, assessments of sensory and motor functions are easy to obtain, cost-effective, and non-invasive. However, sensory and motor function assessments have not yet been established for use in risk prediction models.

Therefore, this study aimed to assess whether midlife sensory and motor function can improve risk prediction models of 10-year incidence of cognitive decline and impairment in comparison to risk predictions using the CAIDE or FRS only.

2 | METHODS

2.1 | Study population

Data included in this study were from participants in the Beaver Dam Offspring Study (BOSS), a longitudinal study of sensory and cognitive aging in the adult offspring of the population-based Epidemiology of Hearing Loss Study.[27,28] Participants in the baseline BOSS (2005–2008) were 21–84 years of age and 55% were women.[27] Follow-up examinations occurred at 5 (2010–2013) and 10 years (2015–2017). Study examinations were conducted by trained examiners following standardized protocols and included measures of sensory and motor function, vascular health, a blood draw, and demographic and behavioral and medical history questionnaires.[11,29,30] The study was approved by the Health Sciences Institutional Review Board of the University of Wisconsin; written informed consent was obtained from all participants prior to each examination.

For this study, we included $N = 1529$ participants, who had repeated blood-measures and underwent longitudinal review for the determination of cognitive impairment status at each wave by an expert neurocognitive review panel.[31,32] More study details have been published[31] and this study sample was similar in their baseline characteristics to the complete baseline BOSS cohort.[31]

2.2 | Cognitive assessments

We administered a battery of cognitive function tests covering the domains of attention, processing speed, executive function, memory, language, and general cognitive function: The Mini-Mental State Examination (MMSE), and Trail Making Tests A (TMTA) and B (TMTB), were administered at all examination waves. Additionally, a modified Rey Auditory Verbal Learning Test (AVLT), phonemic Verbal Fluency Test (VFT; for letters F, A, S), and a Digit Symbol Substitution Test (DSST), were administered at the 5- and 10-year examination. More assessment details have been published.[11,33–35]

We asked participants to self-report a physician diagnosis of dementia or AD at each wave. At the 10-year examination, participants were also asked two questions about memory concerns. "Have you, your family or your physician ever expressed concerns about your memory?" and "Do (your) memory loss symptoms interfere with your ability to do your own day-to-day activities?"[11]

2.2.1 | Cognitive impairment

An expert neurocognitive review panel, comprised a geriatrician specializing in memory disorders, two neuropsychologists, a neuro-ophthalmologist, and a psychologist/epidemiologist determined the cognitive impairment status of the participants for each BOSS wave (baseline, 5- and 10-year follow-up): A sensitive computer-based screening algorithm developed by the panel was used to identify potential cases of cognitive impairment considering data from self- or surrogate reports of physician diagnosis of AD or dementia, MMSE score, self-reported memory complaints, and low performance on the cognitive function tests (relative to respective age-education comparison groups in this cohort). Two panel members independently reviewed the data of potential cases detected by the algorithm to determine their cognitive status. For determining case status, they had access to all cognitive data as well as demographic information, medical history, medication intake, self-reported physical and mental health status, sleep, and other lifestyle factors available from each BOSS wave. If there was disagreement between the reviewer categorizations of normal versus impaired cognition, the full neurocognitive consensus panel determined the final classification of the discordant cases. The panel's decision on cognitive impairment case status was guided by the National Institute on Aging and Alzheimer's Association (NIA-AA) criteria for mild cognitive impairment and dementia while both of these were combined into one outcome of cognitive impairment.[36,37]

2.2.2 | Cognitive decline

Cognitive decline was defined as an increase in TMTB performance time of greater than 29 s between baseline and the 10-year follow-up. This cutoff represents the 90th percentile, that is, 10% of participants with the greatest increase in test completion time from baseline to 10-year follow-up. Participants with a baseline TMTB score > 271 s or longer were excluded from analyses because it could not be determined if they met the definition of decline due to the test time limit of 300 s.[11]

RESEARCH IN CONTEXT

1. **Systematic review**: The authors reviewed the literature using traditional (e.g., PubMed) sources. Several studies have linked sensory and motor changes to cognitive impairment, cognitive decline and dementia. However, sensory and motor functions have not been established for risk prediction models, which have rather largely focused on the usage of education and cardiovascular risk factors. Relevant citations on sensory-motor-cognitive research and cardiovascular risk models are appropriately cited.
2. **Interpretation**: Our findings add to the existing research using cardiovascular assessments to predict dementia, showing that sensory and motor functions in midlife may contribute independent information for risk prediction models of cognitive change.
3. **Future directions**: Importantly, sensory and motor functions can be assessed reliably, are cost-effective and non-invasive and could thus serve as a practical addition for future prediction models to identify high-risk individuals early to target future intervention and prevention strategies.

2.3 | Sensory and motor assessments

Hearing function was measured using pure-tone audiometry (PTA), and hearing impairment was defined as a PTA of the thresholds at 0.5, 1, 2, and 4 kHz greater than 25 decibels hearing level in either ear.[27,29] Visual function was assessed by measuring contrast sensitivity using Pelli-Robson letter charts. Visual impairment was defined as contrast sensitivity < 1.55 log units in the worse eye.[30] The San Diego Odor Identification Test was used to measure olfactory function, and impairment was defined as identifying fewer than six out of eight odorants correctly.[38]

A hand dynamometer (model 78010, Lafayette Instruments, Lafayette, IN, USA) was used to measure the grip strength (kilograms) of the dominant hand. Participants performed the measure twice, while standing, and the average of the two measures was used in the analyses.[31,33] The Grooved Pegboard is considered to measure fine motor and psychomotor function. The test was performed with the dominant hand, and the time in seconds to correctly place 25 slotted pegs correctly was used as the score (Lafayette Instruments, Lafayette, IN, USA).[33,39] The Medical Outcomes Study Short Form Health Survey (SF-36) was administered as a questionnaire, and the physical function scale of the SF-36 is considered to assess mobility, locomotion, and endurance.[40]

2.4 | Other variables

Years of education, smoking history, use of blood pressure medication, and the frequency of exercise (long enough to work up a sweat) were obtained by questionnaire. Height and weight were measured, and body mass index (BMI) was calculated as kg/m^2. Blood pressure was measured three times using a Dinamap Procare 100 (GE Medical Systems, Milwaukee, WI) with a 1 min rest interval between measures. The average of the second and third readings was used as the blood pressure.[29] Total and high-density lipoprotein (HDL) cholesterol were measured in serum, and hemoglobin A1C (HbA1C) was measured in whole blood.[27] Participants were classified as having diabetes if they had an HbA1C $\geq$ 6.5% or a physician diagnosis of diabetes or suspected diabetes with current treatment.[29]

2.5 | Statistical analyses

We calculated the baseline CAIDE score, which is a summary score based on age, education, sex, systolic blood pressure, BMI, total cholesterol, and physical activity for each participant.[17] The original CAIDE scoring algorithm assigned a score of 3 for 0–6 years of education, 2 for 7–9 years, and 0 for $\geq$10 years of education.[17] To account for the fact that our cohort had a higher average level of education and to capture the variation in our cohort appropriately, we assigned a score of 3 for less than 12 years, a score of 2 for 12 years, and a score of 0 for more than 12 years of education, in the calculation of the CAIDE.

The FRS total percent risk estimate (FRS%) was developed by D'Agostino et al. and is based on sex-specific Cox proportional hazards regression models and represents a subject's specific first cardiovascular disease event risk.[19] We calculated the baseline FRS% for each participant based on the published sex-specific weights for age, systolic blood pressure, use of blood pressure medication, total and HDL cholesterol levels, smoking, and diabetes status.[19]

2.5.1 | Logistic regression models

We tested whether including baseline sensory (hearing, vision, olfactory) impairment and motor function (grip strength, Grooved Pegboard, SF-36 physical function scale) improved CAIDE or FRS% risk prediction models of 10-year incidence of cognitive impairment and cognitive decline. Individuals with baseline cognitive impairment were excluded from the incidence of cognitive impairment models. For both cognitive outcomes, logistic regression models were used to determine the area under the receiver operating characteristic curve (AUC) for models including (1) only the CAIDE; (2) the CAIDE plus the sensory-motor function variables (sensory-motor); (3) only the FRS; (4) FRS plus sensory-motor. Sensory impairments (hearing, vision, olfaction) were included in models as binary variables. Because of known sex differences in performance on motor measures (grip strength, Grooved Pegboard, SF-36 physical function scale) and observed differences in motor function between men and women in this cohort we used sex-specific scales for motor function and calculated *z*-scores standardized by sex.[31] These z-scores were used in the regression models. We tested for significance in improvement in the AUCs between risk prediction models with and without sensory-motor variables using chi-squared tests. Receiver operating characteristic (ROC) curves are included in Supplement 1.

Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were calculated via the classification table in Proc Logistic (Supplement 1). To determine if there were differences in the performance of the prediction models by age or by sex, analyses were repeated stratified by age group (< 55 and 55 years) and older and by sex. All analyses were conducted using SAS version 9.4 (SAS Institute, Inc., Cary, NC USA).

3 | RESULTS

Participant baseline characteristics are shown in Table 1. Participants had a mean age of 49 years (standard deviation (SD) = 9.4) and 54% were women. The mean CAIDE was 5.2 (SD = 3.0) and the mean FRS% was 9.6 (SD = 9.6).

3.1 | 10-year incidence of cognitive impairment

In this sample, there were $N = 164$ participants classified as having cognitive impairment at baseline that were not included in the incidence analyses. Of the $N = 1365$ participants without cognitive impairment at baseline, 248 (18%) were classified as having incident cognitive impairment at the 10-year follow-up.

Adding sensory and motor function to the CAIDE only model improved the AUC significantly ($p < .01$) from 0.59 to 0.65. Models also improved for FRS% from 0.59 to 0.65 ($p < .01$, Table 2; Supplement 1). The AUCs in models stratified by age group (< 55 and 55 years or more) were similar (Table 2).

In sex-specific models, the AUC for the CAIDE only model was lower in men than women (AUC 0.53 vs. 0.60, respectively) but the magnitude of improvement in the AUC with the addition of sensory-motor function to the models was the same for both men and women (AUC increased 0.09 for both). For FRS% only models, the AUCs were similar for men and women. The addition of sensory-motor function to the models resulted in a slightly higher increase in the AUC in the model for women versus men (Women: AUC increased 0.15; Men: AUC increased.0.10; Table 2).

3.2 | 10-year incidence of cognitive decline

In the study, there were $N = 16$ participants at baseline who were excluded from the incidence analyses and $N = 139$ (9.5%) of the $N = 1513$ participants at risk for incident decline, experienced cognitive decline between baseline and the 10-year follow-up.

TABLE 1 Baseline participant characteristics.

Baseline characteristic	*N* (%)
Age (years)	
<47	615 (40.2)
47–53	437 (28.6)
>53	477 (31.2)
Women	828 (54.2)
Education (years)	
<12	31 (2.0)
12	433 (28.5)
>12	1055 (69.5)
Systolic blood pressure > 140 mmHg	279 (18.3)
Taking blood pressure medication	340 (22.3)
Total cholesterol > 251 mg/dL	165 (10.8)
HDL cholesterol	
<35 mg/dL	187 (12.3)
35–44 mg/dL	448 (29.6)
45–49 mg/dL	222 (14.7)
50–59 mg/dL	348 (23.0)
≥ 60 mg/dL	310 (20.5)
Exercise < 2 times per week	768 (50.3)
Current smoker	225 (14.7)
BMI> 30 kg/m^2	673 (44.4)
Diabetes	75 (4.9)
Hearing impairment (PTA > 25 dBHL)	217 (14.2)
Vision impairment (CS log triplets < 1.55)	250 (16.4)
Olfactory impairment (SDOIT < 6)	54 (3.5)
	Mean (SD) [range]
Grooved pegboard, time, s	71.7 (15.6) [45–243]
Grip strength, kg	38.5 (12.4) [5.0–77.5]
SF-36 PFS	88.4 (16.0) [0–100]
CAIDE score	5.2 (3.0) [0–13]
FRS%	9.6 (9.6) [0.3–76.5]

Note: Baseline characteristics of $N = 1529$ Beaver Dam Offspring Study participants. Sample sizes vary slightly due to missing data, which was less than 1% for any individual variable. Categories chosen reflect usage of categories in CAIDE and/or FRS.

Abbreviations: BMI, body mass index; CAIDE, Cardiovascular Risk Factors, Aging, and Incidence of Dementia Score; CS, contrast sensitivity; dB HL, decibel hearing level; FRS, Framingham Risk Score; HDL, high density lipoprotein; s, seconds; SDOIT, San Diego Odor Identification Test; SF-36 PFS, Short form Health Survey 36 Physical Function Score; PTA, pure-tone average.

The AUCs for the CAIDE only and FRS% only models for cognitive decline were 0.72 and 0.71, respectively. Adding sensory-motor function to the models increased the AUCs to 0.77 for the CAIDE model ($p < .01$) and to 0.78 for the FRS% model ($p < .01$; Table 3; Supplement 1).

Among those < 55 years, the AUCs for the CAIDE only and FRS% only models were lower than in the overall models. The addition of sensory-motor measures to the prediction models improved the AUCs to the same level as seen in the overall models. In the models restricted to the older group (> = 55 years), the AUCs in the models including only the standard risk scores were lower and the addition of sensory-motor measures to the models only slightly increased the CAIDE model AUC from 0.59 to 0.65 and the FRS% model from 0.62 to 0.66 (Table 3). Sex-specific models were similar to full cohort models (Table 3).

3.3 | Additional metrices of risk prediction for cognitive outcomes

Sensitivity and specificity values of the risk prediction models varied; positive predictive values were low (Supplement 1). Negative predictive values were high: for the 10-year incidence of cognitive impairment models were greater than 85% and the negative predictive values for the 10-year incidence of cognitive decline were greater than 95%.

4 | DISCUSSION

In the current study, adding sensory and motor function to established risk scores improved the risk prediction for 10-year incidence of cognitive impairment and cognitive decline. This adds to existing research using cardiovascular assessments to predict dementia, by showing that sensory and motor functions may add relevant information to risk prediction models of cognitive change. Importantly, sensory and motor functions can be assessed reliably and non-invasively and are cost-effective. They could thus serve as a practical addition for future prediction models.

Sensory and motor functions have been previously associated with developments of cognitive impairment and decline,[11,21–26] but have not been established as risk factors in prediction models, which have rather largely focused on the usage of education and cardiovascular risk factors.[17,18,20] Previous studies investigated the development of dementia over 20 or more years and reported AUCs > = 0.70 for the CAIDE and FRS.[17,18,20] In the current analyses, we studied 10-year incidence of cognitive impairment and cognitive decline. The CAIDE and FRS performed similar in predicting cognitive outcomes in our studies, with AUCs of 0.59 for both CAIDE and FRS in predicting the 10-year incidence of cognitive impairment and 0.71 and 0.72, respectively, for cognitive decline prediction. We found that adding sensory and motor variables to the CAIDE and FRS% models for cognitive impairment improved the AUCs of the models to 0.65, which is closer to the prediction performances of previous studies on the development of dementia later in life.[17,18,20] The addition of the sensory and motor variables to the models on cognitive decline increased the AUCs for both risk prediction scores to 0.77, which met, or slightly exceeded the AUCs observed in previous prediction models.[17,18,20] Importantly, we achieved this level of long-term prediction performance in a comparably "young" cohort, that is, the majority of participants were in their midlife at the time when predictor variables were measured

TABLE 2 Risk prediction for 10-year incidence of cognitive impairment for the CAIDE and FRS% individually and after adding sensory and motor functions.

	10-year incidence of cognitive impairment[a]									
	All[b]		<55 years[c]		≥55 years[c]		Women[d]		Men[d]	
	AUC (95% CI)	p	AUC (95% CI)	p	AUC (95% CI)	p	AUC (95% CI)	p	AUC (95% CI)	p
CAIDE	0.59 (0.55,0.63)	<.01	0.58 (0.54,0.63)	<.01	0.60 (0.53,0.66)	.03	0.60 (0.54,0.67)	<.01	0.53 (0.48.0.59)	<.01
CAIDE +Sens-Motor	0.65 (0.61,0.68)		0.64 (0.60,0.69)		0.67 (0.60,0.74)		0.69 (0.62,0.75)		0.62 (0.57,0.67)	
FRS%	0.59 (0.55,0.63)	<.01	0.59 (0.54,0.64)	.02	0.60 (0.53,0.67)	.05	0.54 (0.47,0.60)	<.01	0.52 (0.46,0.57)	<.01
FRS% +Sens-Motor	0.65 (0.61,0.69)		0.65 (0.61,0.70)		0.67 (0.60,0.74)		0.69 (0.63,0.76)		0.62 (0.57,0.68)	

Abbreviations: AUC, area under the receiver operating characteristic curve; CAIDE, Cardiovascular Risk Factors, Aging, and Incidence of Dementia Score; CI, confidence interval. FRS, Framingham Risk Score; Sens-Motor, sensory and motor assessments.

[a]Results of logistic regression models on 10-year incidence of cognitive impairment. *p*-value is the result of a chi-squared test to determine statistically significant differences between AUCs of models including the standard risk score only and models including the standard risk score and additionally sensory and motor measures (hearing impairment, vision impairment, olfactory impairment, grip strength, Grooved Pegboard test and Short Form Health Survey 36 physical function score).

[b]Sample $N = 1325$ with $N = 240$ cases.

[c]Model stratified by age group. In individuals aged < 55 years: Sample $N = 964$ with $N = 165$ cases; in individuals aged > = 55 years: Sample $N = 361$ with $N = 75$ cases.

[d]Model stratified by sex. Women: Sample $N = 738$ with $N = 83$ cases; Men: Sample $N = 587$ with $N = 157$ cases.

TABLE 3 Risk prediction for 10-year incidence of cognitive decline for the CAIDE and FRS% individually and after adding sensory and motor functions.

	10-year incidence of cognitive decline[a]									
	All[b]		<55 years[c]		≥55 years[c]		Women[d]		Men[d]	
	AUC (95% CI)	p	AUC (95% CI)	p	AUC (95% CI)	p	AUC (95% CI)	p	AUC (95% CI)	p
CAIDE	0.72 (0.68,0.76)	<.01	0.68 (0.61,0.76)	<.01	0.59 (0.52,0.66)	.05	0.71 (0.65,0.78)	<.01	0.72 (0.67,0.78)	<.01
CAIDE + Sens-Motor	0.77 (0.73,0.81)		0.77 (0.71,0.83)		0.65 (0.58,0.72)		0.75 (0.69,0.81)		0.79 (0.74,0.83)	
FRS%	0.71 (0.67,0.76)	<.01	0.63 (0.55,0.71)	<.01	0.62 (0.55,0.69)	.15	0.72 (0.65,0.79)	.03	0.70 (0.64,0.77)	<.01
FRS% + Sens-Motor	0.78 (0.74,0.82)		0.77 (0.71,0.83)		0.66 (0.60,0.73)		0.76 (0.70,0.82)		0.78 (0.73,0.84)	

Abbreviations: AUC, area under the receiver operating characteristic curve; CAIDE, Cardiovascular Risk Factors, Aging, and Incedence of Dementia Score; CI, confidence interval; FRS, Framingham Risk Score; Sens-Motor, sensory and motor assessments.

[a]Results of logistic regression models on 10-year incidence of cognitive decline. *p*-value is the result of a chi-squared test to determine statistically significant differences between AUCs of models including the standard risk score only and models including the standard risk score and additionally sensory and motor measures (hearing impairment, vision impairment, olfactory impairment, grip strength, Grooved Pegboard test and Short Form Health Survey 36 physical function score).

[b]Sample $N = 1470$ with $N = 139$ cases.

[c]Model stratified by age group. In individuals aged < 55 years: Sample $N = 1070$ with $N = 58$ cases; in individuals aged > = 55 years: Sample $N = 400$ with $N = 81$ cases.

[d]Model stratified by sex: Women: Sample $N = 793$ with $N = 64$ cases; Men: Sample $N = 677$ with $N = 75$ cases.

which is when intervention or prevention methods might be more effective.

In fact, the addition of the sensory and motor variables to the prediction models on cognitive decline in those less than 55 years was especially beneficial. Sensory and motor impairments in early midlife are less common (as compared to older age) but may be early indicators of neurodegeneration.[21,27,30] Thus, including them in models with the standard risk scores may improve the risk prediction of cognitive changes in early midlife when the prevalence of cardiovascular risk factors is also lower.

The AUCs for all models were slightly higher for the outcome of 10-year cognitive decline as compared to cognitive impairment. This could be because sensory and motor impairments are better predictors of earlier changes (decline) as compared to onset of disease (impairment). It may have also been due to the nature of the definition of our outcomes. We used a narrow definition to classify cognitive decline, which included only the 10% of participants with the most decline on the TMTB in 10 years. The risk prediction scores may have performed better with this conservative outcome, which only included the participants with the most extreme decline in cognition function. On the other hand, the determination of cognitive impairment was conducted by the neurocognitive consensus panel and was based on performance on all cognitive tests, memory complaints, dementia diagnosis and related variables.[36,37]

While other metrices on predictive performance were rather low, the negative predictive values were good to excellent in this study. For usage in a population with a low prevalence of disease, screening tools are not intended as a diagnostic tool but should rather serve as a gatekeeper to identify individuals that should undergo further confirmatory diagnostic procedures. Thus, the primary goal is to attain a high negative predictive value,[41] which was the case in our study.

This study focused on the predictive value of sensory and motor function for cognitive changes rather than the study of their etiology in the process of aging. Different pathways, including a shared cardiovascular pathway, have been discussed in previous studies that investigated sensory and motor changes as risk factors for cognitive decline.[42,43] In our study, when added to models using the CAIDE or FRS, risk predictions significantly improved, although the magnitude of improvement was rather small. However, it is important to note that sensory and motor functions added to the predictive performance and explained variance of the development of cognitive impairment and decline beyond the already explained variance by education, sex, and cardiovascular risk.

As previously stated, the CAIDE and FRS% AUCs were lower in the BOSS cohort as compared to some previous studies.[17,18,20] There are several possible reasons for these findings. First, we had 10 years of follow-up in the BOSS as compared to 20 or more years in previous studies. Second, our outcomes were cognitive impairment and cognitive decline versus dementia. Finally, although the CAIDE was developed in a midlife population, participants in that study, and in the later validation study were born earlier in the 20th century than participants in the BOSS, who were born in the second half of the 20th century (Baby Boomers and Generation X).[17,18,27] This is also true for the FRS, which was developed using participant data collected in the 1960s–1980s.[19] More recent birth cohorts have higher levels of education,[44,45] a major protective factor of dementia.[7] Thus, to more appropriately reflect the educational distributions in our cohort, we adjusted the CAIDE scoring for education. Moreover, more recent generations have shown better cardiovascular health and lower prevalence of related risk factors, such as smoking.[17,44–47] Younger generations have also shown better cognitive function and a lower prevalence of dementia than previous generations.[8,48,49] Thus, they may be at lower risk for developing dementia or onset may occur later in life than in previous generations. Therefore, it is possible that risk scores developed in earlier generations may not perform as well as in more recent generations. Enhancing these risk scores with additional factors, such as sensory-motor variables, that have been shown to predict cognitive decline and impairment in more recent generations may improve risk prediction of these standard scores. Future studies should determine the best predictor variables to be used in parsimonious models. Such future studies could take ease of administration into account: Measures that are easy to administer, such as the self-report measures of motor function utilized here, could be particularly feasible when added to routine clinical screenings.

4.1 | Limitations and strengths

This study is based on a subsample of the BOSS. However, the sample was not different from the complete baseline sample, which has been previously shown.[31] Our study cohort consists of predominantly non-Hispanic White individuals, which may thus limit our ability to generalize the findings to other populations. While we aimed to assess predictors of early changes, the severity of cognitive changes and impairment might not have been sufficient to develop strong prediction models and longer follow-up might be needed. Apolipoprotein E (APOE) ε4-carrier status, a risk factor for and predictor of AD and dementia, was not available in this study cohort. However, APOE genotype did not improve CAIDE-based risk prediction models in previous work.[17]

There are multiple strengths of our study. We utilized a large, well-characterized general population cohort that has standardized objective assessments of cardiovascular risk factors, three sensory systems, and motor functions. We had repeated measures of cognitive assessment, follow-up over 10 years, and a neurocognitive review panel for the study.

4.2 | Conclusion

Including sensory-motor function variables in models with standard risk scores based on cardiovascular risk factors may improve risk prediction of cognitive decline and impairment. As sensory and motor changes can occur early and may precede other indicators of neurodegeneration, they may be especially useful for risk predictions in early midlife, where intervention and prevention methods might be more effective, to help identify those that may be at increased risk for cognitive decline.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest to report. Author disclosures are available in the supporting information.

CONSENT STATEMENT

All human subjects provided written informed consent.

ORCID

Natascha Merten PhD, MS https://orcid.org/0000-0002-1405-1218

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SUPPORTING INFORMATION

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

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