International Psychogeriatrics (2024), 36:7, 574–586
doi:10.1017/S1041610223000819

Socioeconomic position, modifiable dementia risk and cognitive decline: results of 12-year Maastricht Aging Study

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ABSTRACT

Objectives: This study investigated whether the association between modifiable dementia risk and rate of cognitive decline differs across socioeconomic status (SES) strata.

Design, setting and participants: Data were used from Maastricht Aging Study, a prospective cohort study with a 12-year follow-up. The baseline sample consisted of 1023 adults over 40 years old.

Measurements: The "LIfestyle for BRAin health" (LIBRA) index was used to assess modifiable dementia risk. Cognitive performance was assessed at baseline, 6 and 12 years, and measured in the domains of information processing speed, executive functioning and verbal memory function. An SES score was calculated from equivalent income and educational level (tertiles). Linear mixed models were used to study the association between LIBRA, SES and their interaction on the rate of cognitive decline.

Results: Participants in the lowest SES tertile displayed more decline in information processing speed (vs. middle SES: $X^2 = 7.08$, $P = 0.029$; vs. high SES: $X^2 = 9.49$, $P = 0.009$) and verbal memory (vs. middle SES: $X^2 = 9.28$, $P < 0.001$; vs. high SES: $X^2 = 16.68$, $P < 0.001$) over 6 years compared to their middle- and high-SES counterparts. Higher (unhealthier) LIBRA scores were associated with more decline in information processing speed ($X^2 = 12.66$, $P = 0.002$) over 12 years and verbal memory ($X^2 = 4.63$, $P = 0.032$) over 6 years. No consistent effect modification by SES on the association between LIBRA and cognition was found.

Conclusions: Results suggest that lifestyle is an important determinant of cognitive decline across SES groups. Yet, people with low SES had a more unfavorable modifiable risk score suggesting more potential for lifestyle-based interventions.

Key words: dementia, cognitive testing, risk factors, education, health aging

Introduction

Dementia is one of the biggest health challenges of our time (World Health Organization, 2019). The expected worldwide threefold increase in the number of people with dementia to 152 million in 2050 is particularly attributable to the rising numbers in low-to-middle income countries (LMIC) (World Health Organization, n.d.; Hachinski *et al.*, 2019; Livingston *et al.*, 2020). In fact, epidemiological studies have shown stabilization and even decline in incidence rates in high-income countries (HIC) (Hachinski *et al.*, 2019; Matthews *et al.*, 2016; Prince *et al.*, 2016; Roehr *et al.*, 2018; Satizabal *et al.*, 2016; Wolters *et al.*, 2020). Possible explanations are the increasing wealth and improved general health in HIC (e.g., improved provision and access to education, better nutrition and cardiovascular risk management) and increasing rates of dementia risk factors in LMIC (e.g., higher prevalence of diabetes mellitus, smoking, hypertension, and obesity) (Hachinski *et al.*, 2019; Prince *et al.*, 2016; Roehr *et al.*, 2018; Satizabal *et al.*, 2016).

Indeed, there is accumulating evidence that modifiable risk factors contribute to cognitive decline and dementia risk, which suggests potential for dementia risk reduction (Lincoln *et al.*, 2014; Livingston *et al.*, 2020; Norton *et al.*, 2014;

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Lautenschlager *et al.*, 2003). The 2020 update of the Lancet Report on Dementia Prevention, Intervention and Care concluded that around 40% of all dementia cases are potentially attributable to modifiable risk factors (Livingston *et al.*, 2020). The World Health Organization identified risk reduction of dementia as one of the action areas for 2017–2025 (World Health Organization, 2017), which was followed by publishing guidelines for risk reduction of cognitive decline and dementia in 2019 (World Health Organization, 2019). The International Research Network on Dementia Prevention ensures that scientific results are communicated among researchers and policymakers worldwide (Anstey *et al.*, 2017). These developments within the field have led to multidomain lifestyle-intervention trials for middle-aged and older individuals. The population-based Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) was the first to show improvements in cognition (Ngandu *et al.*, 2015). The recent initiative World Wide FINGERS aims to harmonize adapted versions of the FINGER trial worldwide, such as the Australian Maintain Your Brain and U.S. POINTER trials (Kivipelto *et al.*, 2020).

Besides lifestyle-related risk factors, lower socioeconomic status (SES), in which SES is defined as "social and economic factors that influence which positions individuals or groups will hold within the structure of a society" (Krieger *et al.*, 1997), has also been associated with an increased risk of cognitive decline and dementia (Deckers *et al.*, 2019; George *et al.*, 2020; Hachinski *et al.*, 2019; Yaffe *et al.*, 2013; Zeki Al Hazzouri *et al.*, 2011) and an unhealthier lifestyle (Röhr *et al.*, 2022a).

The relationship between all three factors has also been investigated and there are different pathways by which lifestyle and SES can influence cognition and dementia risk. A recent study showed that the association between SES (i.e., education, occupation and net equivalence income) and cognitive performance can partially be explained by health and lifestyle factors (Röhr *et al.*, 2022b). Other studies suggest that SES might act as a moderator between lifestyle and cognitive performance. For example, higher adherence to a healthy diet was associated with less cognitive decline over 3 years in older adults (68–84 years) with low SES, compared with high SES (based on income, education and occupation) (Parrott *et al.*, 2013). A prospective cohort study found that financially disadvantaged participants benefitted cognitively the most from living healthy (based on vegetable and fish intake, physical activity, smoking status and light-to-moderate alcohol intake) (Weng *et al.*, 2018). Contrary, a prospective cohort study from 2019 found that the effect of a modifiable risk score (including lifestyle factors) and cognitive functioning over 10 years was similar across educational groups, another indicator of SES (Deckers *et al.*, 2018). In addition, SES measured as income did not modify the lifestyle-intervention effect of the FINGER on cognition (Rosenberg *et al.*, 2018).

More clarity on this matter is important from a public health perspective. It is important to identify and target subgroups that would benefit most from lifestyle interventions and vascular risk management aimed at risk reduction of dementia and to develop more extensive or other types of interventions in specific SES groups, to reach the full potential of primary prevention of dementia.

Therefore, this study aims to contribute to the existing evidence by investigating whether the association between modifiable dementia risk and cognitive performance over 12 years is different across groups with different levels of SES, defined by educational level and income.

Methods

Study design

This study used data from the Maastricht Aging Study (MAAS), a population-based observational study into successful and pathological cognitive aging. Data collection for MAAS is ongoing and has to date a fully completed follow-up period of 12 years (Jolles *et al.*, 1995).

Participants

Potential participants for MAAS were randomly drawn from the Research Network Family Medicine Maastricht (RNFM), a registration network of family practices in the Province of Limburg, the Netherlands (Metsemakers *et al.*, 1992). The network consisted of approximately 80,000 primary care patients that are representative of the general Dutch population with respect to demographic characteristics (Metsemakers *et al.*, 1992). A total of 10,396 individuals aged between 24 and 81 years old without morbidity that is known to interfere with cognitive function (e.g. dementia, schizophrenia) received a postal letter with an invitation to participate in MAAS. Interested individuals were screened for exclusion criteria that were not available in the RNFM database (e.g. score of <24 on the Mini-Mental State Examination, history of transient ischemic attacks, or brain surgery) (Jolles *et al.*, 1995). This led to the selection of 1823 Caucasian and Dutch-speaking participants who completed the baseline assessment between 1993 and 1995 (Jolles *et al.*, 1995; van Boxtel *et al.*, 1998). The study protocol of MAAS has been approved by the local ethics committee of

https://doi.org/10.1017/S1041610223000819

Maastricht University Medical Centre [METC2019-1151]. Before participating in the study, all individuals were provided with oral and written information. Written informed consent was obtained from all participants at the start of the baseline assessment.

This study used data from the sample of ≥ 40 years old at baseline ($n = 1223$) and used the 6- and 12-year follow-up assessments as (cognitive) outcome time points.

Measures

Modifiable dementia risk

To assess health and lifestyle factors associated with dementia risk, the "LIfestyle for BRAin health" (LIBRA) index was used (Deckers *et al.*, 2015). While most other dementia risk indices are based on single cohort studies and/or include non-modifiable factors such as age, sex or genetic factors (Cherbuin *et al.*, 2019; Exalto *et al.*, 2014; Kivipelto *et al.*, 2006; Reitz *et al.*, 2010; Stephen *et al.*, 2017), LIBRA is based on a systematic literature review and Delphi consensus (Deckers *et al.*, 2015) and was designed to capture the modifiable risk fraction of 12 risk and protective factors. LIBRA could therefore be useful as a participant selection tool or as a surrogate outcome measure in lifestyle intervention trials (Coley *et al.*, 2020; Deckers *et al.*, 2021). LIBRA has been associated with cognitive decline, cognitive impairment and dementia risk in several cohorts, particularly in middle-aged and young-old populations (Deckers *et al.*, 2017a; Deckers *et al.*, 2018; Deckers *et al.*, 2019; Deckers *et al.*, 2020; Deckers *et al.*, 2021; Pons *et al.*, 2018; Schiepers *et al.*, 2018; Vos *et al.*, 2017). Presence of LIBRA factors in MAAS (yes/no) was based on self-reported questionnaires and/or clinical data at baseline and defined following established cutoffs. A weight (positive for risk factors, negative for protective factors) was assigned to the presence of each LIBRA factor, based on the factor's relative risk (Deckers *et al.*, 2015). With the exception of information on adherence to a Mediterranean diet, all LIBRA factors were available in MAAS. The LIBRA total score was calculated for each participant by summation of the individual LIBRA weights (ranging from −4.2 to +12.7, with higher scores indicating higher dementia risk). Additionally, LIBRA discrete risk groups were calculated based on tertiles (referred to as "low," "middle" and "high" risk). Participants were only included in the analyses if all 11 LIBRA factors were available. See Table S1 published as supplementary material to the electronic version of this paper at https://www.cambridge.org/core/journals/international-psychogeriatrics for an overview of the LIBRA factors, assigned weights and operationalization in MAAS.

Cognitive outcomes

Cognitive performance was assessed with a neuropsychological assessment administered by trained personnel at baseline, 6- and 12-year follow-up. The Verbal Learning Test (VLT) was used to assess verbal memory. A total of 15 meaningful words were successively presented after which a participant was asked to recall as many words as possible, with five consecutive trials. Number of recalled words after 20 minutes assessed delayed recall and was used as an outcome measure in this study (Van der Elst *et al.*, 2005). To assess information processing speed, the written version of the Letter-Digit Substitution Test was used. In this test, participants were given 90 seconds to match as many letters as possible to the given numbers following the key at the top of the test sheet (van der Elst *et al.*, 2006a). The Stroop Color-Word Test (SCWT) was used to assess executive functioning. Three cards were consecutively presented to participants, each displaying 100 color names (card one), colored patches (card two) and color names printed in another color's ink (card three). Cognitive interference, the time needed to ignore irrelevant but very outstanding (verbal) information in favor of less salient information (color naming) in card three, was used to assess executive functioning (Van der Elst *et al.*, 2006b). Participants were only included in the study sample if at least one of the three cognitive tests was administered at baseline.

Socioeconomic status

SES was assessed using a compound score of household income and educational level. Income was measured by self-reported net month income of the household in Euro, with 12 answering options ranging from less than 680 euros to more than 2949 euros. In MAAS, income was measured from the 6-year follow-up and available for 712 (58.2%) participants of the study sample. In order to account for the household size living from a household income, income was then recoded into a continuous equivalent income measure by using the Organisation for Economic Co-operation and Development (OECD) square root scale (OECD, 2011). The midpoint of each category of income was taken and divided by the squared root of the number of people that this income should provide for. Educational level was measured using the highest finalized educational degree of a participant in eight categories (primary school, low vocational education, intermediate secondary education, intermediate vocational or higher secondary education, higher vocational education, university and other), assessed at baseline. To compute an overall compound score of SES, equivalent income and educational level were standardized and averaged and subsequently categorized into tertiles.

https://doi.org/10.1017/S1041610223000819

Statistical analysis

Chi^2 tests and *t*-tests were used to investigate differences in socio-demographics, LIBRA profile and cognitive performance between the baseline study sample and those excluded (i.e., <11 LIBRA factors measured). ANOVA's and chi^2 tests were used to study differences in the aforementioned determinants between the three SES tertiles of the baseline study sample (low, middle and high SES). Linear mixed models were used to study the association between LIBRA, SES and cognition over time (3 time points: baseline, 6 and 12-year follow-up), adjusted for baseline age, age^2 and sex. To correct for skewness, data on the VLT delayed recall was squared and data on the SCWT interference score was log-transformed. As suggested by likelihood ratio tests, the models included a random intercept, random slope and unstructured covariance matrix. Interaction terms were added to the models to investigate whether participants with different LIBRA scores (time*LIBRA; using dummy variables for the two follow-ups of time) or SES scores (time*SES; dummy variables for middle and high SES) differ in the rate of change of cognition over time. The interaction terms were tested using a Wald test, which yields a chi^2 statistic with 2 degrees of freedom. Next, three-way interactions (time*LIBRA*SES) were added to the models to study the effect of SES on the association between LIBRA and cognition over time, followed by stratified analyses in case of statistical significance. Analyses were first performed for continuous LIBRA scores and then repeated using LIBRA tertiles (low risk, middle risk, high risk). Two inverse probability weights were used to reduce selection bias (Deckers *et al.*, 2017b; Köhler *et al.*, 2014; Schievink *et al.*, 2017; Weuve *et al.*, 2012). First, an attrition weight was used. While the mixed model assumes data to be missing at random, conditional on included covariates, the weighting further minimizes bias due to selective dropout. The attrition weight was based on probit regression including demographic and health-related factors associated with missingness. Second, a sampling weight using age, gender and level of occupational achievement as predictors was added to weight the estimates back to the RNFM source population participants were recruited from (Matthews *et al.*, 2016; Weuve *et al.*, 2012). All analyses were performed in Stata 13.1 (StataCorp, College Station, TX, USA) with a level of statistical significance set a $P < 0.05$ in two-tailed tests.

Data availability statement

The data underlying this article will be shared on reasonable request to the corresponding author.

Results

Participants

A flowchart of the recruitment process and selection of the study sample is shown in Figure S1, published as supplementary material to the electronic version of this paper at https://www.cambridge.org/core/journals/international-psychogeriatrics. Included participants were by design older ($t = (1819)\ 39.9$, df = 1819, $p < 0.001$). In addition, included participants were lower educated ($X^2\ (2) = 79.6, p < 0.001$), had more unfavorable LIBRA scores ($t\ (1821) = -6.5$, $p < 0.001$) and lower scores on cognitive performance (information processing speed: $t\ (1817) = 18.9$, $p < 0.001$; executive functioning: $t\ (1798) = -11.3$, $p < 0.001$; memory: $t\ (1814) = 12.9$, $p < 0.001$). There was no difference between included and excluded participants for sex ($X^2\ (1) = 0.72$, $p = 0.397$). Table 1 presents the baseline characteristics of the study sample by SES groups (low, middle and high). Participants in the lowest SES group were older, more often female and had a higher (i.e., unhealthier) LIBRA score and lower performance on cognition tasks. In contrast, the protective factor of low-to-moderate alcohol use was more common in the lowest SES group and participants in the high SES group were more often physically inactive compared to their low and middle counterparts.

Lifestyle and cognitive decline

At baseline, higher (continuous) LIBRA scores were associated with lower scores on information processing speed (B = −0.37, 95%CI = −0.58 to −0.16, $p < 0.001$; results in this paragraph not tabulated) and executive functioning (B = 0.02, 95%CI = 0.01–0.04, $p < 0.001$), but not on verbal memory (B = −1.01, 95%CI = −2.15 to 0.12, $p = 0.081$). In the prospective analyses, a higher continuous LIBRA score was associated with faster decline in information processing speed (Wald test for overall interaction: $X^2 = 12.66$, df = 2, $p = 0.002$; 6-year LIBRA*time interaction: B = −0.25, $X^2 = 7.39$, df = 1, $p = 0.007$; 12-year LIBRA*time interaction: B = −0.47, $X^2 = 11.64$, df = 1, $p = 0.001$). There was no association between the continuous LIBRA and decline in executive functioning (Wald test for overall interaction: $X^2 = 0.03$, df = 2, $p = 0.987$; 6-year LIBRA*time interaction B = −0.0004, $X^2 = 0.00$, df = 1, $p = 0.947$; 12-year LIBRA*time interaction: B = −0.002, $X^2 = 0.02$, df = 1, $p = 0.875$). The difference for verbal memory from baseline to 6-year follow-up (B = −1.52, $X^2 = 4.63$, df = 1, $p = 0.032$) was attenuated at 12-year follow-up (B = −0.67, $X^2 = 0.45$, df = 1,

https://doi.org/10.1017/S1041610223000819

Table 1. Characteristics of the baseline study population ($n = 1223$) by socioeconomic status

VARIABLES[a]	LOW SES, $N = 419$ (34.3%)	MIDDLE SES, $N = 402$ (32.9%)	HIGH SES, $N = 402$ (32.9%)	P
Demographics				
Age; mean (SD) range	62.4 (11.1) 40–82	57.9 (10.6) 40–79	56.3 (12.1) 40–82	<0.001
Female; *n* (%)	247 (59.0%)	199 (49.5%)	156 (38.8%)	<0.001
LIBRA health and lifestyle factors; n (%)				
Hypertension	200 (47.9%)	139 (34.6%)	140 (34.7%)	<0.001
Diabetes	35 (8.4%)	18 (4.5%)	16 (4.0%)	0.011
Hypercholesterolemia	51 (12.2%)	56 (13.9%)	50 (12.4%)	0.724
Coronary heart disease	66 (15.8%)	61 (15.2%)	60 (14.9%)	0.935
Chronic kidney disease	21 (5.0%)	17 (4.2%)	18 (4.5%)	0.855
Obesity	114 (27.3%)	79 (19.7%)	63 (15.6%)	<0.001
Smoking	110 (26.3%)	99 (24.6%)	110 (27.3%)	0.684
Cognitive activity	111 (26.6%)	113 (28.1%)	141 (35.0%)	0.020
Physical inactivity	125 (29.9%)	136 (33.8%)	211 (52.4%)	<0.001
Low-to-moderate alcohol use	296 (70.8%)	259 (64.4%)	201 (49.9%)	<0.001
High depressive symptoms	114 (27.3%)	91 (22.6%)	75 (18.6%)	0.013
LIBRA score; mean (SD) range	1.42 (2.33) −4.2 to +9.2	1.05 (2.27) −4.2 to +7.7	0.94 (2.40) −4.2 to +7.4	0.008
Cognitive function score[b]; mean (SD)				
Information processing speed	39.05 (9.86)	45.54 (9.56)	50.61 (10.05)	<0.001
Executive functioning	60.19 (30.95)	47.89 (18.69)	43.26 (18.44)	<0.001
Verbal memory	8.41 (2.90)	9.05 (2.84)	9.70 (3.09)	<0.001

SES: socioeconomic status (compound score of educational level and equivalent month income); SD: standard deviation; LIBRA: LIfestyle for BRAin health index.

[a] Numbers and percentages do not add up due to missing values.

[b] Information processing speed was assessed with the LDST (higher scores reflect better performance), executive functioning with the SCWT interference score (lower scores reflect better performance), and verbal memory with the delayed recall score of the VLT (higher scores reflect better performance).

Table 2. LIBRA risk groups and change in cognition over time: comparison of middle- and high-risk groups with low-risk group

	BASELINE		RATE OF DECLINE FROM BASELINE TO 6-YEAR FOLLOW-UP		RATE OF DECLINE FROM 6-YEAR TO 12-YEAR FOLLOW-UP		OVERALL LIBRA*TIME	
VARIABLES[a]	DIFFERENCE[b]	95% CI	DIFFERENCE[b]	95% CI	DIFFERENCE[b]	95% CI	X^{2c}	*P*
Information processing speed (n = 1198)								
Middle risk	− 1.17	− 2.38 to 0.05	− 0.71	− 1.79 to 0.38	− 0.36	− 1.56 to 0.84	1.86	0.394
High risk	− 2.03***	− 3.23 to − 0.83	− 1.19*	− 2.21 to − 0.17	− 1.09	− 2.41 to 0.23	8.81	0.012
Executive functioning (n = 1190)								
Middle risk	0.08**	0.02 to 0.13	0.003	− 0.05 to 0.06	− 0.01	− 0.08 to 0.07	0.05	0.973
High risk	0.10**	0.04 to 0.16	0.01	− 0.04 to 0.07	− 0.03	− 0.11 to 0.05	0.62	0.734
Verbal memory (n = 1198)								
Middle risk	− 4.05	− 10.75 to 2.66	− 5.15	− 12.64 to 2.33	9.34*	0.34 to 18.33	4.84	0.089
High risk	− 2.86	− 9.54 to 3.81	− 10.55**	− 18.06 to − 3.04	5.02	− 5.90 to 15.95	7.59	0.023

LIBRA: LIfestyle for BRAin health; CI: confidence interval; df: degrees of freedom.

[a] Information processing speed was assessed with the LDST (higher scores reflect better performance), executive functioning with the SCWT interference score (lower scores reflect better performance) and verbal memory with the delayed recall score of the VLT (higher scores reflect better performance). Analyses were adjusted for sex, age, age^2 and level of education.

[b] Difference in cognitive performance between the group of interest and the reference group (low risk).

[c] X^2 test with 2 degrees of freedom.

*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

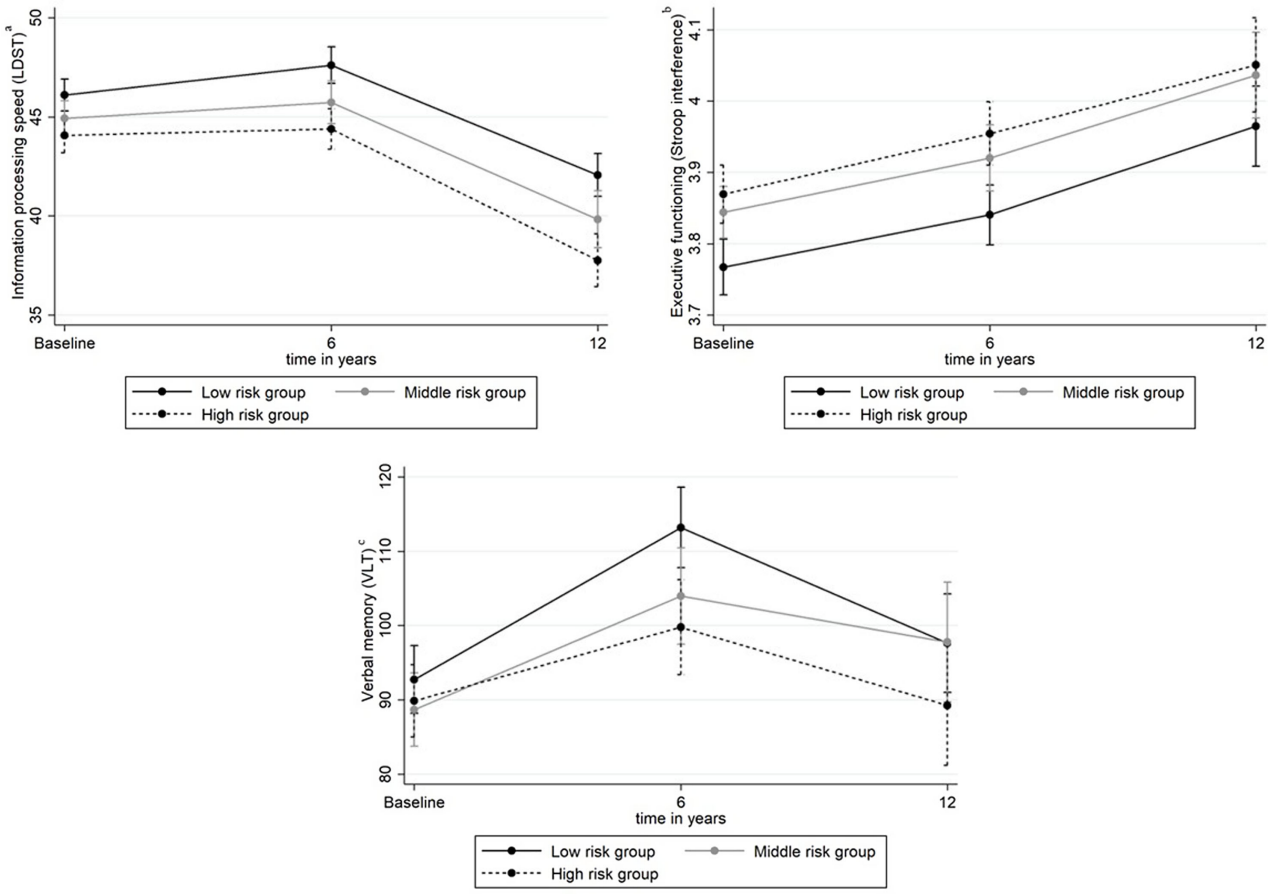

Figure 1. Estimated marginal means with 95% CIs of cognitive trajectories over time for the LIBRA risk groups. [a]Information processing speed, assessed with the LDST (higher scores reflect better performance); [b]Executive functioning, assessed with the SCWT interference score (log-transformed; lower scores reflect better performance); [c]Verbal memory, assessed with the delayed recall score of the VLT (squared; higher scores reflect better performance). Adjusted for sex, age, age^2 and level of education. LIBRA: LIfestyle for BRAin health index.

$p = 0.502$), and thus there was no overall association found ($X^2 = 4.72$, df = 2, $p = 0.094$).

Table 2 presents the results of the comparison of the middle- and high-risk groups with the low-risk group, based on LIBRA tertiles. Faster decline in information processing speed was observed in the high-risk group compared to the low-risk group, which was more pronounced in the 6-year follow-up. There was an increase (not tabulated) in verbal memory score from baseline to 6-year follow-up. This improvement in performance was lower in the high-risk group than in the low-risk group. No effect was observed from 6-year to 12-year follow-up. No differences over time were observed in executive functioning and there were no differences in cognition scores over time between the middle- and high-risk groups. The trajectories over time (baseline until 12-year follow-up) of the cognitive tests for the three LIBRA risk groups are displayed in Figure 1.

SES and cognitive decline

Table 3 presents the results of the comparison between the three SES groups, based on SES tertiles. Participants in the middle- and high-SES groups had less decline in information processing speed and verbal memory from baseline to 6-year follow-up (except middle SES vs. low SES for verbal memory) compared to participants in the low SES group. There was no difference in decline between the middle and high SES groups for information processing speed (rate of decline from baseline to 6 years 0.40, CI −0.62 to 1.42, $p = 0.439$; and 6 years to 12 years −0.20, CI −1.41 to 1.01, $p = 0.741$), memory (rate of decline from baseline to 6 years 4.38, CI −3.21 to 11.96, $p = 0.257$; 6 years to 12 years 0.62, CI −9.00 to 10.24, $p = 0.900$) and executive functioning (rate of decline baseline to 6 years 0.009, CI −0.05 to 0.06, $p = 0.755$, 6 years to 12 years −0.07, CI −0.14 to 0.003, $p = 0.059$).

https://doi.org/10.1017/S1041610223000819

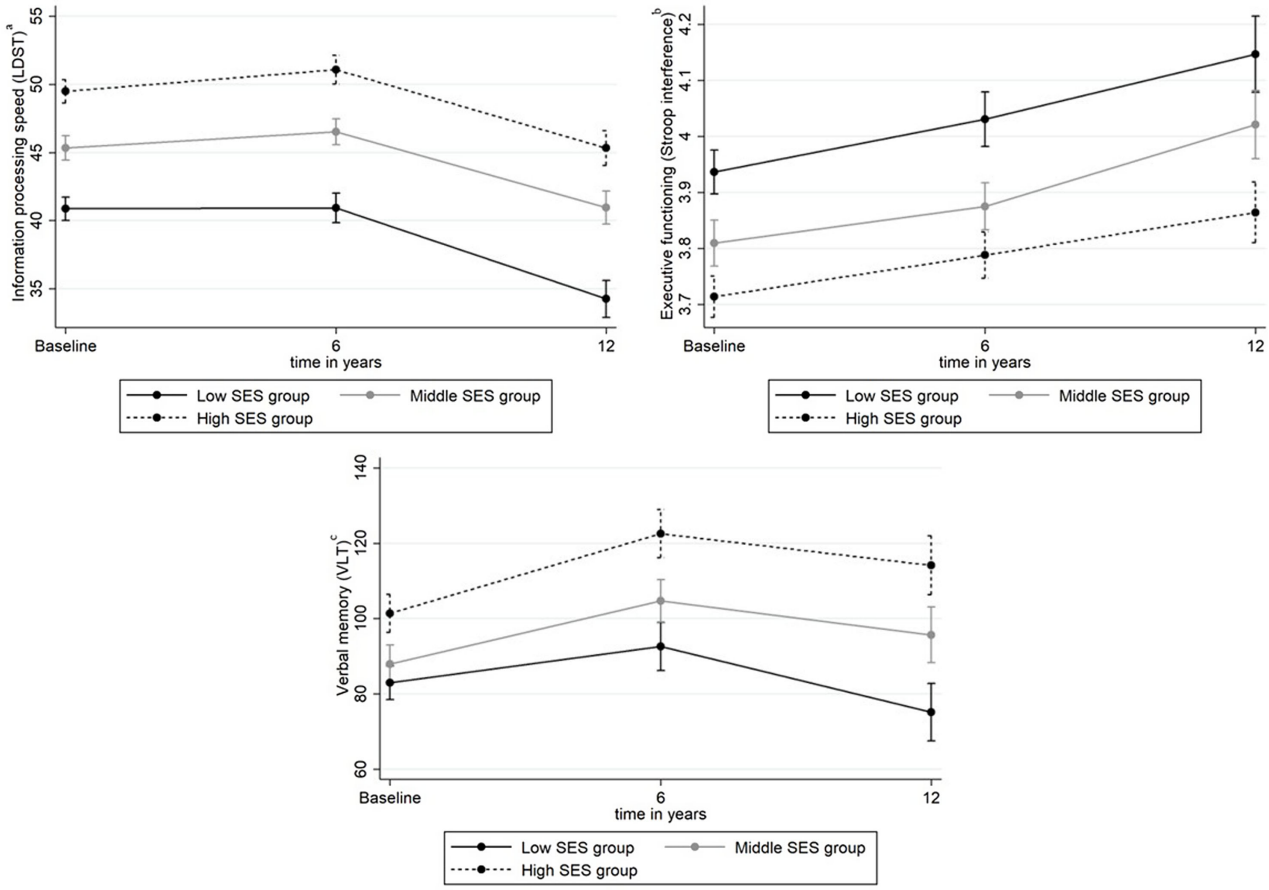

Figure 2. Estimated marginal means with 95% CIs of cognitive trajectories of the SES groups over time. [a]Information processing speed, assessed with the LDST (higher scores reflect better performance); [b]Executive functioning, assessed with the SCWT interference score (log-transformed; lower scores reflect better performance); [c]Verbal memory, assessed with the delayed recall score of the VLT (squared; higher scores reflect better performance). Adjusted for sex, age and age^2. SES: socioeconomic status (assessed using a compound score of equivalent income and/or educational level).

There was also no difference in executive functioning observed over time between the three SES groups. Figure 2 displays the cognitive trajectories of the three SES groups over time.

Differences in socioeconomic status

None of the three-way interaction models showed a modifying effect of SES on the relationship between continuous LIBRA and cognition. When categorizing LIBRA into three risk groups (tertiles), a modifying effect of SES was found in executive functioning. With increasing SES, the middle-risk group needed less time to complete this task compared to the low-risk group from baseline to 6-year follow-up ($B = -0.05$, 95% CI $= -0.10$ to -0.01, $p = 0.013$). This effect was attenuated at 12-year follow-up ($B = 0.002$, 95% CI $= -0.08$ to 0.08, $p = 0.970$) and no effects were found for the high-risk group compared to the low-risk group (baseline to 6 years: $B = 0.01$, 95% CI $= -0.04$ to 0.06, $p = 0.749$; 6 to 12-year follow-up: $B = 0.08$, 95% CI $= -0.01$ to 0.17, $p = 0.074$).

Sensitivity analyses

We performed sensitivity analyses in which the three-way interaction models were performed including education or income separately (in tertiles), instead of the combined SES compound score. Results for the continuous LIBRA score did not change, meaning that none of these models showed a modifying effect of education or income on the relationship between LIBRA and cognition. When categorizing LIBRA into three risk groups (tertiles), the modifying effect of the original SES model in executive functioning no longer appeared ($B = -0.11$, 95% CI $= -0.26$ to 0.03, $p = 0.120$). A modifying effect of income was found in information processing speed, in which participants within the highest income group with the highest (i.e. most unhealthy) risk profile performed worse from

https://doi.org/10.1017/S1041610223000819

Table 3. SES groups and change in cognition over time: comparison of middle- and high-SES groups with low-SES group

	BASELINE		RATE OF DECLINE FROM BASELINE TO 6-YEAR FOLLOW-UP		RATE OF DECLINE FROM 6-YEAR TO 12-YEAR FOLLOW-UP		OVERALL SES*TIME	
VARIABLES[a]	DIFFERENCE[b]	95% CI	DIFFERENCE[b]	95% CI	DIFFERENCE[b]	95% CI	X^{2c}	*P*
Information processing speed (n = 1198)								
Middle SES	4.45***	3.21 to 5.70	1.12*	0.03 to 2.21	1.13	− 0.19 to 2.44	7.08	0.029
High SES	8.61***	7.38 to 9.84	1.52**	0.41 to 2.64	0.92	− 0.41 to 2.26	9.49	0.009
Executive functioning (n = 1190)								
Middle SES	− 0.13	− 0.18 to − 0.07	− 0.03	− 0.09 to 0.03	0.03	− 0.05 to 0.11	1.18	0.554
High SES	− 0.22	− 0.28 to − 0.17	− 0.02	− 0.07 to 0.03	− 0.04	− 0.11 to 0.03	2.11	0.349
Verbal memory (n = 1198)								
Middle SES	4.97	− 1.94 to 11.87	7.17	− 0.29 to 14.63	8.38	− 2.03 to 18.79	9.28	0.001
High SES	18.41***	11.58 to 25.23	11.55**	3.63 to 19.47	9.00	− 1.59 to 19.60	16.68	<0.001

SES: Socioeconomic status; CI: confidence interval; df: degrees of freedom.

[a] Information processing speed was assessed with the LDST (higher scores reflect better performance), executive functioning with the SCWT interference score (lower scores reflect better performance) and verbal memory with the delayed recall score of the VLT (higher scores reflect better performance). Analyses were adjusted for sex, age, and age^2.

[b] Difference in cognitive performance between the group of interest and the reference group (low risk).

[c] X^2 test with 2 degrees of freedom.

*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

baseline to 6-year follow-up compared to participants within the lowest income group ($B = -2.87$, 95% CI = −5.69 to −0.05, $p = 0.046$).

Discussion

This study prospectively examined the association between the modifiable dementia risk score LIBRA and cognitive decline across different SES strata over 12 years in a cognitively healthy population aged 40 years and above. Results show that higher LIBRA scores (both on a continuous scale and divided into risk groups), reflecting a less brain-healthy lifestyle, predicted more decline in information processing speed and verbal memory function. Participants in the lowest SES group displayed more decline in information processing speed and verbal memory function compared to the higher SES groups. However, no consistent effect modification was found, meaning that the association between LIBRA and rate of cognitive decline over 12 years was similar across SES groups.

Higher modifiable dementia risk and lower SES were both associated with faster decline in cognitive performance, which is in line with previous work (Deckers *et al.*, 2018; Deckers *et al.*, 2020; Deckers *et al.*, 2019; Deckers *et al.*, 2021; Röhr *et al.*, 2022b; Schiepers *et al.*, 2018; Vos *et al.*, 2017). The finding that the improved performance in verbal memory score from baseline to 6-year follow-up was lower in the high-risk group than in the low-risk group indicated that the former benefitted less from the practice effect that is commonly observed in repeated assessment of verbal memory (Gavett *et al.*, 2016). Possible pathophysiological mechanisms by which the different LIBRA factors affect cognition are neurodegenerative processes (O'Brien and Markus, 2014), cerebrovascular pathology (Wolters *et al.*, 2017), atherosclerotic burden (Qiu *et al.*, 2005), metabolic and inflammatory processes (Deckers *et al.*, 2015) and enhanced brain maintenance, leading to delayed cognitive decline (Stern, 2012).

No consistent effect modification of SES was found, which is in line with previous work investigating LIBRA and cognitive performance in different educational strata (Deckers *et al.*, 2018). It should be noted that analyses were conducted at the level of the LIBRA total score, which takes all 11 LIBRA factors into account, and that differences in SES for individual risk or protective factors (e.g., hypertension, physical inactivity) were not assessed and could have been present (Deckers *et al.*, 2018). Yet, the used methods served our purpose since LIBRA aims to identify the room for improvement based on the total modifiable risk spectrum. These findings suggest that modifiable lifestyle and health factors are similarly associated with cognitive decline across SES strata. This finding seems to make a case for universal dementia risk reduction across all SES levels. However, our study also shows that participants with lower SES have a poorer health and lifestyle status and faster decline in cognitive performance. In addition, a recent study (Röhr *et al.*, 2022b) may suggest that the association between lifestyle factors and cognitive performance is less apparent in individuals with high SES, although – similar to our study – the interaction analysis was not significant. Thus, the potentially modifiable risk fraction (i.e., the room for improvement) is higher in people with low SES. Consequently, health inequalities will increase further if these high-risk groups – which are often also hard to reach (Lafortune *et al.*, 2016; Luten *et al.*, 2018; Steyaert *et al.*, 2020) – are missed in the development and out-roll of future interventions.

Strengths of this study include the prospective design, which allowed us to assess exposure to LIBRA factors years prior to our cognitive outcome measures and to analyze serial assessment of cognitive functioning with a comprehensive neuropsychological test battery, and the large sample size. Further, this study is strengthened by using a modifiable dementia risk score that is developed based on an extensive systematic literature review and Delphi consensus study (Deckers *et al.*, 2015). Last, we used a resource-based SES operationalization (OECD, 2011) not only based on educational level, which is also a proxy for cognitive reserve (George *et al.*, 2020), but also on an economic (income) measure that accounts for household size. This study, however, also has some limitations that need to be addressed. First, dropout of the study at 6- and 12-year follow-ups could have led to selection bias. This is an unfortunate but common phenomenon in aging studies. Still, the response rate was quite high for a prospective study (Wang *et al.*, 2020) (71.7% from baseline to 6-year follow-up, and 81.4% from 6- to 12 years) and the use of linear mixed models allowed us to use maximum likelihood estimations of missing outcome data to minimize selection bias. Furthermore, although the use of an SES compound score of education and equivalent income should foremost be seen as a strength of this study, it should be noted that there was no data on equivalent income in 41.8% ($n = 511$) of the participants, which resulted in an SES score based on only educational level in this group. Further, the use of self-reported measures to calculate most of the LIBRA factors and net month income could have led to recall bias or socially desirable responses and could have affected the predictive accuracy. Still, most LIBRA factors were operationalized based on a combination of self-report and a clinical measure (e.g., hypertension),

https://doi.org/10.1017/S1041610223000819

diagnosis and/or registered medication use (e.g., diabetes, heart disease). Last, although LIBRA assumes all individual factors to have an added predictive value, the underlying mechanisms by which the individual LIBRA factors affect cognition could interact and this was not considered in the design of the LIBRA score.

Conclusion

A higher modifiable risk score and SES predicted cognitive decline over 12 years. Although modifiable factors were equally associated with cognitive decline across SES strata, the modifiable risk fraction is higher in people with low SES. It is thus important to tailor interventions toward the needs, wishes and barriers of subgroups, defined by SES and/or risk status. It appears that considerable prevention gain can be expected by engaging people with low SES in preventive measures, as they more often have higher LIBRA scores.

Conflict of interest

None.

Description of authors' roles

IH: study concept and design, analysis and interpretation of the data and preparation of the manuscript; MvB: study concept and design, analysis and interpretation of the data, acquisition of subjects and data, critical revision of the manuscript and study supervision; KD: study concept and design and critical revision of the manuscript; HB: study concept and design and critical revision of the manuscript; FV: study concept and design, critical revision of the manuscript and study supervision; SK: study concept and design, analysis and interpretation of the data, acquisition of subjects and data, critical revision of the manuscript and study supervision.

Acknowledgments

The authors are grateful to Ms Mina Stanikić for conducting preliminary work for the purpose of this study. This work was supported by NESTOR (Nederlands Stimuleringsprogramma Ouderenonderzoek, 1995) of the Dutch Ministry of Education & Science and Welfare, Health and Cultural Affairs.

Supplementary material

To view supplementary material for this article, please visit https://doi.org/10.1017/S1041610223000819

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