



Impact of lifestyle factors on quantitative motor and cognitive performance: insights from a longitudinal study on healthy ageing

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Abstract The process of ageing is extremely variable in progression and phenotypic features including significant variations in disease milestones, such as cognitive impairment, frailty, or recurrent falls. Our aim was to analyze the influence of lifestyle factors on motor and cognitive performance in a longitudinal ageing study in older people on healthy ageing. We conducted a longitudinal analysis in a cohort of 744 older participants (mean 70 years) over an 8-year period. Cognitive performance was assessed using the *Consortium to Establish a Registry for Alzheimer's*

Disease (CERADplus) test battery, including the *Trail Making Test* (TMT) for executive function. Gait performance was evaluated by measuring gait velocity. Dual-task performance was assessed by measuring gait velocity while checking boxes. *Body Mass Index* (BMI) was also recorded. Symptoms of depression were examined using *Beck's Depression Inventory* (BDI-II). We observed higher cognitive functions in individuals adhering to a high-frequency physical activity regimen and a resilient plant-based diet. Additionally, these individuals exhibited lower BDI-II scores and experienced mitigated cognitive decline. Participants who combined high physical activity, a high intake of plant-based foods, and extensive education—referred to as having a high “successful ageing index”—maintained nearly constant CERADplus total scores over the 8-year period. Protective lifestyle factors are linked to better cognitive and motor performance and a slower decline in cognitive function, indicating healthy ageing. Since the factors diet and exercise are modifiable, adopting them may enhance cognitive performance and autonomy in older adults.

Key summary points Aim

Our aim was to analyze the influence of lifestyle factors on motor and cognitive performance in a longitudinal ageing study in older people on healthy ageing.

Findings

We observed higher cognitive functions in individuals adhering to a high-frequency physical activity regimen and a resilient plant-based diet.

Message

Since those factors diet and exercise are modifiable, adopting them may enhance cognitive performance and autonomy in older adults.

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Keywords Healthy lifestyle · Protective score · Longitudinal ageing study · Nutrition

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Purpose

The process of ageing varies significantly in phenotype, encompassing variations not only in the expression of age-related ailments such as osteoporosis, coronary heart disease, hypertension, oncological diseases, and diabetes mellitus, but also variances in the progression and temporal patterns leading to disease milestones, such as major cognitive impairment, frailty, or recurrent falls [1, 2]. In accordance with the definition provided by the World Health Organization (WHO), healthy ageing is delineated as “the process of developing and maintaining the functional ability that enables wellbeing in older age” [3]. This encompasses among others the fulfillment of fundamental needs, mobility, continued learning, fostering relationships, and active contribution to society. Beyond the notion of “healthy ageing,” alternative terms and concepts have been introduced, including “resilient,” “productive,” or “successful ageing” [4]. Successful ageing is regarded a more comprehensive concept, encompassing not only physical well-being but also psychosocial aspects [5].

As outcome parameters for quantifying and qualifying healthy ageing, various metrics have been proposed in the literature, including the “healthy ageing score” and the “modified healthy ageing index” [6]. These encompass information related to diseases and incorporate both subjective accounts and objective measurements such as systolic blood pressure, fasting glucose, cystatin C levels, or respiratory vital capacity. The majority of studies have examined the influence of singular lifestyle factors mostly cross-sectionally, including physical activity, adherence to

the Mediterranean diet or caffeine intake, on singular outcome parameters such as the incidence of dementia or other age-related diseases, frailty, frequency of falls, or mortality [7]. Conversely, prospective cohort studies such as the Canadian Longitudinal Study on Ageing [1], the Baltimore Longitudinal Study of Ageing [2], the Basel Longitudinal Study on Ageing [8], and the DZNE Rhineland study [9] integrate comprehensive measures of biological, phenotypical, and functional ageing.

Our objective was to investigate (A) the lifestyle factors that significantly influence healthy ageing, as indicated by a comprehensive selection of longitudinal quantitative measures of motor and cognitive performance assessed in our large prospective cohort study over more than 8 years, and (B) whether the cumulative impact of lifestyle profiles incorporating the most relevant protective factors amplifies their influence on the ageing process.

Methods

Participants and assessments

TREND cohort

The participants were recruited as part of the TREND study (Tuebingen evaluation of Risk factors for Early detection of NeuroDegeneration). The study was initiated in 2009 with biennial assessments of older participants aged between 50 and 80 years with and without prodromal markers for Parkinson’s disease or Alzheimer’s disease but without clinical diagnosis of a neurodegenerative disease. For more details about the TREND study, please visit <https://www.trend-studie.de/> [10]. For longitudinal analysis, we selected three time points: at baseline (T0), after 4 years (T04), and after 8 years (T08).

Lifestyle factors

Information on the following lifestyle factors was assessed based on questionnaires: years of education, nutritional characteristics (consumption of meat, vegetables/fruits/beans/peas/lentils/berries (referred to as “plant-based foods”), bread/noodles/rice (referred to as “cereals”), milk/yogurt/cheese (referred to as “dairy products”), coffee) as well as consumption of

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alcoholic drinks and smoking. The nutritional characteristics and the “alcohol” item were categorized as follows: (A) < 1 meal/cup per week; (B) 1–6 meals/cups per week; (C) ≥ 1 meal/cup per day. Smoking status was evaluated by inquiring about pack-years, calculated as the product of the number of years of smoking and the average number of cigarette packs consumed per day. Concerning the variables “meat,” “alcohol,” “coffee,” and “smoking,” we additionally employed dichotomous categories, denoted as 0 for non-consumption and 1 for consumption. For “years of education,” we also defined tertiles. Furthermore, we assessed the physical activity level (referred to as “PA”) via questionnaires applying following categories: (A) no sports or strenuous physical activity; (B) < 1 h of sports or strenuous physical activity per week; (C) ≥ 1 –2 h of sports or strenuous physical activity per week. In the context of longitudinal analysis, classification relied upon assessments conducted at T08 for all items, with the exception of the “alcohol” item, for which assessments at T06 (6 years after baseline) were employed, due to higher data availability. A total of 744 participants possessed a comprehensive dataset encompassing the aforementioned items, rendering them eligible for inclusion in the subsequent analyses.

Furthermore, we calculated a “successful ageing index I” that encompasses the following items: “plant-based foods,” “physical activity,” and “years of education.” Specifically, individuals were categorized into two groups: those with an index of 1, representing participants with a rating of C for “plant-based foods,” a score of C for “PA” and belonging to the highest tertile of “years of education” in contrast to individuals in the 0 group, which includes all other participants. Additionally, we developed a “successful ageing index II,” which included the same criteria as index I, with the added requirement of having no pack-years of smoking.

Clinical assessments

Cognitive performance was assessed using the neuropsychological CERADplus (= Consortium to Establish a Registry for Alzheimer’s Disease) test battery [11, 12]: cognitive testing with higher values indicating better cognitive function; TMT (= Trail Making Test) B-A (in seconds) [13], which is part of the CERADplus: the time needed to complete TMT

B minus the time needed to complete TMT A with lower values indicating a better executive function; BDI-II (= Beck’s Depression Inventory (BDI) II) [14]: scale for assessing symptoms of depression with higher values indicating a higher severity of depression; gait velocity (in metres per second): distances of 20 or 17 m respectively as available divided by the time needed to walk this distance at the highest possible speed; dual-task (in metres per second): gait speed while completing an additional cognitive task (checking boxes on a paper) [15]; BMI (Body Mass Index; in kg/m^2): weight in kilograms divided by the square of height in metres.

The outcome parameters, namely CERADplus total score, TMT B-A, BDI-II, gait velocity, dual-task, and BMI, exhibited non-normal distributions. At T08, five outliers were identified, displaying extreme values in TMT B-A (in seconds) (242; 234; 222; 214; 210), with a mean age at examination of 77 years. Additionally, seven participants exhibited extreme values in BDI-II (39; 34; 31; 29; 28; 28; 27) at time-point T08, with a mean age of 65.1 years. Notably, no extreme values were observed for gait velocity and dual-task. While there were no extreme outliers for CERADplus total score values at T08, one participant with an age at examination of 78 years and a score of 50 was identified as an outlier at T04. There were three extreme values for BMI at T08 (45.3; 42.6; 41.3) with a mean age of 65 years. The plausibility of those outliers was evaluated, and they were retained in the analyses.

Statistics

Statistical analysis was performed using IBM-SPSS Statistics (IBM Corp. Released 2021. IBM SPSS Statistics for Macintosh, Version 28.0. Armonk, NY: IBM Corp.). For demographic data and cross-sectional analyses at time-point T08, we employed analysis of covariance (ANCOVA), incorporating the covariates of “sex,” “age at examination at T08,” and “years of education.” Individuals falling into the highest category of a specific variable (C) were compared with those in the remaining categories (A/B). For the items “meat,” “coffee,” “alcohol,” and “smoking,” a binary categorization of consumption (no = 0/yes = 1) was additionally implemented. Cohen’s *d* was used to calculate the effect size.

To compare the prevalence of individuals within each category of the lifestyle factors between male and female participants, we employed the chi-square test.

Also, we performed correlation analyses (Pearson's correlation). Furthermore, we analyzed Eta values to investigate the influence of sex on clinical outcome parameters and lifestyle factors.

For longitudinal analyses spanning the time-points T0, T04, and T08, we employed ANCOVA with repeated measurements, incorporating the same covariates as utilized in the cross-sectional analyses. In case of significant values for Mauchly's sphericity test, the Greenhouse–Geisser correction was applied for more accurate adjustment. The Shapiro–Wilk test was utilized to assess the normal distribution of the data.

As an additional longitudinal analysis, we conducted a linear mixed model to examine the effects of the following items on test scores, accounting for variability across participants and repeated measures over time. The model included fixed effects for sex, age, years of education, smoking (yes/no), physical activity (category C versus all other participants), the successful ageing index I, and the successful ageing index II (considering smoking), with random intercepts for participants and repeated measures for those participants at the three time points T0, T04, and T08.

To account for multiple testing, we applied a manual Bonferroni correction, setting the threshold for statistical significance at ≤ 0.005 for cross-sectional analysis. This adjustment was deemed necessary due to the consideration of 10 lifestyle factors in the cross-sectional analyses.

For ANCOVA with repeated measurements, a Bonferroni-corrected threshold of ≤ 0.016 was utilized, considering the examination of three specific lifestyle factors (years of education, plant-based foods, PA).

For linear mixed models, a Bonferroni-corrected threshold of ≤ 0.007 was utilized, considering the examination of seven specific lifestyle factors.

Ethics

The study was approved by the Ethics Committee of the Faculty of Medicine at the University of Tuebingen (No. 90/2019BO2), and all participants gave

written informed consent. All procedures adhered to the principles outlined in the Declaration of Helsinki.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Results

Cross-sectional analyses

1. Demographic analysis: higher intake of plant-based foods among female participants

A total of 401 out of 744 participants (53.9%) were male. The mean age at T08 was 69.9 years. Female participants had a higher age at examination, fewer years of education, higher CERADplus total scores, and lower gait velocity. For further cross-sectional and demographic data, we refer to Table 1.

Female participants exhibited a higher intake of plant-based foods and coffee, along with lower consumption of meat and alcohol in comparison to male participants. Additionally, there was a lower prevalence of smoking among female participants.

No significant differences were observed in terms of physical activity, cereal consumption, and dairy product intake (Table 2). Male participants exhibited a higher cumulative exposure in pack-years compared to females ($7.7 (\pm 13.0)$ vs. $4.4 (\pm 9.2)$, $p \leq 0.001$). No statistically significant differences were observed with respect to the successful ageing index I (overall—0, 80.2%; 1, 19.8%; male—0, 80.5%; 1, 19.5%; female—0, 79.9%; 1, 20.1%, $p = 0.820$) or II.

2. Correlation of lifestyle factors with clinical outcome parameters: positive effects on cognition through physical activity, education and higher intake of plant-based foods

An advanced age at examination was associated with a reduced CERADplus total score (correlation coefficient (c), -0.417 , $p \leq 0.001$), a higher TMT B-A score (c , 0.305 , $p \leq 0.001$), lower gait velocity

Table 1 Cross-sectional and demographic data: a comparison between female and male participants in the TREND study at follow-up T08 (8 years post-baseline). Analysis of covariance (ANCOVA) was performed, with “years of education” and “age at examination” as covariates, where applicable. Significant *p*-values (≤ 0.05) are indicated in bold. CERADplus (= Consortium to Establish a Registry for Alzheimer’s Disease); TRAIL B-A (in seconds): the time needed to complete Trail

Making Test B minus the time needed to complete Trail Making Test A; BDI-II (= Beck’s Depression Inventory-II); gait velocity (in m/s): distance of 20 m or respective 17 m divided by the time needed to walk this distance at the highest possible speed; dual-task (in m/s): gait velocity while completing an additional cognitive task (checking boxes on a paper); BMI (in kg/m²): body mass index

	OVERALL (<i>N</i> = 744)	MALE (<i>N</i> = 401)	FEMALE (<i>N</i> = 343)	<i>p</i> -value
Age at examination	69.9 ($\pm$ 6.2)	69.0 ($\pm$ 6.2)	70.7 ($\pm$ 6.0)	$\leq$ 0.001
Years of education	14.5 ($\pm$ 2.7)	15.2 ($\pm$ 2.5)	13.7 ($\pm$ 2.6)	$\leq$ 0.001
CERADplus	84.6 ($\pm$ 8.2)	83.6 ($\pm$ 8.0)	85.8 ($\pm$ 8.3)	$\leq$ 0.001
TMT B-A	53.4 ($\pm$ 42.0)	52.8 ($\pm$ 42.2)	54.1 ($\pm$ 41.9)	0.989
BDI-II	5.3 ($\pm$ 5.7)	4.7 ($\pm$ 5.4)	6.1 ($\pm$ 5.9)	$\leq$ 0.001
Gait velocity	1.54 ($\pm$ 0.25)	1.57 ($\pm$ 0.27)	1.50 ($\pm$ 0.22)	$\leq$ 0.001
Dual-task	1.33 ($\pm$ 0.24)	1.35 ($\pm$ 0.25)	1.31 ($\pm$ 0.22)	$\leq$ 0.001
BMI	25.9 ($\pm$ 4.2)	26.2 ($\pm$ 3.8)	25.5 ($\pm$ 4.7)	$\leq$ 0.001

(*c*, -0.381 , $p \leq 0.001$) and lower dual-task performance (*c*, 0.389 , $p \leq 0.001$).

A higher frequency of physical training per week was associated with a higher CERADplus total score (*c*, 0.149 ; $p \leq 0.001$), higher gait velocity (*c*, 0.158 , $p \leq 0.001$), a lower TMT B-A score (*c*, -0.153 , $p \leq 0.001$), a lower BDI-II score (*c*, -0.218 , $p \leq 0.001$), and a lower BMI (*c*, -0.175 , $p \leq 0.001$). Similar directions of associations were observed with years of education (CERADplus: *c*, 0.235 , $p \leq 0.001$; TMT B-A: *c*, -0.199 , $p \leq 0.001$; gait velocity: *c*, 0.120 , $p = 0.002$; BMI: *c*, -0.152 , $p \leq 0.001$) and plant-based foods (CERADplus: *c*, 0.181 , $p \leq 0.001$; TMT B-A: *c*, -0.117 , $p \leq 0.001$; BMI: *c*, -0.109 , $p = 0.003$).

Certain correlations were statistically significant exclusively in either male or female participants. Specifically, in male participants, there was a significant positive correlation between age and BDI-II scores (*c* 0.203 , $p \leq 0.001$), an inverse correlation between physical activity and BDI-II scores (*c* -0.299 , $p \leq 0.001$), and a positive correlation between physical activity and dual-task performance (*c* 0.191 , $p \leq 0.001$).

Conversely, solely in female participants, a positive correlation between physical activity and CERADplus total scores (*c* 0.196 , $p \leq 0.001$) and an inverse correlation between physical activity and BMI (*c* -0.248 , $p \leq 0.001$) were found. Additionally, exclusive to female participants, there were significant positive correlations between years of

education and gait velocity (*c* 0.206 , $p \leq 0.001$), plant-based food intake and CERADplus total scores (*c* 0.214 , $p \leq 0.001$), and meat consumption and BMI (*c* 0.212 , $p \leq 0.001$). An inverse correlation between dairy product intake and BMI (*c* -0.166 , $p = 0.002$) was also observed solely in female participants.

Additionally, we calculated Eta values to analyze the influence of sex on various clinical outcome parameters: CERADplus total score (Eta = 0.135), TRAIL B-A (Eta = 0.015), BDI-II (Eta = 0.121), gait velocity (Eta = 0.154), dual-task performance (Eta = 0.089), and BMI (Eta = 0.081).

For further associations and sex stratification, please see Supplemental Table 1.

3. Interconnections among lifestyle factors: positive correlation among lifestyle factors

The frequency of physical activity exhibited a positive correlation with the intake of plant-based foods (*c* 0.147 , $p \leq 0.001$) and an inverse correlation with the number of pack-years (*c* -0.145 , $p \leq 0.001$). Age was inversely correlated with coffee consumption (*c* -0.110 , $p = 0.003$). Years of education were positively correlated with consumption of cereals (*c* 0.141 , $p \leq 0.001$) and alcohol consumption (*c* 0.168 , $p \leq 0.001$).

A stratified analysis by sex revealed distinct correlations between dietary and lifestyle factors in male

Table 2 Comparison of the prevalence of individuals within each category of the lifestyle factors between male and female participants at follow-up after 8 years (T08) employing chi-square test ($N=744$). Following categorization was applied: nutritional characteristics, coffee, and alcohol consumption were categorized as A (< 1 meal/cup per week), B (1–6 meals/cups per week), and C (≥ 1 meal/cup per day); physical activity was categorized as A (no physical activity), B (< 1 h of physical activity per week), and C (≥ 1 –2 h of physical activity per week). Additionally, dichotomous variables were considered for meat, coffee, alcohol, and smoking, with 0 indicating no consumption and 1 indicating consumption. Regarding the successful ageing index I, individuals were grouped into two

categories: those with a score of 1, denoting participants with a rating of C for “plant-based foods,” a score of C for “physical activity,” and belonging to the highest tertile of “years of education.” This was in contrast to individuals in the 0 group, which included all other participants. The successful ageing index II included the same criteria as index I, with the added requirement of having no pack-years of smoking. Analysis of covariance, with “years of education” and “age at examination” as covariates was employed to compare pack-years between male and female participants. Significant p -values ≤ 0.005 (Bonferroni-corrected p -value) are indicated in bold letters

	OVERALL	MALE	FEMALE	p -value
Plant-based foods	A: 9/744 (1.2%) B: 249/744 (33.5%) C: 486/744 (65.3%)	A: 5/401 (1.2%) B: 175/401 (43.6%) C: 221/401 (55.1%)	A: 9/343 (2.6%) B: 74/343 (21.6%) C: 265/343 (77.3%)	≤ 0.001
Meat	A: 92/744 (12.4%) B: 505/744 (67.9%) C: 147/744 (19.8%)	A: 29/401 (7.2%) B: 259/401 (64.6%) C: 113/401 (28.2%)	A: 63/343 (18.4%) B: 246/343 (71.7%) C: 34/343 (9.9%)	≤ 0.001
Meat (dichotomous)	0: 92/744 (12.4%) 1: 652/744 (87.6%)	0: 29/401 (7.2%) 1: 372/401 (92.8%)	0: 63/343 (18.4%) 1: 280/343 (81.6%)	≤ 0.001
Cereals	A: 7/744 (0.01%) B: 181/744 (24.3%) C: 556/744 (74.7%)	A: 3/401 (0.01%) B: 94/401 (23.4%) C: 304/401 (75.8%)	A: 4/343 (0.01%) B: 87/343 (25.4%) C: 252/343 (73.5%)	0.684
Dairy products	A: 22/744 (3.0%) B: 495/744 (66.5%) C: 408/744 (54.8%)	A: 12/401 (3.0%) B: 181/401 (45.1%) C: 208/401 (51.9%)	A: 10/343 (2.9%) B: 133/343 (38.8%) C: 200/343 (58.3%)	0.205
Coffee	A: 92/744 (12.4%) B: 90/744 (12.1%) C: 562/744 (75.5%)	A: 46/401 (11.5%) B: 67/401 (16.7%) C: 288/401 (71.8%)	A: 46/343 (13.4%) B: 23/343 (6.7%) C: 274/343 (79.9%)	≤ 0.001
Coffee (dichotomous)	0: 92/744 (12.4%) 1: 652/744 (87.6%)	0: 46/401 (11.5%) 1: 355/401 (88.5%)	0: 46/343 (13.4%) 1: 297/343 (86.6%)	0.423
Physical activity	A: 87/744 (11.7%) B: 60/744 (8.1%) C: 597/744 (80.2%)	A: 57/401 (14.2%) B: 31/401 (7.7%) C: 313/401 (78.1%)	A: 30/343 (8.7%) B: 29/343 (8.5%) C: 284/343 (82.8%)	0.068
Successful ageing index I	0: 597/744 (80.2%) 1: 147/744 (19.8%)	0: 323/401 (80.5%) 1: 78/401 (19.5%)	0: 274/343 (79.9%) 1: 69/343 (20.1%)	0.820
Successful ageing index II	0: 657/744 (88.3%) 1: 87/744 (11.7%)	0: 353/401 (88.0%) 1: 48/401 (12.0%)	0: 304/343 (88.6%) 1: 39/343 (11.4%)	0.820
Alcohol	A: 47/744 (6.3%) B: 114/744 (15.3%) C: 583/744 (78.4%)	A: 17/401 (4.2%) B: 49/401 (12.2%) C: 335/401 (83.5%)	A: 30/343 (8.7%) B: 65/343 (19.0%) C: 248/343 (72.3%)	≤ 0.001
Alcohol (dichotomous)	0: 47/744 (6.3%) 1: 697/744 (93.7%)	0: 17/401 (4.2%) 1: 384/401 (95.8%)	0: 30/343 (8.7%) 1: 313/343 (91.3%)	0.012
Pack-years	6.2 (± 11.5)	7.7 (± 13.0)	4.4 (± 9.2)	≤ 0.001
Smoking (dichotomous)	0: 358/744 (48.1%) 1: 386/744 (51.9%)	0: 168/401 (41.9%) 1: 233/401 (58.1%)	0: 190/343 (55.4%) 1: 153/343 (44.6%)	≤ 0.001

and female participants. In male participants, significant positive correlations were observed between physical activity and intake of plant-based foods ($c 0.187$, $p \leq 0.001$), intake of plant-based foods and

dairy products ($c 0.218$, $p \leq 0.001$), meat and cereal intake ($c 0.199$, $p \leq 0.001$), and meat intake and pack-years ($c 0.150$, $p = 0.003$). None of these associations were significant among female participants.

Conversely, in female participants, significant positive correlations were found between years of education and intake of plant-based foods (c 0.161, $p = 0.003$), years of education and physical activity (c 0.176, $p \leq 0.001$), and meat and alcohol intake (c 0.282, $p \leq 0.001$). Additionally, there was a significant inverse correlation between age and smoking (c - 0.151, $p = 0.005$). These correlations were not significant in male participants.

Additionally, we calculated Eta values to analyze the influence of sex on the lifestyle factors: age (Eta = 0.137), years of education (Eta = 0.282), plant-based foods (Eta = 0.220), meat (Eta = 0.261), cereals (Eta = 0.030), dairy products (Eta = 0.058), coffee (Eta = 0.044), physical activity (Eta = 0.076), alcohol (Eta = 0.118), and pack-years (Eta = 0.143).

For details, please see Supplemental Tables 2 A-C.

4. ANCOVA analysis: better cognitive function in individuals with high physical activity frequency, a high intake of plant-based foods, and a high level of education

Participants with the highest frequency of physical activity presented with a higher CERADplus total score in comparison to all other participants (85.2 ($\pm$ 7.7) vs. 82.2 ($\pm$ 9.4), $p \leq 0.001$, Cohen's $d = 0.4$), a lower TMT B-A score (49.9 ($\pm$ 35.7) vs. 67.7 ($\pm$ 59.5), $p \leq 0.001$, Cohen's $d = 0.4$), a lower BDI-II score (4.7 ($\pm$ 4.8) vs. 7.9 ($\pm$ 7.7), $p \leq 0.001$, Cohen's $d = 0.6$), higher gait velocity (1.56 ($\pm$ 0.24) vs. 1.42 ($\pm$ 0.25), $p \leq 0.001$, Cohen's $d = 0.6$), better dual-task performance (1.35 ($\pm$ 0.24) vs. 1.24 ($\pm$ 0.23), $p \leq 0.001$, Cohen's $d = 0.5$), and a lower BMI (25.5 ($\pm$ 4.0) vs. 27.5 ($\pm$ 4.8), $p \leq 0.001$, Cohen's $d = 0.5$). Participants with the highest educational level also presented with higher scores in the CERADplus total score, higher gait velocity, a lower TMT B-A score, and a lower BMI. Participants with a successful ageing index I of 1 exhibited a higher CERADplus total score (88.3 ($\pm$ 6.2) vs. 83.7 ($\pm$ 8.4), $p \leq 0.001$, Cohen's $d = 0.6$), a lower TMT B-A score (42.8 ($\pm$ 29.7) vs. 56.0 ($\pm$ 44.2), $p \leq 0.001$, Cohen's $d = 0.3$), a higher gait velocity (1.60 ($\pm$ 0.24) vs. 1.52 ($\pm$ 0.25), $p = 0.002$, Cohen's $d = 0.1$), better dual-task performance (1.39 ($\pm$ 0.23) vs. 1.32 ($\pm$ 0.24), $p \leq 0.001$, Cohen's $d = 0.3$), and a lower BMI (24.4 ($\pm$ 3.4) vs. 26.3 ($\pm$ 4.4), $p \leq 0.001$, Cohen's $d = 0.5$) in comparison to all other participants.

Female participants with the highest intake of plant-based foods had significantly higher CERADplus total scores (86.6 ($\pm$ 7.7) vs. 83.1 ($\pm$ 9.5), $p = 0.005$, Cohen's $d = 0.4$). Similarly, female participants with the highest levels of physical activity also showed higher CERADplus total scores (86.4 ($\pm$ 7.6) vs. 82.6 ($\pm$ 10.3), $p \leq 0.001$, Cohen's $d = 0.5$). These associations were not statistically significant in male participants.

In a further analysis, we compared male and female participants with a successful ageing index I of 1. Among those with the highest levels of education, plant-based food intake, and physical activity, male participants had a lower CERADplus total score compared to females (85.8 ($\pm$ 6.4), $N = 46$, vs. 90.2 ($\pm$ 4.7), $N = 54$, $p \leq 0.001$, Cohen's $d = 0.8$), but also a lower BDI-II score (6.4 ($\pm$ 6.2) vs. 10.5 ($\pm$ 7.6), $p = 0.008$, Cohen's $d = 0.6$), higher gait velocity (1.87 ($\pm$ 0.22) vs. 1.70 ($\pm$ 0.22), $p \leq 0.001$, Cohen's $d = 0.8$), and better dual-task performance (1.55 ($\pm$ 0.26) vs. 1.48 ($\pm$ 0.18), $p = 0.025$, Cohen's $d = 0.3$). However, differences in the TMT B-A score (41.9 ($\pm$ 23.1) vs. 44.5 ($\pm$ 30.0), $p = 0.182$) and BMI (25.0 ($\pm$ 3.1) vs. 23.7 ($\pm$ 3.6), $p \leq 0.101$) did not reach statistical significance.

For details, please see Fig. 1, Table 3, and Supplemental Tables 3A and B with stratification for sex.

Longitudinal analyses

1. Attenuated cognitive decline in individuals with high physical activity frequency

Participants with the highest frequency of physical activity (category C) exhibited a slower decline in CERADplus total scores (T0, 86.5 ($\pm$ 6.5); T04, 86.9 ($\pm$ 7.4); T08, 85.5 ($\pm$ 7.6) vs. T0, 84.9 ($\pm$ 6.9); T04, 85.9 ($\pm$ 6.9); T08, 82.6 ($\pm$ 9.6), $F(2.0, 834.4) = 4.4$, $p = 0.013$) in comparison to all other participants (categories A and B).

Those with the highest educational levels showed a slower decline in dual-task performance. Additionally, participants with the highest frequency of plant-based food intake demonstrated a borderline significance regarding slower decline in CERADplus total scores. Notably, female participants with the highest frequency of plant-based food intake experienced a significant reduction in BDI-II scores in comparison

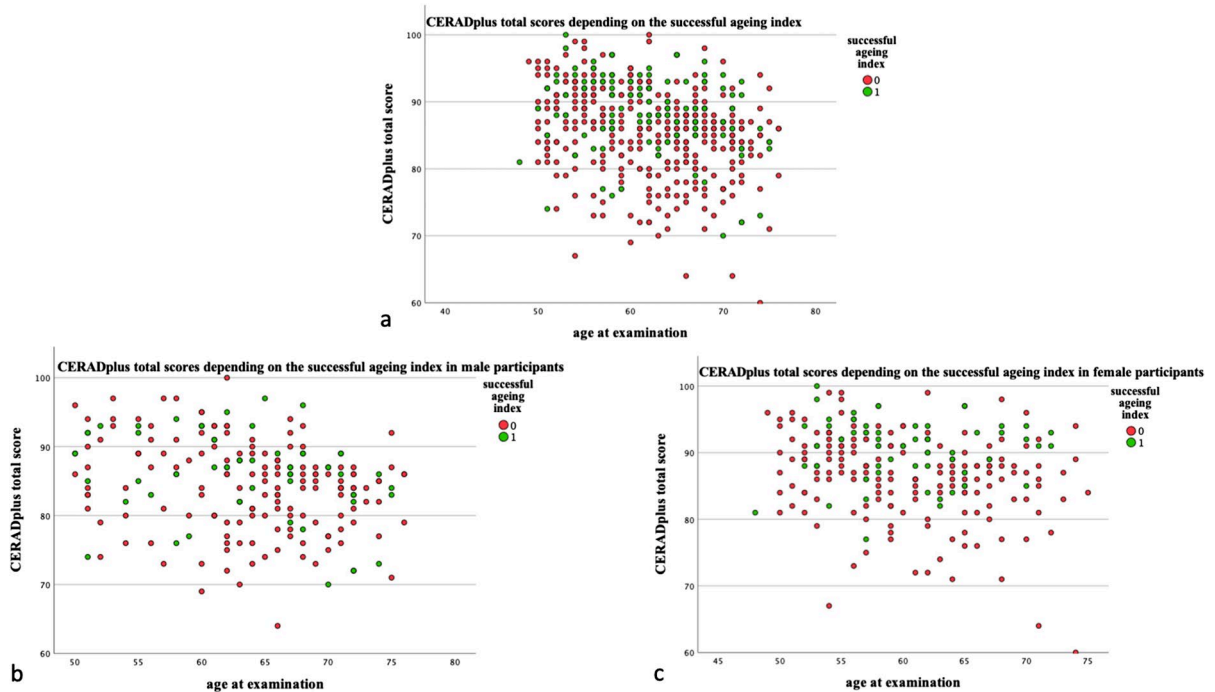


Fig. 1 CERADplus total scores are shown based on the successful ageing index I (0 versus 1) and age at examination, stratified by sex (**a** total cohort; **b** male participants; **c** female participants). The figure illustrates higher CERADplus total

scores among participants with a higher successful ageing index I. CERADplus: Consortium to Establish a Registry for Alzheimer's Disease

to female participants with a lower intake of plant-based food. For further details and sex stratification, please see Supplemental Table 4.

2. Mitigated cognitive decline in individuals exhibiting a synergistic combination of high physical activity frequency, a high intake of plant-based foods, and elevated educational attainment.

Participants with a successful ageing index I of 1 displayed almost consistent CERADplus total score values over the 8-year time interval (T0, 88.2 (± 6.0); T04, 88.8 (± 6.8); T08, 88.1 (± 6.5) vs. T0, 85.6 (± 6.7); T04, 86.0 (± 7.3); T08, 83.9 (± 8.4), $F(2.0, 836.6) = 3.1$, $p = 0.049$ and a slower decline in dual-task performance (T0, 1.51 (± 0.22); T04, 1.51 (± 0.21); T08, 1.35 (± 0.23) vs. T0, 1.52 (± 0.21); T04, 1.45 (± 0.21); T08, 1.31 (± 0.24), $F(1.9, 800.2) = 5.1$, $p = 0.007$) compared to their counterparts with an index of 0. For details, please see Fig. 2 and Supplemental Table 5.

3. Consistent positive effects of physical activity frequency in the linear mixed model

For the variable “CERADplus sum score,” the overall model was statistically significant, $F(1, 1341.1) = 3495.6$, $p \leq 0.001$. A significant effect of sex was observed, $F(1, 707.7) = 33.447$, $p \leq 0.001$, indicating that female participants scored higher on the CERADplus ($M = 86.7$, $SE = 0.7$) compared to male participants ($M = 83.9$, $SE = 0.6$). A significant effect of years of education was also identified, $F(13, 700.3) = 5.776$, $p \leq 0.001$. Participants with 22 years of education achieved higher CERADplus scores ($M = 87.7$, $SE = 5.7$) compared to those with 9 years of education ($M = 77.1$, $SE = 1.5$). Additionally, significant effects were found for age, $F(1, 1398.8) = 113.9$, $p \leq 0.001$, and for physical activity, $F(1, 700.2) = 6.949$, $p = 0.009$. Participants engaging in sports with the highest frequency (category C) demonstrated higher CERADplus scores ($M = 86.0$, $SE = 0.6$) than those with lower levels of sports participation (Categories A and B; $M = 84.6$, $SE = 0.8$).

Table 3 Analysis of the association between lifestyle factors and clinical outcome parameters at T08. This involved categorizing participants based on the criteria outlined in Table 2. Analysis of covariance (ANCOVA), with “sex,” “years of education,” and “age at examination” as covariates comparing participants of category C with all other participants (A, B). Significant *p*-values ≤ 0.005 (Bonferroni-corrected *p*-value) are indicated in bold letters. CERADplus (= Consortium to Estab-

lish a Registry for Alzheimer’s Disease); TRAIL B-A (in seconds): the time needed to complete Trail Making Test B minus the time needed to complete Trail Making Test A; BDI-II (= Beck’s Depression Inventory-II); gait velocity (in m/s): distance of 20 m or respective 17 m divided by the time needed to walk this distance at the highest possible speed; dual-task: gait velocity, while completing an additional cognitive task (checking boxes on a paper); BMI (in kg/m²): body mass index

	CERADplus	TMT B-A	BDI-II	gait velocity	dual-task	BMI
Years of education	A/B: 83.2 ($\pm$ 8.5), <i>N</i> = 494 C: 87.3 ($\pm$ 6.6), <i>N</i> = 248 <i>p</i> $\leq$ 0.001	A/B: 57.9 ($\pm$ 45.7), <i>N</i> = 494 C: 44.4 ($\pm$ 31.9), <i>N</i> = 247 <i>p</i> $\leq$ 0.001	A/B: 5.3 ($\pm$ 5.8), <i>N</i> = 496 C: 5.4 ($\pm$ 5.5), <i>N</i> = 248 <i>p</i> = 0.326	A/B: 1.51 ($\pm$ 0.24), <i>N</i> = 482 C: 1.59 ($\pm$ 0.26), <i>N</i> = 245 <i>p</i> = 0.002	A/B: 1.31 ($\pm$ 0.24), <i>N</i> = 480 C: 1.37 ($\pm$ 0.24), <i>N</i> = 244 <i>p</i> = 0.012	A/B: 26.4 ($\pm$ 4.5), <i>N</i> = 495 C: 24.9 ($\pm$ 3.5), <i>N</i> = 248 <i>p</i> $\leq$ 0.001
Plant-based foods	A/B: 82.8 ($\pm$ 8.5), <i>N</i> = 257 C: 85.5 ($\pm$ 7.8), <i>N</i> = 485 <i>p</i> = 0.008	A/B: 58.1 ($\pm$ 48.1), <i>N</i> = 258 C: 50.9 ($\pm$ 38.3), <i>N</i> = 483 <i>p</i> = 0.124	A/B: 5.7 ($\pm$ 6.1), <i>N</i> = 258 C: 5.1 ($\pm$ 5.5), <i>N</i> = 486 <i>p</i> = 0.033	A/B: 1.53 ($\pm$ 0.26), <i>N</i> = 250 C: 1.54 ($\pm$ 0.24), <i>N</i> = 477 <i>p</i> = 0.444	A/B: 1.31 ($\pm$ 0.24), <i>N</i> = 250 C: 1.34 ($\pm$ 0.24), <i>N</i> = 474 <i>p</i> = 0.132	A/B: 26.6 ($\pm$ 4.5), <i>N</i> = 258 C: 25.5 ($\pm$ 4.0), <i>N</i> = 485 <i>p</i> = 0.015
Meat	A/B: 84.6 ($\pm$ 8.2), <i>N</i> = 595 C: 84.6 ($\pm$ 8.0), <i>N</i> = 147 <i>p</i> = 0.767	A/B: 53.5 ($\pm$ 41.7), <i>N</i> = 594 C: 53.1 ($\pm$ 43.6), <i>N</i> = 147 <i>p</i> = 0.590	A/B: 5.3 ($\pm$ 5.5), <i>N</i> = 597 C: 5.4 ($\pm$ 6.3), <i>N</i> = 147 <i>p</i> = 0.265	A/B: 1.54 ($\pm$ 0.24), <i>N</i> = 583 C: 1.54 ($\pm$ 0.28), <i>N</i> = 144 <i>p</i> = 0.164	A/B: 1.33 ($\pm$ 0.24), <i>N</i> = 580 C: 1.34 ($\pm$ 0.25), <i>N</i> = 144 <i>p</i> = 0.473	A/B: 25.7 ($\pm$ 4.2), <i>N</i> = 596 C: 26.7 ($\pm$ 4.4), <i>N</i> = 147 <i>p</i> = 0.012
Meat (dichotomous)	0: 83.9 ($\pm$ 9.7), <i>N</i> = 92 1: 84.7 ($\pm$ 7.9), <i>N</i> = 650 <i>p</i> = 0.032	0: 62.7 ($\pm$ 49.9), <i>N</i> = 92 1: 52.1 ($\pm$ 40.7), <i>N</i> = 649 <i>p</i> = 0.009	0: 6.9 ($\pm$ 6.5), <i>N</i> = 92 1: 5.1 ($\pm$ 5.5), <i>N</i> = 652 <i>p</i> = 0.018	0: 1.46 ($\pm$ 0.28), <i>N</i> = 90 1: 1.55 ($\pm$ 0.24), <i>N</i> = 637 <i>p</i> = 0.002	0: 1.25 ($\pm$ 0.21), <i>N</i> = 87 1: 1.34 ($\pm$ 0.24), <i>N</i> = 637 <i>p</i> $\leq$ 0.001	0: 24.1 ($\pm$ 3.8), <i>N</i> = 92 1: 26.2 ($\pm$ 4.2), <i>N</i> = 651 <i>p</i> $\leq$ 0.001
Cereals	A/B: 83.2 ($\pm$ 8.2), <i>N</i> = 188 C: 85.1 ($\pm$ 8.1), <i>N</i> = 554 <i>p</i> = 0.037	A/B: 52.7 ($\pm$ 39.6), <i>N</i> = 187 C: 53.7 ($\pm$ 42.9), <i>N</i> = 554 <i>p</i> = 0.236	A/B: 5.3 ($\pm$ 6.2), <i>N</i> = 188 C: 5.3 ($\pm$ 5.5), <i>N</i> = 556 <i>p</i> = 0.869	A/B: 1.51 ($\pm$ 0.23), <i>N</i> = 182 C: 1.55 ($\pm$ 0.25), <i>N</i> = 545 <i>p</i> = 0.206	A/B: 1.31 ($\pm$ 0.23), <i>N</i> = 183 C: 1.34 ($\pm$ 0.24), <i>N</i> = 541 <i>p</i> = 0.368	A/B: 26.9 ($\pm$ 4.4), <i>N</i> = 188 C: 25.6 ($\pm$ 4.1), <i>N</i> = 555 <i>p</i> $\leq$ 0.001
Dairy products	A/B: 84.2 ($\pm$ 8.8), <i>N</i> = 334 C: 84.9 ($\pm$ 7.6), <i>N</i> = 408 <i>p</i> = 0.444	A/B: 53.2 ($\pm$ 42.2), <i>N</i> = 335 C: 53.7 ($\pm$ 42.0), <i>N</i> = 406 <i>p</i> = 0.781	A/B: 5.1 ($\pm$ 5.4), <i>N</i> = 336 C: 5.5 ($\pm$ 5.9), <i>N</i> = 408 <i>p</i> = 0.600	A/B: 1.53 ($\pm$ 0.23), <i>N</i> = 325 C: 1.54 ($\pm$ 0.26), <i>N</i> = 402 <i>p</i> = 0.225	A/B: 1.26 ($\pm$ 0.24), <i>N</i> = 313 C: 1.28 ($\pm$ 0.25), <i>N</i> = 386 <i>p</i> = 0.205	A/B: 26.5 ($\pm$ 4.6), <i>N</i> = 335 C: 25.4 ($\pm$ 3.9), <i>N</i> = 408 <i>p</i> = 0.002
Coffee	A/B: 83.4 ($\pm$ 7.5), <i>N</i> = 181 C: 85.0 ($\pm$ 8.4), <i>N</i> = 561 <i>p</i> = 0.311	A/B: 55.4 ($\pm$ 41.4), <i>N</i> = 182 C: 52.8 ($\pm$ 42.3), <i>N</i> = 559 <i>p</i> = 0.903	A/B: 5.2 ($\pm$ 5.3), <i>N</i> = 182 C: 5.3 ($\pm$ 5.8), <i>N</i> = 562 <i>p</i> = 0.742	A/B: 1.51 ($\pm$ 0.25), <i>N</i> = 177 C: 1.55 ($\pm$ 0.25), <i>N</i> = 550 <i>p</i> = 0.371	A/B: 1.29 ($\pm$ 0.22), <i>N</i> = 176 C: 1.34 ($\pm$ 0.24), <i>N</i> = 548 <i>p</i> = 0.184	A/B: 25.6 ($\pm$ 4.3), <i>N</i> = 181 C: 26.0 ($\pm$ 4.2), <i>N</i> = 562 <i>p</i> = 0.279
Coffee (dichotomous)	0: 83.6 ($\pm$ 7.4), <i>N</i> = 91 1: 84.7 ($\pm$ 8.3), <i>N</i> = 651 <i>p</i> = 0.482	0: 58.7 ($\pm$ 45.2), <i>N</i> = 92 1: 52.7 ($\pm$ 41.6), <i>N</i> = 649 <i>p</i> = 0.452	0: 5.5 ($\pm$ 6.3), <i>N</i> = 92 1: 5.3 ($\pm$ 5.6), <i>N</i> = 652 <i>p</i> = 0.036	0: 1.49 ($\pm$ 0.28), <i>N</i> = 90 1: 1.54 ($\pm$ 0.24), <i>N</i> = 637 <i>p</i> = 0.182	0: 1.29 ($\pm$ 0.25), <i>N</i> = 88 1: 1.34 ($\pm$ 0.24), <i>N</i> = 636 <i>p</i> = 0.192	0: 25.4 ($\pm$ 4.4), <i>N</i> = 91 1: 26.0 ($\pm$ 4.2), <i>N</i> = 652 <i>p</i> = 0.271
Physical activity	A/B: 82.2 ($\pm$ 9.4), <i>N</i> = 146 C: 85.2 ($\pm$ 7.7), <i>N</i> = 596 <i>p</i> $\leq$ 0.001	A/B: 67.7 ($\pm$ 59.5), <i>N</i> = 146 C: 49.9 ($\pm$ 35.7), <i>N</i> = 595 <i>p</i> $\leq$ 0.001	A/B: 7.9 ($\pm$ 7.7), <i>N</i> = 147 C: 4.7 ($\pm$ 4.8), <i>N</i> = 597 <i>p</i> $\leq$ 0.001	A/B: 1.42 ($\pm$ 0.25), <i>N</i> = 138 C: 1.56 ($\pm$ 0.24), <i>N</i> = 589 <i>p</i> $\leq$ 0.001	A/B: 1.24 ($\pm$ 0.23), <i>N</i> = 139 C: 1.35 ($\pm$ 0.24), <i>N</i> = 585 <i>p</i> $\leq$ 0.001	A/B: 27.5 ($\pm$ 4.8), <i>N</i> = 146 C: 25.5 ($\pm$ 4.0), <i>N</i> = 597 <i>p</i> $\leq$ 0.001

Table 3 (continued)

	CERADplus	TMT B-A	BDI-II	gait velocity	dual-task	BMI
Successful ageing index I	0: 83.7 ($\pm$ 8.4), N = 595 1: 88.3 ($\pm$ 6.2), N = 147 $p \leq 0.001$	0: 56.0 ($\pm$ 44.2), N = 595 1: 42.8 ($\pm$ 29.7), N = 146 $p \leq 0.001$	0: 5.4 ($\pm$ 5.8), N = 597 1: 5.1 ($\pm$ 5.4), N = 147 $p = 0.657$	0: 1.52 ($\pm$ 0.25), N = 581 1: 1.60 ($\pm$ 0.24), N = 146 $p = 0.002$	0: 1.32 ($\pm$ 0.24), N = 580 1: 1.39 ($\pm$ 0.23), N = 144 $p \leq 0.001$	0: 26.3 ($\pm$ 4.4), N = 596 1: 24.4 ($\pm$ 3.4), N = 147 $p \leq 0.001$
Successful ageing index II	0: 84.1 ($\pm$ 8.2), N = 655 1: 88.0 ($\pm$ 6.9), N = 87 $p = 0.561$	0: 54.5 ($\pm$ 43.2), N = 655 1: 45.6 ($\pm$ 30.9), N = 86 $p = 0.321$	0: 5.4 ($\pm$ 5.6), N = 657 1: 4.9 ($\pm$ 5.9), N = 87 $p = 0.151$	0: 1.53 ($\pm$ 0.25), N = 640 1: 1.59 ($\pm$ 0.26), N = 87 $p = 0.661$	0: 1.33 ($\pm$ 0.24), N = 638 1: 1.37 ($\pm$ 0.23), N = 86 $p = 0.864$	0: 26.1 ($\pm$ 4.3), N = 656 1: 24.3 ($\pm$ 3.6), N = 87 $p = 0.065$
Alcohol	A/B: 83.4 ($\pm$ 8.4), N = 160 C: 84.9 ($\pm$ 8.1), N = 582 $p = 0.075$	A/B: 67.4 ($\pm$ 52.3), N = 160 C: 49.6 ($\pm$ 37.9), N = 581 $p \leq 0.001$	A/B: 5.7 ($\pm$ 6.0), N = 161 C: 5.2 ($\pm$ 5.6), N = 583 $p = 0.445$	A/B: 1.48 ($\pm$ 0.25), N = 156 C: 1.55 ($\pm$ 0.25), N = 571 $p = 0.008$	A/B: 1.29 ($\pm$ 0.23), N = 155 C: 1.34 ($\pm$ 0.24), N = 569 $p = 0.094$	A/B: 26.3 ($\pm$ 4.8), N = 160 C: 25.8 ($\pm$ 4.1), N = 583 $p = 0.291$
Alcohol (dichotomous)	0: 81.7 ($\pm$ 8.8), N = 47 1: 84.8 ($\pm$ 8.1), N = 695 $p = 0.020$	0: 73.6 ($\pm$ 55.4), N = 47 1: 52.1 ($\pm$ 40.7), N = 694 $p = 0.003$	0: 6.9 ($\pm$ 6.1), N = 47 1: 5.2 ($\pm$ 5.6), N = 697 $p = 0.057$	0: 1.44 ($\pm$ 0.23), N = 44 1: 1.54 ($\pm$ 0.25), N = 683 $p = 0.025$	0: 1.30 ($\pm$ 0.22), N = 45 1: 1.33 ($\pm$ 0.24), N = 679 $p = 0.715$	0: 26.4 ($\pm$ 4.4), N = 47 1: 25.9 ($\pm$ 4.2), N = 696 $p = 0.687$
Smoking (dichotomous)	0: 84.3 ($\pm$ 9.2), N = 357 1: 84.9 ($\pm$ 7.1), N = 385 $p = 0.211$	0: 56.7 ($\pm$ 47.4), N = 355 1: 50.4 ($\pm$ 36.2), N = 386 $p = 0.071$	0: 5.1 ($\pm$ 5.5), N = 358 1: 5.5 ($\pm$ 5.8), N = 386 $p = 0.061$	0: 1.53 ($\pm$ 0.25), N = 349 1: 1.54 ($\pm$ 0.24), N = 378 $p = 0.556$	0: 1.33 ($\pm$ 0.24), N = 348 1: 1.33 ($\pm$ 0.24), N = 376 $p = 0.417$	0: 25.4 ($\pm$ 4.0), N = 357 1: 26.3 ($\pm$ 4.4), N = 386 $p = 0.020$

BDI-II Beck's Depression Inventory-II, *CERADplus* Consortium to Establish a Registry for Alzheimer's Disease, *PA* physical activity, *PD* Parkinson's disease, *TMT B-A* Trail Making Test B minus A, *UPDRS III* MDS-UPDRS part III, Movement-Disorder-Society-Unified Parkinson's disease rating scale-part III

In contrast, smoking status and the successful ageing index I and II were not associated with significant effects. The Akaike information criterion (AIC) was 12,125.156, and the Bayesian information criterion (BIC) was 12,147.346.

For the variable "Trail Making Test B-A," the overall model did not reach statistical significance, $F(1, 1142.8) = 3.056$, $p = 0.081$. A significant effect of years of education was found, $F(13, 635.6) = 3.805$, $p \leq 0.001$. Participants with 22 years of education achieved lower scores in Trail Making Test B-A ($M = 43.5$, $SE = 24.5$) compared to those with 9 years of education ($M = 77.9$, $SE = 6.5$). Additionally, significant effects were found for age, $F(1, 1253.9) = 65.580$, $p \leq 0.001$, and for physical activity, $F(1, 640.9) = 9.644$, $p = 0.002$. Participants engaging in sports with the highest frequency demonstrated lower Trail Making Test B-A scores ($M = 46.7$, $SE = 2.4$) than those with lower levels of sports participation ($M = 54.3$, $SE = 3.2$). The AIC was 18,221.073, and the BIC was 18,243.246.

For the variable "BDI-II," the overall model reached statistical significance, $F(1, 1634.0) = 122.876$, $p \leq 0.001$. A significant effect of sex was found, $F(1, 694.8) = 26.910$, $p \leq 0.001$, indicating that female participants had higher BDI-II scores ($M = 8.9$, $SE = 0.6$) compared to male participants ($M = 6.5$, $SE = 0.6$). Additionally, significant effects were found for age, $F(1, 1574.3) = 48.0$, $p \leq 0.001$, and for physical activity, $F(1, 687.5) = 39.175$, $p \leq 0.001$. Participants engaging in sports with the highest frequency demonstrated lower BDI-II scores ($M = 6.0$, $SE = 0.5$) than those with lower levels of sports participation ($M = 9.4$, $SE = 0.7$). The AIC was 11,747.443, and the BIC was 11,769.640.

For the variable "gait velocity," the overall model reached statistical significance, $F(1, 1440.7) = 2559.515$, $p \leq 0.001$. A significant effect of sex was found, $F(1, 676.4) = 86.397$, $p \leq 0.001$, indicating that male participants were faster ($M = 1.67$, $SE = 0.02$) compared to female participants ($M = 1.53$, $SE = 0.02$). Additionally, significant effects were

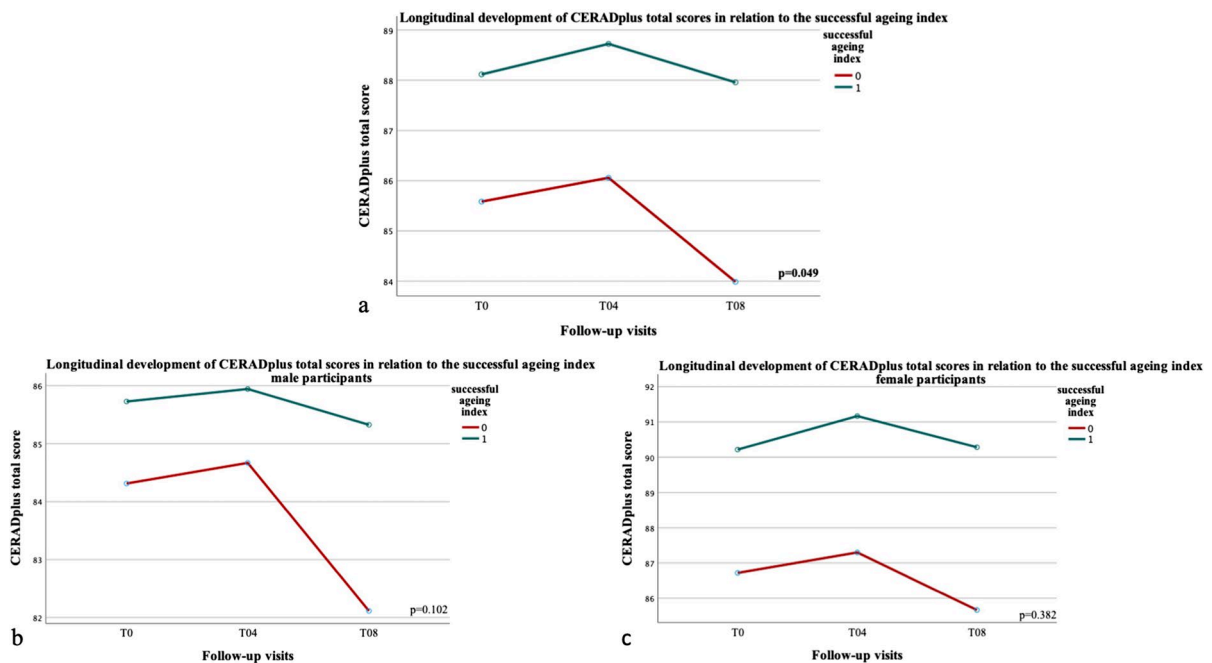


Fig. 2 Mean CERADplus total scores at three follow-up visits (T0: baseline; T04: 4 years; T08: 8 years) are presented based on the successful ageing index I (0 versus 1), stratified by sex (**a** total cohort; **b** male participants; **c** female participants). The

figure demonstrates higher baseline CERADplus scores and a slower decline over time among participants with a higher successful ageing index I. CERADplus: Consortium to Establish a Registry for Alzheimer’s Disease

found for age, $F(1, 1482.8) = 617.898$, $p \leq 0.001$, and for physical activity, $F(1, 671.6) = 64.694$, $p \leq 0.001$. Participants engaging in sports with the highest frequency were faster ($M = 1.67$, $SE = 0.02$) than those with lower levels of sports participation ($M = 1.53$, $SE = 0.02$). The AIC was -765.752 , and the BIC was -743.589 .

For the variable “dual-task,” the overall model reached statistical significance, $F(1, 1459.5) = 2573.617$, $p \leq 0.001$. A significant effect of sex was found, $F(1, 705.4) = 44.039$, $p \leq 0.001$, indicating that male participants were faster ($M = 1.44$, $SE = 0.02$) compared to female participants ($M = 1.35$, $SE = 0.02$). Additionally, significant effects were found for age, $F(1, 1497.4) = 696.195$, $p \leq 0.001$, and for physical activity, $F(1, 698.9) = 40.542$, $p \leq 0.001$. Participants engaging in sports with the highest frequency were faster ($M = 1.45$, $SE = 0.02$) than those with lower levels of sports participation ($M = 1.34$, $SE = 0.02$). The AIC was -1143.774 , and the BIC was -1121.624 .

For the variable “BMI,” the overall model reached statistical significance, $F(1, 1195.7) = 1217.625$, $p \leq$

0.001 . A significant effect of sex was found, $F(1, 729.5) = 11.554$, $p \leq 0.001$, indicating that male participants had a higher BMI ($M = 27.1$, $SE = 0.4$) compared to female participants ($M = 26.0$, $SE = 0.4$). Additionally, significant effects were found for years of education, $F(13, 724.3) = 2.815$, $p \leq 0.001$. Participants with 22 years of education achieved a lower BMI ($M = 24.9$, $SE = 3.9$) compared to those with 9 years of education ($M = 28.1$, $SE = 1.0$). There was also a significant effect for physical activity, $F(1, 724.1) = 19.370$, $p \leq 0.001$. Participants engaging in sports with the highest frequency had a lower BMI ($M = 25.7$, $SE = 0.4$) than those with lower levels of sports participation ($M = 27.4$, $SE = 0.5$). Furthermore, patients with a history of smoking had a higher BMI ($M = 27.0$, $SE = 0.5$) than those without ($M = 26.1$, $SE = 0.4$), $F(1, 725.0) = 8.743$, $p = 0.003$. The AIC was 8784.805 , and the BIC was 8806.991 .

Discussion

Our TREND-study offers a comprehensive evaluation of longitudinal data on motor and cognitive performance in relation to lifestyle factors, aiming to investigate patterns of healthy ageing in a large prospective cohort of participants aged 50 (mean 70 years) and older over a time span of 8 years. We demonstrate that the most compelling influences on healthy ageing are linked to distinct protective lifestyle factors, such as engagement in physical activities, level of education, and specific dietary attributes. Our correlation analyses revealed significant associations between protective lifestyle factors and various cognitive, emotional, and physical parameters, including CERADplus, BDI-II, gait velocity, dual-task performance, and BMI, all of which can be readily incorporated into clinical practice. These findings suggest a higher level of healthy ageing among individuals exhibiting these protective lifestyle attributes, with physical activity emerging as the most influential factor on outcome parameters in both cross-sectional and longitudinal analyses.

Impact of physical activity and levels of formal education on motor and cognitive outcomes

The positive effects of physical activity on cognitive function in older populations have been confirmed in numerous studies and meta-analyses [16, 17]. Similarly, higher levels of formal education have been linked to better cognitive outcomes and a reduced risk of dementia [16, 18].

The benefits of physical activity have also been demonstrated in patients with neurodegenerative diseases. In patients with Parkinson's disease, physical activity has been shown to improve motor performance, as measured by the Unified Parkinson's Disease Rating Scale (UPDRS), and to reduce depression scores, as assessed by the BDI-II, suggesting beneficial effects on both motor function and mood [19].

Consistent with these findings, participants in our study who engaged in higher levels of physical activity per week exhibited better motor and cognitive function in cross-sectional and longitudinal analyses. Additionally, they demonstrated a slower decline in cognitive function over an 8-year period. Our analyses also revealed positive effects of physical activity

on mental health, as assessed by the BDI-II, further supporting the findings of existing literature [20].

Associations of nutritional factors with healthy ageing

The Mediterranean diet, extensively investigated in numerous studies, is distinguished by the consumption of elevated levels of monounsaturated fatty acids, primarily derived from abundant intake of olive oil, fish, vegetables, fruits, nuts, and cereals, coupled with a reduced consumption of meat [7].

In a population of 935 participants aged 65 years and older, high values in the Mediterranean diet score (MDS) were linked to a better lower body performance, as assessed by the short physical performance battery, and a slower decline of mobility over a 9-year follow-up [21]. Furthermore, another study showed that protein-energy supplementation might reduce the progression of functional decline measured by, among others, the timed-up-and-go-test.

One Australian study demonstrated greater odds of successful ageing in participants with energy-adjusted cereal/grain fibre intake above the median [22].

Intake of high concentrations of unsaturated fatty acids, antioxidants, vitamin B, and a high adherence to the Mediterranean diet were also associated with a lower risk for dementia in a meta-analysis [23], whereas low consumption of meat was associated with an increased risk of dementia and Alzheimer's disease in comparison to regular meat consumption [24].

Smoking has been associated with an increased risk for dementia [23] supported by results of meta-analyses [25].

Concerning the connection between nutrition and mood, a particular study showcased an inverse correlation between fiber intake and the prevalence of depressive symptoms [26]. Conversely, a meta-analysis revealed an elevated risk of depression in individuals who abstained from meat consumption [27], without constructing causality between meat consumption and better mood [28].

Our findings support the positive effects of a high intake of plant-based foods, both cross-sectionally and longitudinally. In detail, the intake was associated with a better cognitive and executive performance as indicated by CERADplus total score and Trail Making Test. Notably, participants with a high intake of

plant-based foods also exhibited a slower decline in CERADplus total scores, which reached borderline significance. Results for other nutritional factors such as coffee, meat, cereals, and dairy products were inconsistent, implying the need for further studies.

Successful ageing index

Participants with the highest frequency of physical activity, the highest intake of plant-based foods, and belonging to the highest educational level demonstrated protective effects across nearly all

clinical outcome parameters (Fig. 3). Notably, these effects were, in some instances, more pronounced than the impact of each individual lifestyle factor alone. Especially, weekly exercises of more than 1 h should be a realistic goal for most older adults. Specifically, these individuals exhibited superior mnemonic and executive function, enhanced dual-task performance, and a lower BMI. Remarkably, they also maintained constant CERADplus total scores over the 8-year longitudinal period, in contrast to their counterparts who exhibited cognitive decline and a faster deterioration in dual-task performance.

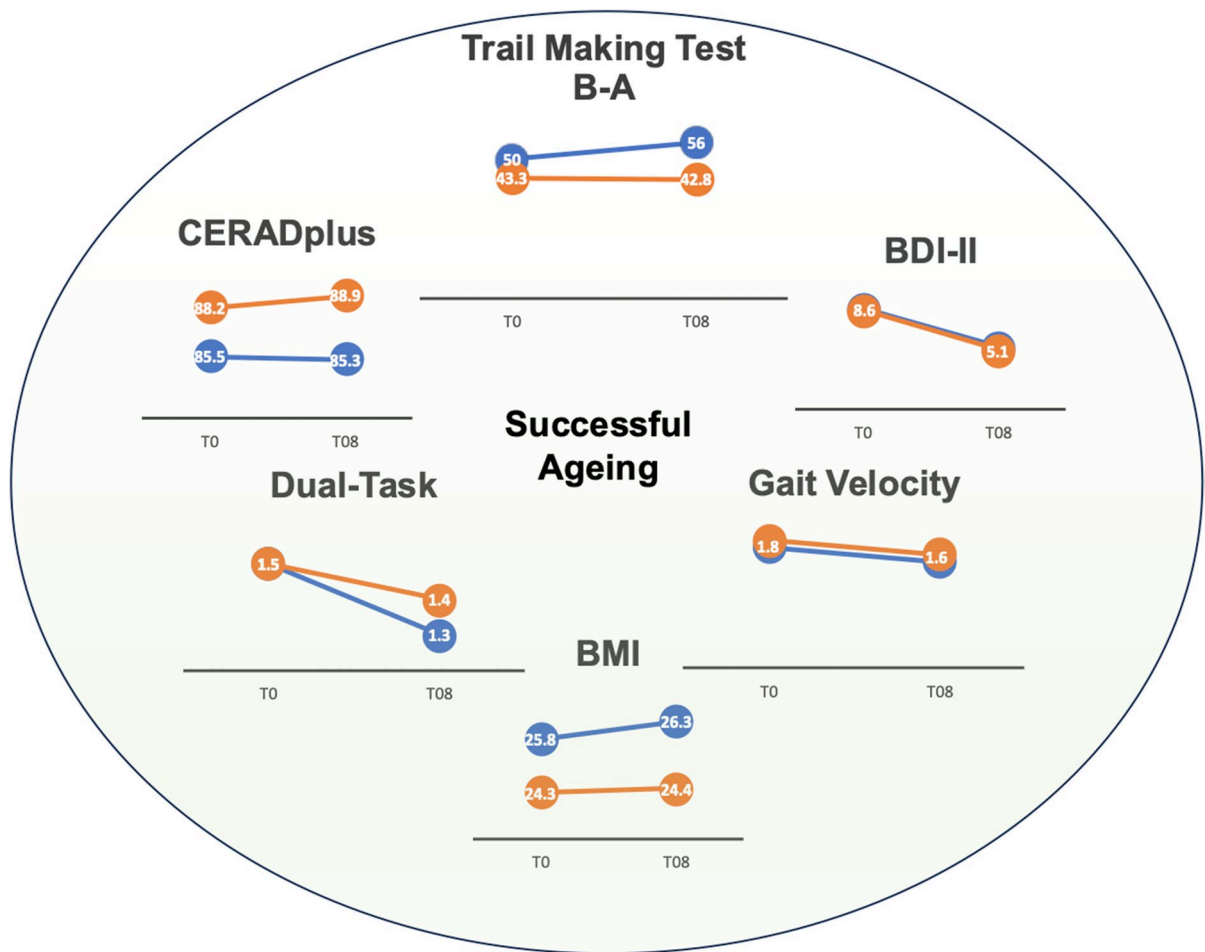


Fig. 3 Impact of a healthy lifestyle—characterized by frequent physical activity, high intake of plant-based foods, and a high level of education—on test scores at baseline (T0) and at follow-up T08 (8 years post-baseline). The blue line represents a successful ageing index I of 0, while the orange line represents an index of 1. CERADplus (= Consortium to Establish a Registry for Alzheimer’s Disease); Trail Making Test B-A (in sec-

onds): the time needed to complete Trail Making Test B minus the time needed to complete Trail Making Test A; BDI-II (= Beck’s Depression Inventory-II); gait velocity (in m/s): distance of 20 m or respective 17 m divided by the time needed to walk this distance at the highest possible speed; dual-task: gait velocity, while completing an additional cognitive task (checking boxes on a paper); BMI (in kg/m²): body mass index

The second index that included non-smoking status showed similar associations with clinical test scores in baseline analyses. However, these associations did not reach statistical significance in longitudinal analyses, possibly due to small effect sizes.

Observation of sex differences

Female participants were older at examination and had fewer years of education, higher CERADplus total scores, higher BDI-II scores, and lower gait velocity compared to male participants.

Clinical correlations suggest that female participants generally adhered more to a healthier lifestyle. They reported higher intake of plant-based foods, smoked less, and consumed less alcohol compared to male participants, whereas the prevalence of physical activity did not differ between sexes. Interestingly, while both higher intake of plant-based foods and higher levels of physical activity were linked to increased CERADplus total scores, these associations were statistically significant only in female participants. This may be attributable to the generally healthier lifestyle observed among female participants.

Notably, male participants showed an increase in depressive symptoms with age, as measured by the BDI-II. Physical activity was associated with lower BDI-II scores, an effect that reached statistical significance especially in males. Among female participants, higher intake of plant-based foods was associated with a reduction in BDI-II scores over time, suggesting that the protective impact of lifestyle factors on depressive symptoms, but also on quantitative cognitive and motor measurements, may vary by sex. In this context, among participants with the highest levels of education, plant-based food intake, and physical activity, male participants showed a lower CERADplus total score compared to females, along with a lower BDI-II score, higher gait velocity, and better dual-task performance. These potential differences warrant further investigation in future studies. A more detailed analysis of the CERADplus subdomains could provide additional insights and would be beneficial in future research.

Implications

Overall, our results are in line with findings of various studies and meta-analyses. In particular, we demonstrate cumulative effects of specific diets as well as physical activity and education mediating protective effects on mnemonic and executive function, gait velocity, dual-task performance, mental health, and BMI in older participants of our prospective longitudinal ageing study. These assessments, which can be easily integrated into clinical routines, may help identify individuals at risk for developing age-related diseases, particularly dementia. In this context, Verghese et al. [29] introduced the concept of Motoric Cognitive Risk (MCR) syndrome, a pre-dementia condition characterized by the combination of cognitive complaints and slow gait. Identifying patients with MCR syndrome may offer improved opportunities for early preventive and therapeutic interventions, potentially preventing or delaying the onset of dementia.

Our results might help stratify and motivate participants with different lifestyle profiles for interventional studies. Along these lines, we also suggest replicating the results in cohorts of patients with neurodegenerative diseases.

Limitations and strengths

Several limitations in our study must be acknowledged: (i) the assessment of lifestyle factors was not conducted at all time points, necessitating reliance on classifications at the 8-year follow-up for most factors. This limitation could be addressed in future follow-up visits or studies by including these assessments at each time point; (ii) given that information on lifestyle factors was gathered through questionnaires, there is a potential for inaccuracies and reporting bias, especially for smoking and alcohol; (iii) the types of sports or activities, along with their potentially varied influences on outcome parameters, were not accounted for in our analyses; (iv) The categorization and selection of lifestyle factors and the successful ageing index are inherently artificial and represent a simplification of complex processes, necessitating validation in additional studies. Particular attention should be given to social determinants—such as marital status, friendships, social engagement, and, conversely, social isolation or perceived loneliness—as they represent important factors contributing

to healthy and successful ageing; (v) the outcome parameters exhibited non-normal distributions, and notable outliers were identified in TMT B-A, BDI-II, and BMI, along with a singular extreme outlier in CERADplus total score. Despite the presence of these outliers, they were retained in the study as their occurrence is likely associated with advanced age at examination (TMT B-A and CERADplus total score) or the possible occurrence of depressive episodes (BDI-II); (v) the interpretation of this coherent set of lifestyle factors warrants caution, given the inherent challenges associated with multiple testing. In an effort to mitigate this concern, we applied a manual Bonferroni correction. However, this approach does not entirely eliminate the risk of false negatives due to multiple comparisons. Future studies could focus on a select number of lifestyle factors and their impact on test outcomes. These factors could also be more rigorously controlled, for example, by assigning one group to a specific weekly sports intervention and comparing them to a control group.

The inclusion of adjustments for age at examination, sex, and years of education, along with stratification by sex in all analyses, is a crucial strength of this ageing study.

The study outcomes align with expectations. The robustness of our study lies in the prospective and longitudinal evaluation of an extensive array of quantitative measures encompassing motor and cognitive performances, along with aspects of mental health, within a substantial population-based cohort of elderly participants over the long time interval of 8 years.

Conclusions

Protective lifestyle factors like plant-based diet and exercise are associated with improved motor and cognitive performances reflecting healthy ageing. As these lifestyle factors are modifiable, a protective lifestyle has the potential of relevant improvement of cognitive performance in higher age groups.

Our finding of significant differences in cognitive decline over an 8-year period, based on adherence to protective lifestyle factors, may help motivate individuals to adopt healthier lifestyles as part of preventive strategies. However, to establish causal relationships, future studies in clinical or community-based

settings are warranted. Interventional trials or long-term observational studies conducted in these contexts could help clarify the directionality of effects and assess the practical applicability of these factors for promoting healthy ageing in older populations. In this regard, cohorts of patients with neurodegenerative diseases, specifically Parkinson's disease and Alzheimer's disease, should also be included as additional groups. This could provide valuable insights into causal relationships and the significance of specific lifestyle interventions in promoting healthy ageing and preventing accelerated ageing. Future longitudinal cohort studies could further delve into the intricate interplay among genetics, epigenetics and lifestyle factors to inform targeted, personalized prevention strategies aimed at fostering healthy ageing, and the promotion of disease-free survival rather than merely increasing life expectancy.

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Author contribution MZ, US, BR, and KB designed the following sub-study. KB, TG, DB, WM, AF, and GE designed the underlying TREND-study. MZ, KB, MH, BR, US, IW, CS, AT, SL, TG, DB, GE, AF, and WM generated and collected clinical data. MZ performed the statistical analyses. MZ and BR drafted the manuscript. All authors were involved in interpretation of the data and critical revision of the manuscript. All authors gave their final approval.

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Declarations

Competing interests We have no conflict of interest to declare in regard to the manuscript. Prof. Daniela Berg has received grants or contracts from the German Research Society (DFG), German Parkinson's Disease Association (dPV), Michael J Fox Foundation, BMBF, Parkinson Fonds Deutschland gGmbH,

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