Research article

Associations of lifestyle factors with amyloid pathology in persons without dementia

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Abstract

Background: The association between lifestyle factors and Alzheimer's disease (AD) pathophysiology remains incompletely understood.

Objective: The aim of this study was to assess the association of alcohol consumption, smoking behavior, sleep quality and physical, cognitive, and social activity with cerebral amyloid pathology.

Methods: For this cross-sectional study, we selected participants from the Amyloid Biomarker Study data pooling initiative. We used generalized estimating equations to assess associations of dichotomized lifestyle measures with amyloid pathology.

Results: We included 9171 participants with normal cognition (NC) and 2555 participants with mild cognitive impairment (MCI) from the Amyloid Biomarker Study. Of participants with NC, 58% were women, 34% were *APOE* ϵ4 carrier, and 27% had amyloid pathology. Of participants with MCI, 48% were women, 47% were *APOE* ϵ4 carrier, and 57% had amyloid pathology. In NC, cognitively active participants were less likely to have amyloid pathology (OR = 0.77, 95%CI 0.66–0.89, $p < 0.001$). In MCI, participants who had ever smoked or had sleep problems were less likely to have amyloid pathology (OR = 0.85, 95%CI 0.73–0.99, $p = 0.029$; OR = 0.62, 95%CI 0.45–0.86, $p = 0.004$).

Conclusions: In NC, cognitive activity was associated with a lower frequency of amyloid pathology. In MCI, favorable lifestyle behaviors were not associated with a lower frequency of amyloid pathology. The results of the current study contribute to the broader evidence base on lifestyle and AD by further characterizing the role of lifestyle behaviors in AD pathology across different clinical stages.

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Alzheimer's disease, amyloid, amyloid biomarker study, cerebrospinal fluid, positron emission tomography, lifestyle

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Introduction

Evidence on the role of lifestyle behaviors in the development of cognitive impairment and dementia has been steadily accumulating, with evidence from meta-analyses and systematic reviews showing clear associations between lifestyle factors and dementia risk.[1] However, the relation between lifestyle factors and Alzheimer's disease (AD) pathophysiology is not yet well defined. A better understanding of the association between lifestyle factors and AD pathology (i.e., amyloid plaques and tau tangles) in early disease stages may help to identify those at risk and contribute to the development of targeted prevention strategies.

Findings from previous studies on the association between lifestyle factors and AD biomarkers of amyloid in cerebrospinal fluid (CSF) or on positron emission tomography (PET) are mainly based on cross-sectional analyses and are heterogeneous.[2–16] While some studies report clear associations between lifestyle behaviors such as physical and cognitive activity and amyloid burden,[2–4,6,7,9,10,12–16] others find no associations between lifestyle behaviors and amyloid pathology,[5,8,11] or identify associations specific to *APOE* ϵ4 carriers or non-carriers.[7]

Differences in composition and size of study cohorts, associated differences in distributions of demographic factors, timing (midlife versus late life), and method of lifestyle assessment as well as lack of power contribute to heterogeneity and likely account for a proportion of the divergence in results. Assessment in a large, harmonized study sample could therefore provide more insight into the role of lifestyle factors in the development of AD.

The aim of the current cross-sectional study was to examine the associations of alcohol consumption, smoking behavior, sleep quality, physical activity, cognitive activity, and social activity with amyloid pathology in a large group of persons without dementia by harmonizing lifestyle and amyloid measures across 42 cohorts and 11,726 participants included in the Amyloid Biomarker Study (ABS).

Methods

Standard protocol approvals, registrations, and patient consents

Written informed consent was obtained from all participants and data were de-identified. All individual sites contributing to the ABS have obtained local ethical approval and the ABS was approved by the Medical Ethics Committee of the Maastricht University Medical Center which declared that the Medical Research Involving Human Subjects Act does not apply to the study and waived the informed consent requirement because de-identified data were used.

Participants

Participants for this cross-sectional study were recruited from the ABS, a data pooling initiative that was started in 2013. Study design and data collection have been described previously.[17–19] The ABS currently includes over 24,000 participants from 95 cohorts. For the present study, we selected 11,726 participants from 42 centers based on availability of amyloid biomarkers, age, cognitive status, and information on any lifestyle factor (n = 3399 excluded due to missing information on lifestyle; cohort characteristics are provided in Supplemental Table 1). 9171 participants had normal cognition (NC) as defined by normal scores on cognitive tests and absence of cognitive complaints (cohort-specific tests and measurements), and 2555 participants had mild cognitive impairment (MCI) as diagnosed by criteria set out in Petersen et al. or Winblad et al.[20,21] Participants who reported subjective cognitive complaints were considered to have NC for the purpose of these analyses.

Amyloid pathology

Presence or absence of amyloid pathology was determined based on $A\beta_{42}$ levels or $A\beta_{42/40}$ ratio in CSF (n = 20 centers) or an amyloid-PET scan (n = 13 centers); 9 centers had both CSF and PET data. Amyloid pathology was defined using methods described previously.[17] Briefly, we used either center-specific or data-driven cut-offs obtained from Gaussian Mixture Modelling (GMM) to dichotomize CSF data. Center-specific cutoffs were used to dichotomize all PET data (n = 6298 participants) and CSF data for 33% of participants (n = 1776). GMM-based cutoffs were used to dichotomize CSF data for 67% of participants (n = 3652). Measurement details of amyloid biomarkers and applied cutoffs have been specified elsewhere.[17]

Lifestyle factors

For each individual included, data was available on at least one of the following lifestyle factors: alcohol consumption,

smoking behavior, sleep quality, physical activity, cognitive activity, or social activity. The lifestyle assessment was performed within six months of the amyloid assessment in 41 centers and within 12 months of the amyloid assessment in one center. Supplemental Tables 2 and 3 present measurement information and the number of participants with available data for each center. Lifestyle data was dichotomized as detailed below. If multiple measures for a lifestyle factor were available in one center, we prioritized rating scale data and other continuous data over self-reported and/or categorical data.

Alcohol consumption. Participants were classified as drinkers (>= 1 alcohol unit per week) or abstainers based on (1) information on alcohol units in drinks consumed per day or week (18 centers, n = 6215) or (2) medical history (25 centers, n = 1444). We did not include participants in the analysis of alcohol consumption if information was limited to alcohol abuse status.

Smoking status. Participants were classified as ever-smokers (past or present) or never-smokers based on (1) information on smoking units in cigarettes per day or week (10 centers, n = 5954) or (2) medical history (32 centers, n = 4713).

Sleep quality. Participants were classified as being with or without sleep problems based on (1) rating scales for sleep quality and sleep problems (8 centers, n = 2555), (2) sleep hours (8 centers, n = 5168), (3) a positive answer to the screening question on the sleep domain of the neuropsychiatric inventory questionnaire (NPI) or NPI-Q (15 centers, n = 1293), or (4) self-report (9 centers, n = 801). Rating scales provided included the Pittsburgh Sleep Quality Index (PSQI[22]; sleep problems if score > 5), Epworth Sleep Quality Index (ESS[23]; sleep problems if score > 10). and Profile of Elderly Quality of Life (PEQOL[24]) Sleep disturbance (tertile-based cut-off). Participants who reported sleeping less than 6 or over 9 h of sleep per night were considered to have sleep problems.[25,26]

Physical activity. Participants were classified as being physically inactive or active based on (1) rating scales for physical activity (3 centers, n = 456), (2) frequency and/or intensity of physical exercise (11 centers, n = 6876), or (3) self-report (8 centers, n = 375). Rating scales provided included the International Physical Activity Questionnaire (IPAQ[27]) and the Physical Activity Scale for the Elderly (PASE[28]). To account for variability in activities classified as physical activity, cohort-specific cutoffs based on the upper tertile were applied to rating scale and frequency and/or intensity data.

Cognitive activity. Participants were classified as being cognitively inactive or active based on (1) the Wilson cognitive activity questionnaire[29] (current life epoch; 4 centers, n = 412), (2) frequency of participation in cognitive activities (3 centers, n = 349), or (3) self-report (4 centers, n = 201). Data on frequency of participation in cognitive activities was recoded to match the rating outcomes of the Wilson cognitive activity questionnaire (frequency rated on a scale of 1–5). Participants with an average score > 3.57 on the Wilson cognitive activity questionnaire or a score of > 3.57 as averaged over activities were considered to be cognitively active.[30]

Social activity. Participants were classified as being socially inactive or active based on (1) frequency of participation in social activities (3 centers, n = 330), (2) frequency of meeting with friends (1 center, n = 118), (3) self-report (3 centers, n = 203), or (4) information on social network size (2 centers, n = 83). Participants were considered socially active if they participated in a social activity or met with friends at least once a week. A center-specific median cut-off was applied to classify participants as socially active or inactive based on information on their social network size.

Other covariates

Age, sex, and education-years were based on participant self-report.[17–19]

Statistical analysis

Differences in demographic and clinical characteristics between those with and without amyloid pathology were tested using ANOVA (continuous variables) or chi-square tests (categorical variables). Generalized estimating equations were used to assess the associations between the individual lifestyle factors and amyloid pathology. We assumed a logit link function for binary outcomes with an exchangeable working correlation matrix and robust variance estimators to account for within-study correlation.

Analyses were performed separately in participants with NC and participants with MCI. Age, sex, and education were included as covariates in all models, with age and education years included as continuous measures and age centered at the mean. We first tested the overall association between the individual lifestyle factors and amyloid pathology. In secondary analyses, we used continuous lifestyle measures (alcohol units per week, number of cigarettes per week, average number of hours slept each night) instead of dichotomous lifestyle measures.

The significance level was set at $p < 0.05$ for unpaired, 2-sided tests. Analyses were conducted with IBM SPSS Statistics version 27 and images were created using R (version 4.0.0, R Foundation for Statistical Computing). We used Bonferroni adjustment to correct for multiple comparisons when evaluating the primary outcomes. We report uncorrected p-values and note if the association was no longer significant after correction for multiple comparisons.

Table 1. Participant characteristics.

	Total n = 11726		NC		MCI		p difference amyloid pathology versus no amyloid pathology	
	NC n = 9171	MCI n = 2555	No amyloid pathology, n = 6729	Amyloid pathology, n = 2442	No amyloid pathology, n = 1103	Amyloid pathology, n = 1452	NC	MCI
Age, mean ± SD	68.4 ± 8.7	69.8 ± 8.5	67.6 ± 8.8	70.5 ± 8.2	68.0 ± 8.9	71.1 ± 7.9	p < 0.001	p < 0.001
Sex, female, n (%)	5287 (57.7%)	1213 (47.5%)	3912 (58.1%)	1375 (56.3%)	533 (48.3%)	680 (46.8%)	p = 0.12	p = 0.46
Education, mean ± SD	15.2 ± 3.7	12.3 ± 4.3	15.3 ± 3.7	15.1 ± 3.7	12.0 ± 4.3	12.4 ± 4.4	p = 0.034	p = 0.025
Education >= 15 years, n (%)	5006 (54.8%)	728 (29.3%)	3694 (55.2%)	1312 (54.0%)	299 (27.8%)	429 (30.4%)	p = 0.32	p = 0.15
APOE ϵ4 carrier, n (%)	2942 (34.3%)	920 (47.2%)	1659 (26.1%)	1283 (57.4%)	214 (25.9%)	706 (62.8%)	p < 0.001	p < 0.001
Missing *APOE* ϵ4, n (%)	587 (6.4%)	604 (23.6%)	380 (5.6%)	207 (8.5%)	276 (25.0%)	328 (22.6%)		
Setting: clinical, n (%)	1074 (11.7%)	1910 (74.8%)	748 (11.1%)	326 (13.3%)	784 (71.1%)	1126 (77.5%)	p 0.001	p < 0.001
research, n (%)	7701 (84.0%)	645 (25.2%)	5732 (85.2%)	1969 (80.6%)	319 (28.9%)	326 (22.5%)		
population, n (%)	396 (4.3%)	0 (0.0%)	249 (3.7%)	147 (6.0%)	0 (0.0%)	0 (0.0%)		
No alcohol consumption, n (%)	2921 (45.1%)	678 (57.2%)	2171 (45.5%)	750 (44.0%)	309 (59.3%)	369 (55.5%)	p = 0.28	p = 0.19
Never smoker, n (%)	6351 (76.2%)	1371 (58.8%)	4659 (76.5%)	556 (24.7%)	591 (58.0%)	780 (59.4%)	p = 0.23	p = 0.49
No sleep problems, n (%)	5812 (69.8%)	1010 (67.7%)	4285 (70.0%)	1527 (69.3%)	414 (60.0%)	596 (74.3%)	p = 0.55	p < 0.001
Physically active, n (%)	2744 (39.1%)	319 (46.4%)	1970 (38.7%)	774 (40.2%)	177 (46.6%)	142 (46.3%)	p = 0.26	p = 0.93
Cognitively active, n (%)	276 (42.7%)	182 (57.6%)	184 (43.7%)	92 (37.9%)	114 (67.5%)	68 (46.3%)	p = 0.052	p < 0.001
Socially active, n (%)	136 (28.9%)	170 (64.4%)	100 (30.5%)	36 (25.4%)	114 (71.3%)	56 (53.8%)	p = 0.26	p = 0.004

NC: normal cognition; MCI: mild cognitive impairment; *APOE*: apolipoprotein E.

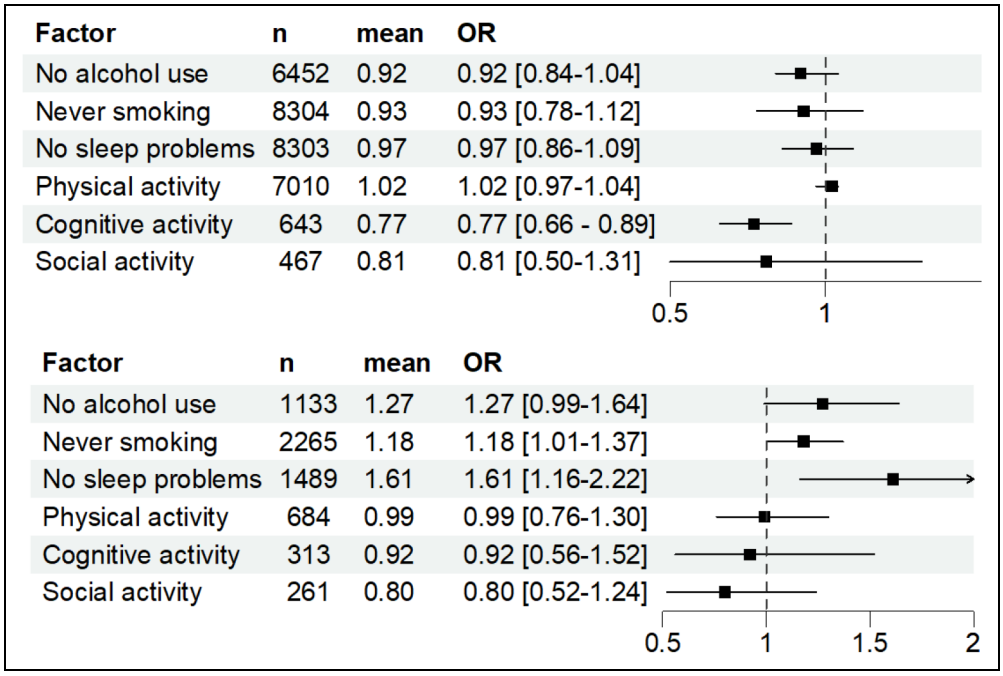

Figure 1. Odds ratios for amyloid pathology by cognitive group and lifestyle factor (top: NC, bottom: MCI).

Results

Participant characteristics

Baseline characteristics are presented in Table 1, stratified by cognitive and amyloid status. Of participants with NC, 58% were women, 34% were *APOE* ϵ4 carrier, and 27% had amyloid pathology. Of participants with MCI, 48% were women, 47% were *APOE* ϵ4 carrier, and 57% had amyloid pathology. The mean age was 69 years and participants had a mean of 15 years of education. 47% of participants did not consume alcohol, 72% never smoked, 70% did not have sleep problems, 40% were physically active, 48% were cognitively active and 42% were socially active. NC participants with amyloid pathology were more likely to be older, more likely to be *APOE* ϵ4 carrier, more likely to have fewer years of education, and less likely to be recruited from a research setting than NC participants without amyloid pathology. MCI participants with amyloid pathology were more likely to be older, more likely to be *APOE* ϵ4 carrier, more likely to have more years of education, more likely to be recruited from a clinical setting, and less likely to have sleep problems or be cognitively or socially active than MCI participants without amyloid pathology.

Associations between dichotomous lifestyle factors and amyloid pathology

The odds ratios (ORs) for amyloid pathology corresponding to each lifestyle factor are presented in Figure 1.

Individuals with NC. In participants with NC, cognitive activity was associated with amyloid pathology. Cognitively active participants had amyloid pathology less often than cognitively inactive participants (OR = 0.77, 95% CI 0.66–0.89, $p < 0.001$). Alcohol consumption, ever smoking, sleep quality, physical activity, and social activity were not associated with amyloid pathology (no alcohol use: OR = 0.92, 95% CI 0.84–1.04, p = 0.060; never smoking: OR = 0.93, 95% CI 0.78–1.12, p = 0.45; no sleep problems: OR = 0.97, 95% CI 0.86–1.09, p = 0.59; physically active: OR = 1.02, 95% CI 0.97–1.04, p = 0.41; socially active: OR = 0.81, 95% CI 0.50–1.31, p = 0.39).

Individuals with MCI. In participants with MCI, those who had ever smoked and those who had sleep problems were less likely to have amyloid pathology (OR = 0.85, 95% CI 0.73–0.99, p = 0.029, not significant after correction for multiple comparisons; OR = 0.62, 95% CI 0.45–0.86, p = 0.004). Alcohol use, physical activity, cognitive activity, and social activity were not associated with amyloid pathology (no alcohol use: OR = 1.27, 95% CI 0.99–1.64, p = 0.062; physically active: OR = 0.99, CI 0.76–1.30, p = 0.95; cognitively active: OR = 0.92, CI 0.56– 1.52, p = 0.74; socially active: OR = 0.80, CI 0.52–1.24, p = 0.33).

Associations of continuous lifestyle factors with amyloid pathology

Individuals with NC. In participants with NC, we found that those who smoked a higher number of cigarettes per week

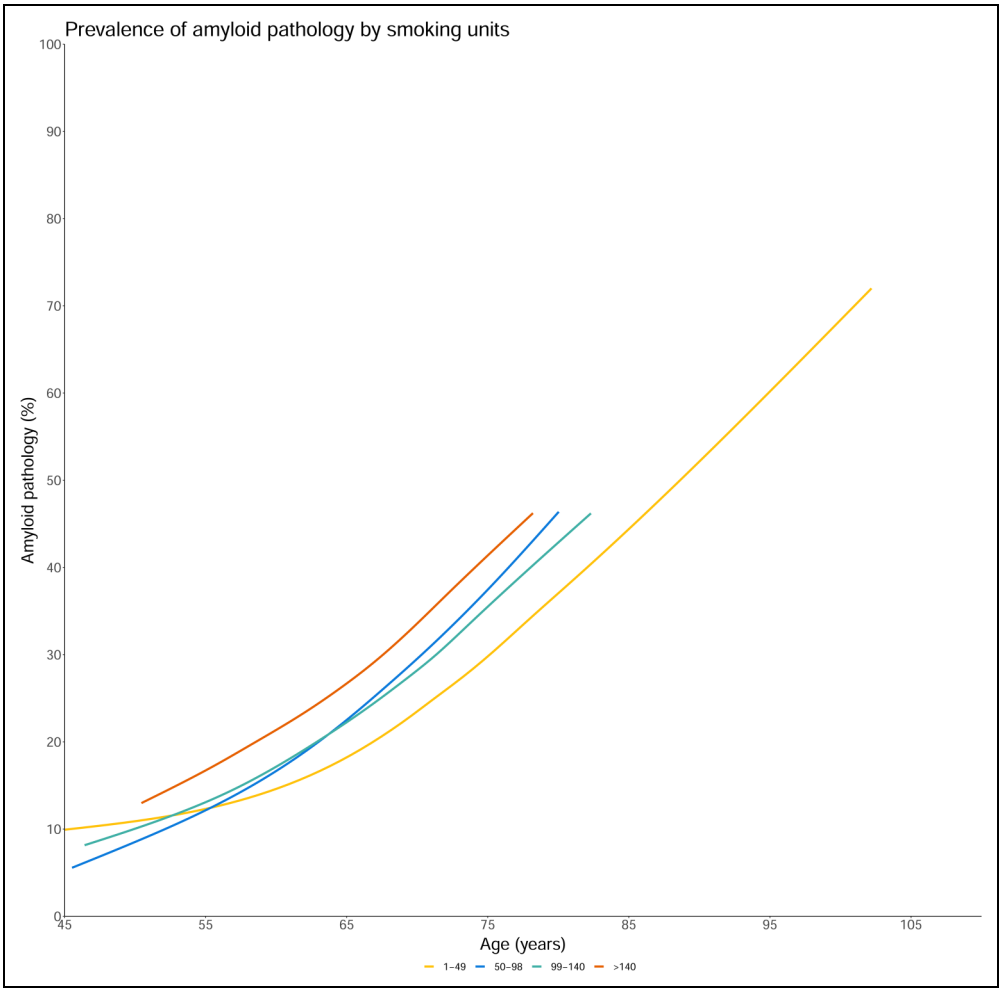

Figure 2. Association between smoking units per week and amyloid pathology in participants with NC.

were more likely to have amyloid pathology (b = 0.002, 95% CI 0.0–0.003, p = 0.018, Figure 2). Number of alcoholic drinks consumed and sleep duration were not associated with amyloid pathology (b = -0.001, 95%CI −0.005–0.004, p = 0.81; b = -0.048, 95%CI −0.198–0.11, p = 0.112, respectively).

Individuals with MCI

In participants with MCI, those who consumed a higher number of alcoholic drinks and smoked a higher number of cigarettes per week were less likely to have amyloid pathology (b = -0.23, 95% CI −0.040 – −0.006, p = 0.009; b = -0.004, 95% CI −0.005– −0.002, p < 0.001, respectively). Increased sleep duration was associated with higher odds of amyloid pathology (b = 0.61, 95%CI 0.54–0.68, p < 0.001).

Discussion

The aim of our study was to examine the associations of lifestyle factors with amyloid pathology in a large group of persons without dementia by harmonizing lifestyle and amyloid measures across 42 cohorts. We robustly harmonized amyloid measures and measures of alcohol consumption, smoking behavior, sleep quality and physical, cognitive, and social activity across cohorts. In participants with NC, we found that cognitively active persons were 23% less likely to have amyloid pathology. In NC, there was no association between the other lifestyle factors studied and amyloid pathology. In participants with MCI, we found that those who smoked and those who had sleep problems were less likely to have amyloid pathology (OR 0.62 and 0.85, respectively), though the association between smoking behavior and amyloid pathology was no longer significant after correction for multiple comparisons. In MCI, none of the favorable lifestyle behaviors studied were associated with a lower frequency of amyloid pathology.

Alcohol consumption and smoking behavior

Earlier work identified positive associations between alcohol consumption and p-tau/Aβ_{42} and t-tau/Aβ_{42} ratios

in cognitively unimpaired individuals as well as positive associations between smoking behavior and amyloid pathology in cognitively unimpaired individuals and persons with AD dementia.[15,16,32] While we did find an indication that NC participants who smoked a higher number of cigarettes per week were more likely to have amyloid pathology, we did not replicate the previously reported findings for alcohol consumption in this population.[31]

Sleep duration and quality

In participants with NC, we did not find any association between sleep quality and amyloid pathology. In participants with MCI, worse sleep quality was associated with lower odds of amyloid pathology while increasing sleep duration was associated with higher odds of amyloid pathology. Effects of sleep on amyloid pathology generally seem difficult to disentangle due to potential disparities in the association of different aspects of sleep with amyloid pathology, though accumulating evidence suggests that sleep problems, more generally defined, are associated with increasing amyloid pathology.[2–4,32–39]

Our observation that *un*favorable lifestyle behaviors were associated with a lower frequency of amyloid pathology in MCI, contrary to earlier observations, could have several explanations. Results may be reflective of underlying non-AD pathological mechanisms (e.g., vascular mechanisms, specifically for smoking) which resulted in participants presenting at the memory clinic with cognitive problems. Results may also be reflective of resilience mechanisms; indicating that the favorable lifestyle behaviors, i.e., no sleep problems, may mitigate or compensate for the effects of amyloid pathology on cognitive decline[40]. This would delay conversion to dementia and result in an increased frequency of amyloid pathology in those without sleep problems in the MCI phase when assessed cross-sectionally.

Past adherence to *un*favorable lifestyle behaviors could also have biased results. For instance, differences in health status between participants who adhered to favorable versus unfavorable lifestyle behaviors previously may have affected study inclusion. Participants with MCI may moreover have recently modified their lifestyle patterns as results of the diagnosis. Longitudinal studies may help to overcome these biases.

Cognitive activity

We found that cognitively active NC participants were less likely to have amyloid pathology than cognitively inactive NC participants. This observed effect extends on earlier findings that more specifically identified early and midlife as well as overall lifetime cognitive activity to be associated with decreased Pittsburgh compound B (PiB) retention,[10,12,41,42] supporting the idea that cognitive activity in NC may provide resistance (delaying the appearance of or retard pathological progression of) to amyloid pathology.[40]

Physical activity

We did not find an association between physical activity and amyloid pathology in either the NC or MCI group. Earlier work mostly identified inverse associations or reported no effect.[6,8–10,43–46] The measure of physical activity used, and more specifically which activities are considered to constitute physical activity, may strongly influence the observed associations, providing a potential explanation for the inconsistency in observations.

Social activity

We did not find an association of social activity with amyloid pathology in NC or MCI. The limited availability of data on social activity and the wide disparity in methods of measurement complicates interpretation. Relatively few studies up to date have focused on social activity in relation to amyloid pathology. Two identified an inverse association between social activity and amyloid pathology (PET and CSF, respectively), while two found no effects.[5,6,13,14] To further study this association, detailed and fine-grained measures of social activity should ideally be used.

Harmonization of lifestyle data

In the current paper, we present a first approach to harmonizing lifestyle data across a large number of cohorts. To be able to integrate as much data as possible, we needed to create dichotomous outcome measures, which inevitably resulted in loss of granularity. However, it was the only way to utilize all lifestyle information that was currently, and is commonly, available across memory clinic and research cohorts. Given the existing heterogeneity in the literature and the sustained interest in the role of lifestyle in cognitive impairment and AD, the field may benefit from the creation of standard operating procedures for the collection and analysis of lifestyle data.

Strengths and limitations

The current study has several limitations. The inclusion of data from and harmonization across multiple cohorts may have introduced sources of variance including heterogeneity in the assessment of amyloid pathology and lifestyle. Lifestyle was measured cross-sectionally, by different and -most often- subjective instruments, which may have introduced additional bias through potential differences in underlying constructs measured and reporting and recall bias. We could not draw any conclusions regarding

causality given the cross-sectional nature of the study. Lastly, we did not consider potential moderating effects of vascular risk factors, hearing loss, or interactions between lifestyle factors. Still, the collation of data and the resulting large sample size gave us the opportunity to study associations between lifestyle and amyloid pathology with sufficient power to detect small associations using lifestyle measures commonly available in memory clinic and research cohorts.

Conclusion

In this cross-sectional study, cognitive activity was associated with a lower frequency of amyloid pathology in those with NC, while other favorable lifestyle behaviors were not associated with a lower frequency of amyloid pathology. Generally, results suggest that cognitive activity may contribute to resistance to amyloid pathology in persons with NC, while in persons with MCI, identified associations may be reflective of non-AD pathological mechanisms or resilience mechanisms. The results of the current study contribute to the broader evidence base on lifestyle and Alzheimer's disease by further characterizing the role of lifestyle behaviors in AD pathology across different clinical stages. Longitudinal evaluation of associations between lifestyle factors and amyloid pathology, using detailed lifestyle measures, will be needed to fully establish the association between lifestyle and AD pathophysiology. The field may further benefit from the creation of standard operating procedures for the collection and analysis of lifestyle data.

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Ethical considerations

The study protocol for each cohort was approved by the local ethics committee at each site and study procedures were conducted in accordance with the Declaration of Helsinki. The present study was approved by the Medical Ethics Committee of the Maastricht University Medical Center, which declared that the Medical Research Involving Human Subjects Act (WMO) does not apply to the study and waived the informed consent requirement because deidentified data were used.

Consent to participate

Written informed consent was obtained from all participants in each study, and data were de-identified by the respective cohorts.

Author contribution(s)

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Dr Grimmer reported receiving consulting fees from AbbVie, Alector, Anavex, Biogen, BMS; Cogthera, Eli Lilly, Functional Neuromodulation, Grifols, Iqvia, Janssen, Noselab, Novo Nordisk, NuiCare, Orphanzyme, Roche Diagnostics, Roche Pharma, UCB, and Vivoryon; lecture fees from Biogen, Eisai, Grifols, Medical Tribune, Novo Nordisk, Roche Pharma, Schwabe, and Synlab; and has received grants to his institution from Biogen, Eisai, and Roche Diagnostics.

Dr Guedj reported having a scientific collaboration on amyloid positron emission tomography (PET) imaging with Life Molecular Imaging before 2018, and honorarium from General Electric and Life Molecular Imaging for expertise and training in the last 3 years.

Dr Hort has consulted Eisai, Biogen, Eli Lilly, Roche and Neurona lab and holds stock options in Alzheon company.

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Dr Kern reported honorarium for consulting for Geras Solutions and Biogen and Bioarctic.

Dr Levin reports speaker fees from Bayer Vital, Biogen, EISAI, TEVA, Zambon, Esteve, Merck and Roche, consulting fees from Axon Neuroscience, EISAI and Biogen, author fees from Thieme medical publishers and W. Kohlhammer GmbH medical publishers and is inventor in a patent "Oral Phenylbutyrate for Treatment of Human 4-Repeat Tauopathies" (PCT/EP2024/053388) filed by LMU Munich. In addition, he reports compensation for serving as chief medical officer for MODAG GmbH, is beneficiary of the phantom share program of MODAG GmbH and is inventor in a patent "Pharmaceutical Composition and Methods of Use" (EP 22 159 408.8) filed by MODAG GmbH, all activities outside the submitted work.

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Dr Maserejian is an employee and shareholder of Biogen, Inc.

Dr Mroczko has received consultation and/or lecture honoraria from Abbott, Wiener, Roche, Cormay, Biameditek, and TK Biotech companies.

Dr Nobili reported receiving fees for teaching courses from GE Healthcare and Biogen, for advisory board participation from Roche and Biogen, and for consultation from Bial.

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Dr Scarmeas reported being a local recruiting site PI for an industry (NovoNordisc) funded multinational, multicenter industry sponsored phase III treatment trial for Alzheimer's disease—funding to institution.
Dr Snyder reported being a consultant to Alzheon Inc, AlzeCure Pharma, and AlzPATH Inc outside the submitted work.
Dr Soininen reported receiving personal consultation fees from AC Immune and Novo Nordisk outside the submitted work.
Dr Sperling reported receiving honorarium for consulting from AC Immune, Acumen, Alnylam, Cytox, Genentech, Janssen, JOMDD, Oligomerix, Neuraly, Neurocentria, Renew, Prothena, and Shionogi; reported receiving research funding from the National Institute on Aging (NIA), Alzheimer's Association, Eisai Inc, Eli Lilly and Company, and Janssen; and reported the following financial relationships for her spouse (Dr Keith Johnson): Cerveau, Janssen, AC Immune, and Novartis.
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Dr Zetterberg reported having served at scientific advisory boards and/or as a consultant for Abbvie, Acumen, Alector, Alzinova, ALZPath, Annexon, Apellis, Artery Therapeutics, AZTherapies, Cognito Therapeutics, CogRx, Denali, Eisai, Nervgen, Novo Nordisk, Optoceutics, Passage Bio, Pinteon Therapeutics, Prothena, Red Abbey Labs, reMYND, Roche, Samumed, Siemens Healthineers, Triplet Therapeutics, and Wave, has given lectures in symposia sponsored by Alzecure, Biogen, Cellectricon, Fujirebio, Lilly, and Roche, and is a co-founder of Brain Biomarker Solutions in Gothenburg AB (BBS), which is a part of the GU Ventures Incubator Program (outside submitted work).
Dr Scheltens is a full-time employee of EQT Life Sciences (formerly LSP) and Professor Emeritus at Amsterdam University Medical Centers. He has received consultancy fees (paid to the university) from Alzheon, Brainstorm Cell and Green Valley. Within his university affiliation he was global PI of the phase 1b study of AC Immune, Phase 2b study with FUJI-film/Toyama and phase 2 study of UCB. He is past chair of the EU steering committee of the phase 2b program of Vivoryon and the phase 2b study of Novartis Cardiology and presently co-chair of the phase 3 study with NOVO-Nordisk.
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Data availability statement

Data access is granted upon approval of individual cohort owners. Researchers interested in working with Amyloid Biomarker Study data can send a research proposal to Dr Willemijn Jansen (willemijn.jansen@maastrichtunivesrity.nl).

Supplemental Material

Supplemental material for this article is available online.

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