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RESEARCH ARTICLE

Adaptive stress coping is associated with cognitive resilience in at-risk cognitively unimpaired older adults

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Abstract

INTRODUCTION: Coping strategies are potentially modifiable factors that may contribute to cognitive resilience. We examined whether adaptive coping modifies the association between Alzheimer's disease (AD) pathology and cognitive decline.

METHODS: We included 99 cognitively unimpaired older adults (mean age = 75.2, 59% females) from two observational cohorts who completed coping strategy assessments. Participants underwent yearly longitudinal cognitive assessments (extended PACC) over 5.3 years on average and cross-sectional Aβ (PiB-PET) and tau (F^{18}-Flortaucipir) neuroimaging. We used linear mixed-effects models.

RESULTS: More frequent use of adaptive coping was associated with better cognitive trajectories, independent of AD pathology. Further, three-way interactions between tau, adaptive coping, and time indicated that individuals with elevated tau and less adaptive coping showed accelerated cognitive decline, while those with more adaptive coping maintained cognitive function.

DISCUSSION: Adaptive coping strategies may confer resilience against cognitive decline. Interventions targeting coping skills could represent promising approaches for maintaining cognition in individuals at risk for AD.

KEYWORDS
Alzheimer's disease, amyloid, cognition, coping strategies, tau

Highlights

- Adaptive coping associates with better cognition independent of Alzheimer's disease (AD) pathology.
- Adaptive coping buffers tau-related effects on cognitive trajectories.
- Coping strategies may be modifiable targets for cognitive decline.

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1 | INTRODUCTION

The pathological hallmarks of Alzheimer's disease (AD)—extracellular amyloid-beta (Aβ) plaques and intracellular neurofibrillary tangles—begin accumulating years to decades before clinical symptoms appear.[1–3] However, a growing body of research shows considerable heterogeneity in the relationship between neuropathological burden and cognitive manifestations, with some individuals maintaining cognitive function despite significant pathology.[4–6] This observed variability in cognitive trajectories among individuals with comparable neuropathology has led to increasing research interest in potential resilience and vulnerability factors that may moderate the relationship between AD pathology and cognitive decline.

Recently, there has been a growing focus on psychological contributors to resilience beyond traditional factors like occupational complexity, intellectual engagement, and education, which have been widely studied.[7] Recent evidence has established important links between psychological factors, such as higher stress-coping abilities with lower AD pathology,[8] and higher repetitive negative thinking with greater AD pathology and cognitive decline.[9] Despite these advances, only a few studies have directly investigated whether psychological factors moderate the relationship between AD biomarkers and cognitive decline. The limited existing research suggests that personality traits modulate the impact of AD pathology on cognitive performance,[10] and that higher levels of purpose in life reduce the effect of AD pathologic changes on cognitive decline among individuals across the AD continuum.[11] Further, studies have shown that social engagement, which involves psychological components such as emotional support and interpersonal coping resources, can buffer the effects of Aβ on cognitive decline among cognitively unimpaired individuals.[12]

Coping styles, referring to the cognitive and behavioral strategies individuals use to manage (i.e., reduce, minimize, master, or tolerate) the internal and external demands that are appraised as taxing or exceeding the individual's resources,[13] are understudied as potential resilience factors in AD. Positive coping styles, including problem-solving, positive reappraisal, seeking social support, and acceptance, have been associated with better psychological outcomes in the general population in various contexts,[14] including the coronavirus disease 2019 (COVID-19) pandemic.[15–17] Additionally, among cognitively unimpaired non-Hispanic Black individuals, problem-focused coping has been associated with better levels of cognition.[18] In contrast, negative coping styles, such as avoidance, have been linked with worse psychological outcomes in the general population[15] and with cognitive decline among individuals along the AD continuum.[19] To our knowledge, the potential of adaptive coping styles as cognitive resilience factors in attenuating the relationship between AD pathology and clinical manifestations has not been studied. As coping styles have been shown to be amenable through cognitive behavioral therapy,[20] they may represent a viable modifiable factor for preventing or delaying cognitive decline.

The recent COVID-19 pandemic, characterized as a traumatic event,[21] provides a unique opportunity to examine these relationships in response to a common stressor that increased psychiatric symptoms globally.[22] Therefore, using previously collected AD biomarker data and longitudinal cognitive assessments past the pandemic, the present study aims to investigate whether coping styles employed during the pandemic moderate the association between AD pathology and cognitive decline. We hypothesize that individuals who employ more adaptive strategies will demonstrate better cognitive trajectories independent of pathology and show better cognitive trajectories relative to their level of pathological burden.

RESEARCH IN CONTEXT

1. **Systematic review**: We reviewed literature using PubMed to identify studies examining psychological resilience factors in Alzheimer's disease (AD). While traditional resilience factors (i.e., education, occupational complexity) have been extensively studied, research on modifiable psychological factors like coping strategies as buffers against AD pathology–cognition relationships remains limited.
2. **Interpretation**: Our findings provide first evidence that adaptive coping strategies may serve as cognitive resilience factors in preclinical AD. Clustering and factor analyses converged to identify a unidimensional adaptive coping capacity, with problem-focused and positive emotion-focused strategies as core components. Individuals using adaptive coping more frequently showed better cognitive trajectories over an average of 5.3 years and lower vulnerability to tau-related cognitive decline.
3. **Future directions**: Future research may benefit from investigating the (1) neurobiological mechanisms underlying coping-mediated resilience; (2) effectiveness of targeted coping interventions in preventing cognitive decline; and (3) generalizability across diverse populations and stressor contexts.

2 | METHODS

2.1 | Participants, design, and setting

Participants of the current study are comprised of participants in longitudinal observational studies in the Harvard Aging Brain Study (HABS; P01 AG036694, PI: Sperling and Johnson) and instrumental activities in daily living Study (IADL; R01 AG053184, PI: Marshall) at Massachusetts General Hospital (Boston, Massachusetts, USA). The participants in HABS were all cognitively unimpaired at recruitment and have been evaluated longitudinally with multi-modal neuroimaging and extensive clinical evaluations. The IADL Study is a natural history, non-interventional study of older adults who were either cognitively unimpaired or had a diagnosis of amnestic mild cognitive impairment

(MCI) at the time of enrollment. Detailed exclusion and inclusion criteria for both cohorts have been described elsewhere.[23] During the pandemic, a study invitation for two sub-study questionnaires measuring COVID-19 related experiences, including perceived stress, coping strategies, lifestyle changes, and other pandemic-related factors, was sent to actively enrolled participants in HABS and IADL, who had a listed email address and had not previously opted out of consideration for sub-studies.[24] The study was reviewed and approved by the Mass General Brigham Institutional Review Board (IRB), and participants provided informed consent both at recruitment to HABS and IADL and at enrollment to the sub-study.

Briefly, participants were invited to participate via email, which included information on the context of the study and a link to access the online consent form and the survey via Research Electronic Data Capture (REDCap), which is a secure web-based software platform for research studies both offline and online.[25] Survey completion was voluntary, and participants were instructed that they could skip questions or stop at any time. The first questionnaire was completed by participants between May 7 and May 26, 2020, about 2 months after the onset of the COVID-19 pandemic in the United States, and the second one between March 23 and May 13, 2021. During the first assessment period (May 2020), Boston was under significant COVID-19 restrictions, including a stay-at-home advisory that had been extended until May 18th and closure of non-essential businesses. By the second assessment period (March–May 2021), restrictions had eased considerably, though many remained in place until the state fully lifted COVID-19 restrictions on May 29, 2021.[26]

The present study used data from both waves of the questionnaire sent to IADL and HABS participants. To maximize the sample size, participants responding to either wave of the questionnaire were included. For participants who responded to both, values reported across each variable measured at both time points were averaged. To be eligible in the current study participants had to have data available for AD biomarkers and be cognitively unimpaired at baseline (i.e., at the closest available cognitive assessment before the pandemic started), with a Clinical Dementia Rating scale (CDR) global score = 0. Altogether, 203 unique participants responded to either the first, second or both waves of the questionnaire. Of these, 139 participants had available Aβ and tau positron emission tomography (PET) data. Participants with MCI or dementia were excluded to isolate the potential buffering effects of adaptive coping strategies on early cognitive decline trajectories among cognitively unimpaired individuals, before the onset of clinically significant cognitive symptoms. After exclusion of participants with a CDR global > 0 and a clinical diagnosis of MCI or dementia (at the time of closest pre-pandemic cognitive assessment), the final sample included in the study was 99 participants (SFigure 1).

Longitudinal cognition data were drawn starting from 2.5 years before participants' COVID-19 questionnaire completion. The date of the first cognitive test included was used as the baseline. Similarly, cross-sectional tau PET and Aβ measurements were obtained within a timeframe of 2.5-0 years before participants' recorded COVID questionnaire date. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline and was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments.

2.2 | Cognition

Participants underwent repeated yearly measurements of cognition (5.3 [SD = 1.4] assessments on average, across a mean of 5.3 [SD = 1.4] years) measured with the extended Preclinical Alzheimer Cognitive Composite-5 (PACC5),[27] which is a summary measure representing the mean of z-scores from performances on five tests sensitive in capturing subtle cognitive decline in preclinical AD.[27] The five tests included: Mini-Mental State Examination (MMSE; range 0–30), Wechsler Memory Scale-Revised (WMS-R) Logical Memory Delayed Recall (LMDR; 0–25), the Digit-Symbol Coding Test (DSC; 0–93), the Free and Cued Selective Reminding Test-Free 1 Total Recall (FCSRT96; 0–96), and category fluency (CAT). A higher value of PACC-5 indicates better cognitive performance. We included the continuous *z*-scores of PACC-5 as the outcome in all models.

2.3 | Coping

Coping strategies were measured with the Brief COPE inventory,[28] which assesses 14 different coping strategies (active coping, planning, positive reframing, humor, emotional support, instrumental support, acceptance, religion, self-distraction, denial, substance use, behavioral disengagement, venting, and self-blame). Each strategy is represented by two questions, totaling 28 items. Participants responded using a 4-point Likert scale indicating how often strategies were used, ranging from 0 "never," to 4 "very often." Some participants completed only the first COVID questionnaire, some only the second, and some both (SFigure 1). If participants had data from both waves, the values for each item were averaged across timepoints, and if data were available from only one wave, that single score was used. For each strategy, the scores of the two corresponding items were averaged, with higher scores representing more frequent use of a strategy. Coping strategies that showed poor reliability (ICCk2 < 0.50, indicating that more than 50% of the variance in measurements is attributable to inconsistency between items) were excluded from further analyses to ensure measurement quality. The excluded coping styles were self-distraction, denial, venting, and behavioral disengagement. The remaining 10 coping strategies showed moderate to excellent reliability (ICCk2: 0.62–0.90) and were retained for subsequent analyses.

2.4 | Covariates and demographics

Covariates included time-constant variables, including age at baseline, sex (as a binary covariate: female/male), years of education (continuous), time in years between PET imaging and first cognitive assessment (continuous), and perceived stress. Perceived stress was measured cross-sectionally at the time of administering the coping questionnaire

using the Perceived Stress Scale (PSS-10),[29] with a single measurement used for each participant. The PSS-10 is a self-reported scale measuring the degree to which a situation is appraised as stressful by an individual. Scores ranging from 0 to 13 reflect low stress; 14–26 moderate stress; and 27–40 high perceived stress. Perceived stress was included as a continuous covariate in all models to account for potential confounding effects on the association between coping and cognition over time.

2.5 | Aβ PET

Fibrillar Aβ burden was measured cross-sectionally with a single measurement used per participant using Pittsburgh Compound B positron emission tomography (PiB-PET) according to established protocols at the Massachusetts General Hospital PET facility, as previously described.[30,31] Briefly, data were acquired using a Siemens/CTI (Knoxville, TN) ECAT HR+ scanner (3D mode; 63 image planes; 15.2 cm axial field of view; 5.6 mm transaxial resolution and 2.4 mm slice interval; 69 frames: 12 × 15 s, 57 × 60 s). After a transmission scan, 8.5 to 15mCi 11C-PiB was injected as a bolus and followed immediately by a 60-min dynamic acquisition. Amyloid PiB distribution volume ratio (DVR) was calculated according to previously established methods that aggregate cortical areas at risk for Aβ burden, across the frontal, lateral temporal, and lateral and medial parietal lobes.[32] We included the aggregate PiB DVR as a continuous measure in all analyses and data across the full range of values were analyzed to capture the spectrum of Aβ burden in this sample.

2.6 | Tau PET

Similarly, tau PET was assessed cross-sectionally with a single measurement used per participant. F^{18}-Flortaucipir (FTP) PET tracer was synthesized and administered at Massachusetts General Hospital using a Siemens ECAT EXACT HR+ scanner (3D mode; 63 image planes; 15.2 cm axial field of view; 5.6 mm transaxial resolution and 2.4 mm slice interval; 69 frames: 12×15 s, 57×60 s) according to the Massachusetts General Hospital Radioactive Drug Research Committee-approved protocols.[33] Following a 10 mCi injection, 18F-FTP data were acquired with a 3D list mode, dynamic protocol using the above PET camera. Static 80 to 100-min acquisition was used. PET data were reconstructed and attenuation corrected, and each frame was evaluated to verify adequate count statistics and absence of head motion. Cerebellar gray matter was used as the reference region from the Freesurfer atlas as previously described.[34] FTP-PET measures were computed (using FreeSurfer) as standardized uptake value ratios (SUVRs) in two anatomic regions commonly exhibiting early tau pathology among cognitively unimpaired individuals: entorhinal cortex (EC), and inferior temporal (IT) cortex.[35] For the present study, the bilateral SUVRs from these two regions were averaged to represent early tau accumulation and used as a continuous measurement. Participants were blind to all PiB and FTP data.

2.7 | Statistical analyses

Characteristics of the whole sample and by clusters were summarized as means and standard deviations (SDs) for continuous variables and as frequencies and percentages for categorical variables. All p values were two-sided with statistical significance set at < 0.05. All analyses were pre-specified and performed with R 4.4.2 (https://www.R-project.org/).

2.8 | Clustering and factor analyses

We used two complementary data reduction methods to examine coping patterns from different perspectives and to increase the robustness of our findings through methodological cross-validation. These included non-hierarchical k-means clustering, which aggregates participants into coping profiles, and factor analysis, which aggregates coping variables into underlying dimensions. By using both approaches, one grouping participants and the other grouping variables, we were able to test the stability and robustness of our findings across different analytic methods.

We conducted k-means clustering on the 10 coping strategies with acceptable reliability (ICC ≥ 0.50). All coping variables were standardized to z-scores before analysis. The optimal number of clusters was determined using three complementary methods: The Elbow Method by plotting the total within-cluster sum of squares against a range of potential cluster solutions (k = 1–15); Silhouette Analysis by calculating average silhouette widths for cluster solutions to assess cluster cohesion and separation[36,37]; and consensus indices from the NbClust package.[38] Between-cluster demographic and clinical differences were assessed using Independent t-tests, Mann-Whitney U-tests, chi-squared tests, or Fisher's exact tests, when appropriate.

As a complementary method, we conducted a factor analysis using principal axis factoring as the extraction method, as it does not assume multivariate normality and is appropriate for identifying latent constructs in psychological data. Prior to analysis, we examined the distributional properties of all ten coping variables. Substance use (67% zero scores) and self-blame (43% zero scores) were excluded despite meeting reliability thresholds due to substantial floor effects and low variability, which could distort factor loadings. The remaining eight coping variables (acceptance, instrumental support, humor, emotional support, positive reframing, active coping, planning, and religion) were included. To determine the optimal number of factors, we examined multiple criteria, including eigenvalues, scree plot inspection, and parallel analysis.

The concordance between the clustering and factor analysis approaches was assessed using a point-biserial correlation between binary-coded cluster membership (high = 1, low = 0) and continuous factor scores. For interpretability, we also calculated Cohen's d as the standardized mean difference in factor scores between the two clusters, as well as r^2 and η^2 to estimate the proportion of variance in factor scores explained by cluster membership.

2.9 | Longitudinal analyses on cognition

Linear mixed random- and fixed-effects models were used to examine the relationship between cognition and coping variables (cluster membership and factor scores) across time, employing a backward elimination algorithm ($p < 0.05$ cutoff) on an initial pool of fixed predictors and the variances of random terms. During backward elimination, non-significant terms were retained if higher-order terms subsuming them (e.g., quadratics, interactions) remained in the model, to maintain proper hierarchical model structure.

Our analysis plan employed two approaches, with a backward elimination algorithm applied separately within each approach. The first approach tested whether coping styles (cluster membership and factor variable) interacted with time in their relations to cognitive trajectories independent of AD pathology. The second approach included the AD pathology predictors (Aβ and tau) and tested higher-order interactions involving them to assess whether the combined effects of AD pathology, time, and coping strategies contribute additively or synergistically to cognitive trajectories.

Fixed terms in the models included time, that is, years in the study (linear and quadratic components), coping variables (time-invariant), Aβ and tau (time-invariant), as well as pertinent two- and three-way interactions among the time, coping and AD pathology predictors (second approach). Covariates were: age at baseline, sex, years of education, perceived stress, number of cognitive assessments (to adjust for potential practice effects), as well as time between biomarker and cognitive assessments, all of which were time-invariant. Random terms included intercepts and the linear time term per participant, allowing for correlation between them, thus accounting for individual differences in both baseline cognition levels and rates of change over time. While all main effects were retained in the models, higher-order interaction terms were subject to backward elimination.

3 | RESULTS

The final sample consisted of 99 participants, of whom 58 (59%) were women, with a mean age of 75.2 years (SD = 7.6, range: 51.0–89.5). Participants had a mean education of 16.8 years (SD = 2.6, range: 12–20), and 19 (19.2%) were APOE ε4 carriers. The mean PACC-5 score at baseline was 0.31 (SD = 0.8, range: −2.10 to 1.95). The mean PiB DVR was 1.2 (SD = 0.2, range: 1.0–1.9) and mean tau SUVR was 1.4 (SD = 0.3, range: 1.0–2.4). The mean score of perceived stress was 14.1 (SD = 8.0, range: 0–37), indicative of low-moderate stress levels in the sample.

The mean time between the first cognitive assessment and Aβ and tau imaging was 0.63 (SD = 0.57) years, ranging from 2.07 years before to 0.88 years after the first cognitive assessment, with three participants exceeding a 1.5-year lag. The mean time between the first cognitive assessment and COVID questionnaire completion was 0.9 years (SD = 2.05), with cognitive assessments ranging from 2.4 years before to 4.4 years after the COVID questionnaire completion. Participants underwent a mean of 5.3 (SD = 1.4) cognitive assessments, ranging from one to eight assessments per participant, resulting in a total of 521 observations. The cognitive assessments spanned a mean total time of 5.3 (SD = 1.4) years, ranging from 0 to 7 years across participants (SFigure 2).

3.1 | Clustering analysis and selection

Multiple methods converged to indicate that a two-cluster solution best represented the structure of coping strategies in our sample. The Elbow Method showed a marked decrease in within-cluster sum of squares from k = 1 to k = 2, with smaller decreases thereafter. Silhouette analysis yielded the highest coefficient (0.20) for k = 2, with near-zero values for higher k. The NbClust package indicated k = 2 as optimal in the majority of indices. Based on this convergence, we performed k-means clustering with k = 2 on standardized coping variables, using 25 random starts (nstart = 25) to avoid local optima.

The resulting clusters were defined as "High Users of Coping Styles" (n = 46) and "Low Users of Coping Styles " (n = 53) based on their distinctive patterns of coping strategy use. The High Coping cluster demonstrated higher scores across several adaptive coping strategies, particularly active coping, planning, and positive reframing, while the Low Coping cluster showed comparatively lower utilization of these coping styles (Figure 1A). There were no significant differences in demographic or clinical characteristics between the High and Low coping clusters (Table 1, Figure 1B).

3.2 | Factor analysis

The factor analysis showed a unidimensional structure underlying coping strategies in the sample. The scree plot and parallel analysis supported a one-factor solution (eigenvalue = 3.5, subsequent < 1). Based on this convergent evidence, we concluded that the coping measures in our sample were best represented by a single underlying dimension rather than multiple distinct factors. The one-factor solution precluded applying any "factor rotation" method subsequent to the initial factor extraction.

Factor loadings revealed a hierarchical structure of coping strategies, with active coping (0.82) and planning (0.82) showing the strongest associations with the general factor (Figure 1C). This pattern suggests a unidimensional structure of adaptive coping in our sample, with problem-focused and positive emotion-focused strategies being the most central components. Higher values on estimated factor scores corresponded to greater use of appropriate coping behaviors.

Despite differences in variable inclusion between clustering and factor analysis (substance use and self-blame excluded from the latter due to floor effects), factor scores were strongly correlated with cluster membership (point biserial $r = 0.83$, 95% CI: 0.76–0.89, $p < 0.001$). The High Copers cluster ($n = 46$) had a mean factor score of 0.83 (SD = 0.44, range: −0.09 to 1.76), while the Low Copers cluster ($n = 53$) had a mean factor score of −0.72 (SD = 0.58, range: −2.63 to 0.16), corresponding to a Cohen's d ≈ 3.0, indicating a large effect. Cluster membership explained approximately 69% of the variance in factor scores. Together, these results confirm that both clustering and factor analysis captured the same underlying coping dimension, supporting the robustness of findings across analytic methods.

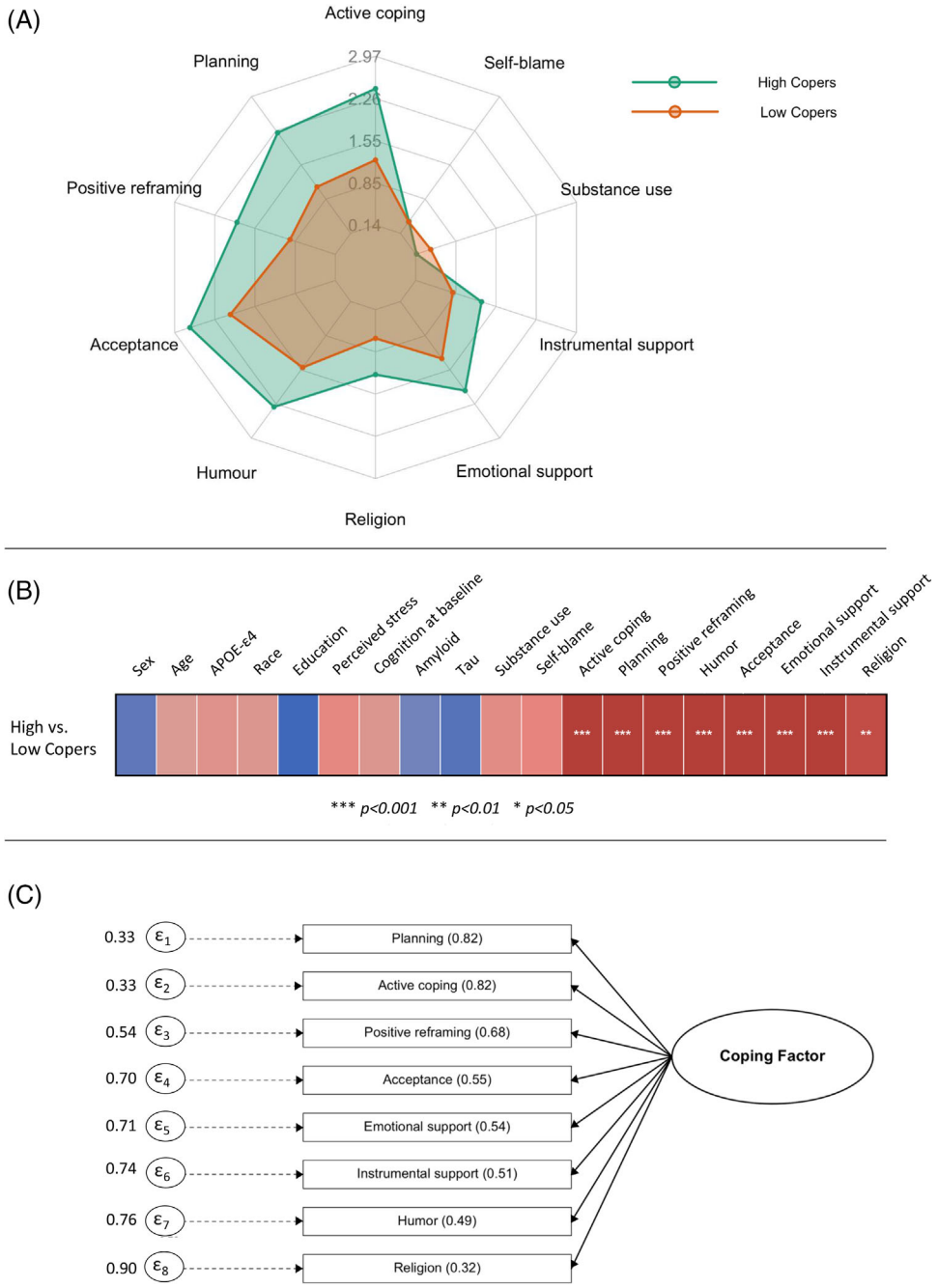

FIGURE 1 Results of clustering and factor analyses. (A) Radar chart showing coping strategy profiles of "High" and "Low" coper clusters. (B) Heat plot of the cluster comparisons. (C) Structural equation diagram of factor analysis. Factor loadings are indicated in parentheses. The "e" terms represent error terms with their variance estimates.

3.3 | Longitudinal analyses on cognition: interaction of coping styles with time

In approach one, examining the association of coping with cognitive decline independent of pathology using the Low/High coping groups formed by the cluster method, the quadratic time component and its interaction with coping were tested but excluded during backward elimination as they were not significant. The final model retained a moderate interaction between coping cluster and linear time (partial regression coefficient β = -0.07, 95% CI: −0.13 to −0.01, p = 0.019), indicating that coping cluster membership moderated cognitive change over time (Table 2). Specifically, individuals in the Low Coping cluster showed more pronounced cognitive decline compared to those in the High Coping cluster (Figure 2).

Similarly, in the final model using the continuous factor coping variable in place of the cluster group distinction, quadratic time terms were excluded during backward elimination. The model retained a strong interaction between the coping factor and linear time (β = 0.05, 95% CI:

TABLE 1 Demographic, clinical, and psychological characteristics within the whole sample and by clusters.

Characteristic	All ($n = 99$) Count (%) / Mean (SD: range)	Cluster 1: High users of coping strategies ($n = 46$) Count (%) / Mean (SD: range)	Cluster 2: Low users of coping strategies ($n = 53$) Count (%) / Mean (SD: range)	Cluster 1 < Cluster 2 *p*-Value*
Sex (female)	58 (58.6%)	28 (60.9%)	30 (56.6%)	0.822
Race				
White	93 (93.9%)	44 (95.7%)	49 (93.5%)	–
Black	3 (3.0%)	1 (2.2%)	2 (3.8%)	–
Asian	3 (3.0%)	1 (2.2%)	2 (3.8%)	–
APOE ε4 status (positive)[a]	19 (19.2%)	13 (28.3%)	6 (11.3%)	0.067
Age	75.2 (7.6; 51.0 to 89.5)	74.9 (7.4; 51.0 to 88.5)	75.37 (7.9; 55.8 to 89.5)	0.781
Education	16.8 (2.6; 12 to 20)	17.3 (2.2; 12 to 20)	16.4 (2.8; 12 to 20)	0.148
Hollingshead Index	22.7 (12.2; 11.0 to 57.0)	20.9 (11.5; 11.0 to 57.0)	24.2 (12.7; 11.0 to 57.0)	0.167
PACC-5 score at baseline	0.31 (0.8; −2.1 to 1.95)	0.43 (0.7; −1.32 to 1.95)	0.20 (0.8; −2.10 to 1.35)	0.216
Perceived stress during COVID-19	14.1 (8.0; 0.0 to 37.0)	12.6 (6.8; 0.0 to 26.5)	15.2 (8.7; 2.0 to 37.0)	0.154
PiB	1.2 (0.2; 1.0 to 1.9)	1.2 (0.2; 1.0 to 2.0)	1.2 (0.2; 1.0 to 2.0)	0.349
Tau (mean across IT and EC tau)	1.4 (0.3; 1.0 to 2.4)	1.4 (0.2; 1.0 to 2.2)	1.4 (0.3; 1.0 to 2.4)	0.257
Active coping	1.8 (0.8; 0.0 to 3.0)	2.4 (0.5; 1.5 to 3.0)	1.2 (0.6; 0.0 to 2.5)	<0.001
Acceptance	2.3 (0.6; 0.0 to 3.0)	2.7 (0.4; 1.5 to 3.0)	2.0 (0.6; 0.0 to 3.0)	<0.001
Planning	1.6 (0.8; 0.0 to 3.0)	2.2 (0.6; 1.0 to 3.0)	1.1 (0.6; 0.0 to 2.5)	<0.001
Positive reframing	1.4 (0.8; 0.0 to 3.0)	1.9 (0.7; 0.5 to 3.0)	0.9 (0.5; 0.0 to 2.0)	<0.001
Humor	1.8 (0.7; 0.0 to 3.0)	2.3 (0.6; 0.5 to 3.0)	1.5 (0.6; 0.0 to 3.0)	<0.001
Religion	0.9 (1.0; 0.0 to 3.0)	1.2 (1.0; 0.0 to 3.0)	0.6 (0.8; 0.0 to 3.0)	0.001
Emotional support	1.6 (0.8; 0.0 to 3.0)	2.0 (0.6; 0.5 to 3.0)	1.3 (0.7; 0.0 to 3.0)	<0.001
Substance use	0.3 (0.6; 0.0 to 3.0)	0.2 (0.3; 0.0 to 1.0)	0.4 (0.8; 0.0 to 3.0)	0.318
Instrumental support	1.0 (0.6; 0.0 to 3.0)	1.3 (0.6; 0.0 to 3.0)	0.8 (0.6; 0.0 to 3.0)	<0.001
Self-blame	0.4 (0.5; 0.0 to 2.5)	0.4 (0.5; 0.0 to 2.5)	0.4 (0.5; 0.0 to 2.0)	0.953

Abbreviations: APOE, apolipoprotein E; COVID-19, coronavirus disease 2019; EC, entorhinal cortex; IT, inferior temporal cortex; PACC-5, Preclinical Alzheimer's Cognitive Composite 5; PiB, Pittsburgh Compound B.

[a]Data available for 98 participants.

*p-Values obtained from independent t-test, Mann-Whitney U-test, chi-squared test, or Mann–Whitney U-test as appropriate for each variable.

0.02–0.08, $p < 0.001$), demonstrating that higher adaptive coping was associated with better maintenance of cognitive function over time (Figure 2).

3.4 | Longitudinal analyses on cognition: interactions of coping styles with time, amyloid, and tau

In the second approach, which further included interactions of AD pathology with time and coping, the final cluster model retained a three-way interaction between quadratic time, coping cluster, and tau ($\beta = 0.08$, 95% CI: 0.00–0.15, $p = 0.039$), suggesting non-linear cognitive trajectories that differed by coping cluster and tau levels (Table 3). Nonsignificant three-way interactions were observed between quadratic time, coping cluster, and Aβ ($\beta = 0.03$, 95% CI: −0.05 to 0.10, $p = 0.517$).

Similarly, the final factor model using the adaptive coping factor scores instead of coping clusters, also retained a three-way interaction between quadratic time, coping factor, and tau (β = -0.05, 95% CI: −0.10 to −0.01, p = 0.016). Similarly, non-significant three-way interactions were observed between quadratic time, coping factor, and Aβ (β = 0.02, 95% CI: −0.03 to 0.07, $p = 0.395$).

In both of the results above, the significant three-way interaction of tau X coping X quadratic time reflected a lower and more rapidly declining cognitive trajectory across time for the combination of higher tau and low scoring on adaptive coping, whereas scoring higher on coping was associated with less pernicious effects of high tau levels on cognition over time (Figure 3).

TABLE 2 Results for predictors retained in final models of separate longitudinal linear mixed-effects models for the coping variables (cluster and factor) predicting PACC-5 scores over time.

	Cluster model			Factor model		
Predictors	***β***	**95% CI**	***p*-Value**	***β***	**95% CI**	***p*-Value**
Age	−0.01	−0.02 to 0.01	0.396	−0.01	−0.02 to 0.01	0.362
Sex (male)	−0.48	−0.70 to −0.25	<0.001	−0.49	−0.71 to −0.26	<0.001
Years of education	0.05	0.01 to 0.10	0.013	0.06	0.02 to 0.10	0.006
COVID-19–related perceived stress	0.01	−0.00 to 0.03	0.114	0.01	−0.00 to 0.02	0.163
No. of cognition assessments	0.10	0.02 to 0.18	0.018	0.09	0.01 to 0.17	0.031
PiB	−0.32	−0.90 to 0.26	0.281	−0.25	−0.83 to 0.33	0.388
Tau	0.01	−0.48 to 0.49	0.979	−0.00	−0.48 to 0.48	0.998
Coping[a]	−0.11	−0.34 to 0.12	0.360	−0.01	−0.13 to 0.12	0.924
Time between pathology assessments and baseline cognition	0.10	−0.10 to 0.30	0.323	0.12	−0.08 to 0.32	0.225
Time from baseline	0.06	−0.04 to 0.15	0.233	−0.05	−0.08 to −0.02	0.004
Time from baseline x coping[a]	−0.07	−0.13 to −0.01	0.019	0.05	0.02 to 0.08	<0.001

Note: β = Partial unstandardized regression coefficient. Cluster model: Marginal R^2 = 0.21, Conditional R^2 = 0.91. Factor model: Marginal R^2 = 0.22, Conditional R^2 = 0.91.

Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 2019; PACC-5, Preclinical Alzheimer's Cognitive Composite 5; PiB, Pittsburgh Compound B.

[a]High Copers as the reference group in cluster models.

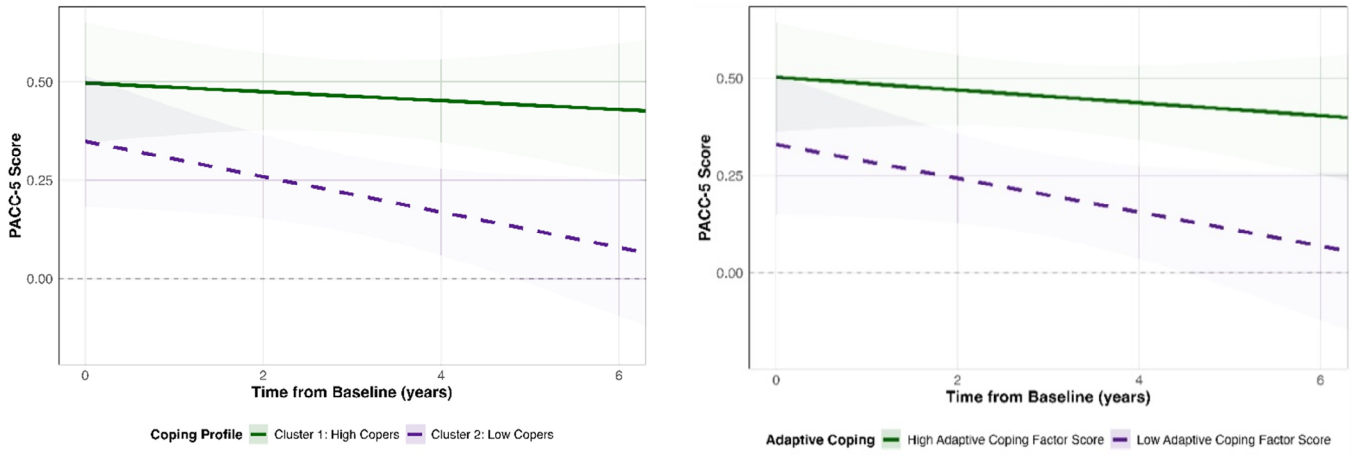

FIGURE 2 Model predicted cognitive trajectories for participants stratified by coping variables. Values for PACC-5 predicted by the fixed effects in the longitudinal models that retained only the linear effect of time with 95% confidence intervals (shaded areas). Left panel shows participants stratified by coping cluster (High Copers [solid line] vs. Low Copers [dashed line]). Right panel shows grouping based on median-split of the adaptive coping factor score. These visualizations illustrate the significant two-way interactions (Coping × Time) observed in the full mixed-effects models. (Predicted values are estimated at the following fixed covariate values: PiB DVR = 1.16, age = 75.08 years, education = 16.73 years, perceived stress = 14.04, number of cognitive assessments = 5.626, time between pathology and baseline assessment = 0.63 years, and sex = male.). PACC-5, Preclinical Alzheimer's Cognitive Composite 5; PiB DVR, Pittsburgh Compound B distribution volume ratio.

4 | DISCUSSION

This study investigated whether adaptive coping strategies employed during a stressful event, the COVID-19 pandemic, are associated with better cognitive trajectories over a mean of 5.3 years among cognitively unimpaired individuals with and without AD pathology. The findings suggest that (1) more frequent use of adaptive coping strategies, including planning, active coping, and positive reframing, is associated with better cognitive trajectories independent of AD pathology, and (2) these coping behaviors moderate the association between tau pathology and cognitive decline. These findings suggest that enhancing adaptive coping strategies represents a potentially

TABLE 3 Results for predictors retained in final models of separate longitudinal linear mixed-effects models for the coping variables (clusters and factor) predicting PACC-5 scores in interaction with AD pathology over time.

	Cluster model			Factor model		
Predictors	***β***	**95% CI**	***p-Value***	***β***	**95% CI**	***p-Value***
Age	−0.01	−0.02 to 0.01	0.390	−0.01	−0.03 to 0.00	0.142
Sex (male)	−0.50	−0.72 to −0.28	<0.001	−0.50	−0.70 to −0.29	<0.001
Years of education	0.05	0.01 to 0.09	0.019	0.06	0.02 to 0.10	0.004
COVID-19–related perceived stress	0.01	−0.00 to 0.02	0.172	0.01	−0.01 to 0.02	0.374
No of cognition assessments	0.09	0.01 to 0.17	0.034	0.07	−0.01 to 0.14	0.090
PiB	0.33	−2.82 to 3.48	0.836	−0.18	−2.84 to 2.49	0.896
Tau	0.36	−2.31 to 3.01	0.790	0.14	−2.16 to 2.44	0.905
Coping[a]	1.55	−0.08 to 3.18	0.062	−1.48	−2.38 to −0.58	0.001
Time between pathology assessments and baseline cognition	0.09	−0.11 to 0.29	0.374	0.08	−0.11 to 0.27	0.389
Time from baseline	1.20	−0.16 to 2.57	0.085	1.75	0.39 to 3.11	0.012
Time from baseline square	−0.19	−0.41 to 0.03	0.084	−0.26	−0.48 to −0.03	0.029
Time from baseline x coping	0.87	0.11 to 1.62	0.025	−0.39	−0.78 to −0.01	0.045
Time from baseline x amyloid	−2.04	−3.26 to −0.82	0.001	−1.43	−2.50 to −0.36	0.009
Time from baseline x tau	−0.55	−1.58 to 0.49	0.298	−1.10	−1.99 to −0.20	0.016
Time from baseline square x coping	−0.12	−0.24 to 0.01	0.041	0.04	−0.03 to 0.11	0.229
Time from baseline square × amyloid	0.32	0.12 to 0.51	0.001	0.25	0.07 to 0.43	0.007
Time from baseline square × tau	0.12	−0.04 to 0.29	0.145	0.16	0.01 to 0.31	0.032
Coping × amyloid	−0.73	−1.97 to 0.51	0.247	0.55	−0.18 to 1.29	0.140
Coping × tau	−0.55	−1.56 to 0.46	0.282	0.61	0.11 to 1.10	0.016
Amyloid × tau	0.36	−1.59 to −2.31	0.718	−0.07	−1.73 to 1.59	0.933
Time from baseline × amyloid × tau	1.27	0.46 to 2.09	0.002	0.85	0.18 to 1.52	0.012
Time from baseline × coping × amyloid	−0.03	−0.53 to 0.47	0.917	−0.17	−0.46 to 0.13	0.265
Time from baseline × coping × tau	−0.70	−1.16 to −0.23	0.003	0.50	0.27 to 0.72	<0.001
Time from baseline square × amyloid × tau	−0.22	−0.35 to −0.10	0.001	−0.16	−0.27 to −0.04	0.006
Time from baseline square × coping × amyloid	0.03	−0.05 to 0.10	0.517	0.02	−0.03 to 0.07	0.395
Time from baseline square × coping × tau	0.08	0.00 to 0.15	0.039	−0.05	−0.10 to −0.01	0.016

Note: Cluster model: Marginal $R^2 = 0.40$, Conditional $R^2 = 0.91$. Factor model: Marginal $R^2 = 0.48$, Conditional $R^2 = 0.91$. β = partial unstandardized regression coefficient.

Abbreviations: APOE, apolipoprotein E; CI, confidence interval; COVID-19, coronavirus disease 2019; PACC-5, Preclinical Alzheimer's Cognitive Composite 5; PiB, Pittsburgh Compound B.

[a]High Copers as the reference group in cluster models.

modifiable target for interventions aimed at delaying cognitive decline in individuals with preclinical AD.

The cluster analysis identified two distinct coping profiles: those who demonstrated a more frequent use of active coping, planning, positive reframing, and acceptance strategies, that is, "High Users of Coping Styles" and those who showed a comparatively less frequent use of these strategies, that is, "Low Users of Coping Styles." The factor analysis further supported a unidimensional structure of adaptive coping, with problem-focused strategies (active coping, planning) and positive emotion-focused strategies (positive reframing, acceptance) as core components. This identified unidimensional structure of adaptive coping suggests that general adaptive coping capacity may be more important than specific strategies, consistent with theories emphasizing coping flexibility rather than specific styles.[39] The convergence of results across both clustering and factor analysis, despite differences in variable inclusion, underscores the robustness of our findings and suggests they are not dependent on the choice of method.

Consistent with our first hypothesis, the longitudinal analyses revealed that individuals who more frequently employed adaptive coping strategies showed better maintenance of cognitive function over time, independent of AD pathology. This finding is consistent with previous research showing associations between psychological factors and cognitive trajectories outcomes in AD.[9,18] Although

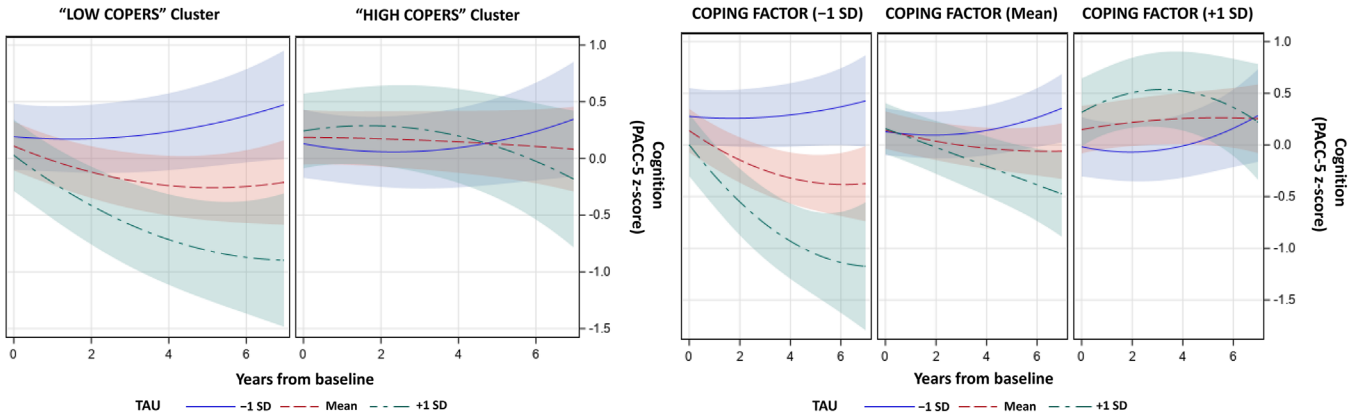

FIGURE 3 Values predicted from the linear mixed effect models for longitudinal PACC-5 scores as a function of coping variables and tau levels. Values predicted for PACC-5 over time by the model fixed effects with 95% confidence intervals (shaded areas). Upper panels show participants stratified based on cluster membership, while lower panels show participants with stratification based on mean and one standard deviation above and below on the coping factor variable. In the figure, participants were further stratified by tau based on mean and one standard deviation above and below the mean on tau. These visualizations illustrate the observed patterns in the data that correspond to the significant three-way interaction (Coping X Quadratic Time X Tau) found in the full mixed-effects models. (Predicted values are estimated at the following fixed covariate values: PiB DVR = 1.16, age = 75.08 years, education = 16.73 years, perceived stress = 14.04, number of cognitive assessments = 5.63, time between pathology and baseline assessment = 0.63 years, and sex = male). PACC-5, Preclinical Alzheimer's Cognitive Composite 5; PiB DVR, Pittsburgh Compound B distribution volume ratio.

studies investigating the association between coping styles and cognition are lacking, our findings are in line with a recent study showing problem-focused coping associates with better levels of cognition among cognitively unimpaired non-Hispanic Black individuals.[18]

Consistent with our second hypothesis, the findings suggested that adaptive coping strategies moderate the association between AD pathology (tau specifically) and cognitive decline. The findings showed a three-way interaction between tau pathology, adaptive coping, and cognitive trajectories over time. Specifically, participants with elevated tau who demonstrated more frequent use of adaptive coping maintained better cognitive function compared to those with similar pathological burden but less frequent adaptive coping use. This finding is in line with the concept of resilience in AD, referring to the ability to maintain cognitive function despite the presence of pathology.[5] The interaction effect was observed with tau pathology, but not with Aβ. This is likely due to tau being more proximally linked to cognitive manifestations than Aβ in AD,[40] suggesting that employing adaptive coping strategies may be especially beneficial for individuals with early tau burden.

Importantly, however, the quadratic interaction terms in our models revealed that the protective effect of adaptive coping strategies as a resilience factor may have temporal limitations. While individuals with more frequent use of adaptive coping maintained better cognitive function initially, the trajectories began to converge at later time points among those with higher tau burden. This suggests that psychological resilience factors may delay, but not entirely prevent, cognitive decline associated with advanced pathology. This pattern is consistent with the concept of resilience in providing a "cognitive buffer" that may eventually become overwhelmed as pathology progresses.[6]

Several biological mechanisms may explain this protective effect. First, the mechanisms underlying this relationship may involve reduced stress activation as a result of better stress-coping associated with adaptive stress-coping strategies, as stress has been linked to hippocampal atrophy, dysregulated hypothalamic pituitary adrenal-axis function, and accelerated cognitive aging.[41] Therefore, adaptive coping strategies may mitigate the physiological consequences of stress, which itself could influence tau accumulation, as stress has been associated with higher levels of tau both in cognitively unimpaired individuals with a history of psychiatric disease[42] and in experimental animal models.[43] This interpretation is in line with research showing better stress-coping associates with lower levels of tau in cognitively unimpaired individuals.[8] Second, individuals employing more adaptive coping strategies may benefit from "brain maintenance," referring to maintaining or preserving brain reserve, that may allow them to tolerate higher levels of pathology before showing cognitive decline.[44,45] Third, adaptive coping strategies may further support cognitive reserve by neural compensation—an active process related to "coping with pathology" by using new or alternate brain networks not compromised by pathology.[6,46] Building on that, adaptive coping may engage large-scale brain networks known to underlie psychological and cognitive resilience. Stronger functional connectivity within the default mode (DMN) and frontoparietal control networks (FPCN) has been associated with slower Aβ-related cognitive decline.[47,48] Moreover, COVID-19-related studies show that FPCN and DMN connectivity associates with pandemic-related distress[49,50] and modulates the association between perceived stress and mental health outcomes.[51] Collectively, adaptive coping may recruit salience–control–DMN circuitry that supports emotional regulation under stress while also facilitating cognitive reserve and compensation in the face of AD pathology.

Our results extend previous research on resilience factors in AD by identifying a potentially modifiable psychological factor that may further buffer against the negative impact of pathology on cognition.

While education, occupational complexity, and intellectual engagement have been extensively studied as resilience factors,[52] psychological and behavioral factors have received less attention. To our knowledge, the role of coping strategies as resilience factors in AD has not been studied. Our findings, however, align with recent studies showing that higher purpose in life[11] and social engagement[12] may buffer the effects of AD pathology on cognitive decline, suggesting that multiple psychological resources may contribute to resilience.

The findings of this study may have important clinical implications for interventions aimed at preventing or delaying cognitive decline in older adults. Unlike demographic factors such as education or occupational history, coping strategies may represent modifiable targets that can be enhanced through behavioral interventions. Indeed, cognitive-behavioral therapy and mindfulness-based interventions have shown effectiveness in improving coping abilities across various populations.[20,53] The protective effects of adaptive coping observed during the pandemic suggest that interventions aimed at enhancing coping abilities may be particularly valuable during times of heightened stress, which may exacerbate vulnerability to cognitive decline in at-risk individuals.

4.1 | Strengths and limitations

The strengths of this study include the longitudinal design spanning a maximum of 7 years, employing complementary analytical approaches (clustering and factor analysis) that yielded convergent findings, and the inclusion of both Aβ and tau PET biomarkers. The study also has several limitations. First, the frequency of use of "maladaptive" coping strategies was notably low across our sample. These maladaptive coping strategies were initially excluded from clustering analysis due to low reliability and subsequently excluded from factor analysis due to low variability and floor effects, preventing direct comparisons between adaptive and maladaptive coping on cognition in the current study. Second, the timing of assessments was not uniform across participants, with variability in the interval between biomarker assessment, cognitive testing, and coping evaluation, and future studies with more homogenous assessment intervals would strengthen these findings. Third, despite the longitudinal design, the observational nature of our study precludes causal conclusions about the effects of coping strategies on cognitive resilience. It is possible that individuals with better maintained cognitive function are more capable of employing adaptive coping strategies, rather than the reverse direction hypothesized in our study. Additionally, personality factors, such as neuroticism which has been associated with cognitive decline,[54] may represent unmeasured confounders that could partly explain the associations observed in this study. Interventional or longitudinal studies across longer time periods will help clarify these temporal relationships. Fourth, the sample consisted of predominantly highly educated and White participants, limiting generalizability to more diverse populations. And finally, the COVID-19 pandemic represents a specific type of a stressor, and coping strategies may differ across various stressors. Future research may benefit from examining whether the protective effects of adaptive coping observed in our study extend to other contexts.

This study provides novel evidence that adaptive coping strategies may confer cognitive resilience among cognitively unimpaired individuals at risk for AD. Individuals who more frequently employed adaptive coping strategies demonstrated better cognitive trajectories over time and appeared less vulnerable to the negative effects of tau pathology on cognition. These findings highlight the importance of psychological factors in AD and suggest that interventions targeting coping abilities may represent promising approaches for maintaining cognition in individuals at risk for AD. Given the potentially modifiable nature of coping strategies, coping-focused interventions may offer a practical and accessible approach to cognitive preservation, particularly when implemented during periods of elevated stress or in early stages of pathological accumulation. Future research should explore the neurobiological mechanisms underlying these resilience effects and examine the effectiveness of targeted interventions to enhance adaptive coping in vulnerable populations.

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All human subjects provided informed consent.

CONFLICT OF INTEREST STATEMENT

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REFERENCES

1. Birdsill AC, Koscik RL, Alex Cody K, et al. Trajectory of clinical symptoms accelerates after 10 years of amyloid. *Alzheimers Dement*. 2020;16(S6):e046459. doi:10.1002/ALZ.046459
2. Bateman RJ, Xiong C, Benzinger TLS, et al. Clinical and biomarker changes in dominantly inherited Alzheimer's disease. *N Engl J Med*. 2012;367(9):795-804. doi:10.1056/NEJMOA1202753/SUPPL_FILE/NEJMOA1202753_DISCLOSURES.PDF
3. Villemagne VL, Burnham S, Bourgeat P, et al. Amyloid β deposition, neurodegeneration, and cognitive decline in sporadic Alzheimer's disease: a prospective cohort study. *Lancet Neurol*. 2013;12(4):357-367. doi:10.1016/S1474-4422(13)70044-9
4. Stern Y. Cognitive reserve and Alzheimer disease. *Alzheimer Dis Assoc Disord*. 2006;20(2):112-117. doi:10.1097/01.wad.0000213815.20177.19
5. Arenaza-Urquijo EM, Vemuri P. Improving the resistance and resilience framework for aging and dementia studies. *Alzheimers Res Ther*. 2020;12(1):1-4. doi:10.1186/S13195-020-00609-2/METRICS
6. Arenaza-Urquijo EM, Vemuri P. Resistance vs resilience to Alzheimer disease: clarifying terminology for preclinical studies. *Neurology*. 2018;90(15):695-703. doi:10.1212/WNL.0000000000005303
7. Arenaza-Urquijo EM, Boyle R, Casaletto K, et al. Sex and gender differences in cognitive resilience to aging and Alzheimer's disease. *Alzheimers Dement*. 2024;19:27. doi:10.1002/ALZ.13844
8. Arenaza-Urquijo EM, Przybelski SA, MacHulda MM, et al. Better stress coping associated with lower tau in amyloid-positive cognitively unimpaired older adults. *Neurology*. 2020;94(15):e1571-e1579. doi:10.1212/WNL.0000000000008979
9. Marchant NL, Lovland LR, Jones R, et al. Repetitive negative thinking is associated with amyloid, tau, and cognitive decline. *Alzheimers Dement*. 2020;16(7):1054-1064. doi:10.1002/ALZ.12116
10. Tautvydaite D, Kukreja D, Antonietti JP, Henry H, Von Gunten A, Popp J. Interaction between personality traits and cerebrospinal fluid biomarkers of Alzheimer's disease pathology modulates cognitive performance. *Alzheimers Res Ther*. 2017;9(1):1-10. doi:10.1186/S13195-017-0235-0/TABLES/3
11. Boyle PA, Buchman AS, Wilson RS, et al. Effect of purpose in life on the relation between Alzheimer disease pathologic changes on cognitive function in advanced age. *Arch Gen Psychiatry*. 2012;69(5):499. doi:10.1001/ARCHGENPSYCHIATRY.2011.1487
12. Biddle KD, d'Oleire Uquillas F, Jacobs HIL, et al. Social engagement and amyloid-β-related cognitive decline in cognitively normal older adults. *Am J Geriatr Psychiatry*. 2019;27(11):1247. doi:10.1016/J.JAGP.2019.05.005
13. Folkman S, Lazarus RS, Gruen RJ, DeLongis A. Appraisal, coping, health status, and psychological symptoms. *J Pers Soc Psychol*. 1986;50(3):571-579. doi:10.1037/0022-3514.50.3.571
14. Chen Y, Peng Y, Xu H, O'Brien WH. Age differences in stress and coping: problem-focused strategies mediate the relationship between age and positive affect. *Int J Aging Hum Dev*. 2018;86(4):347-363. doi:10.1177/0091415017720890
15. Lo HKY, Wong GHS, Chan JKN, et al. COVID-19 perseverative cognition and depressive symptoms in Hong Kong: the moderating role of resilience, loneliness and coping strategies. *J Affect Disord*. 2023;337:86-93. doi:10.1016/J.JAD.2023.05.058
16. Panico F, Luciano SM, Sagliano L, Santangelo G, Trojano L. Cognitive reserve and coping strategies predict the level of perceived stress during COVID-19 pandemic: a cross-sectional study. *Pers Individ Dif*. 2022;195:111703. doi:10.1016/J.PAID.2022.111703
17. Benjamin LR, Wang S. Coping, connection appraisal, and well-being during COVID-19 in the U.S., Japan, and Mexico. *Front Psychol*. 2024;15:1420327. doi:10.3389/FPSYG.2024.1420327
18. Lee JH, Sol K, Zaheed AB, et al. Coping styles and cognitive function in older non-Hispanic black and white adults. *Journals Gerontol Ser B Psychol Sci Soc Sci*. 2023;78(5):789. doi:10.1093/GERONB/GBAD005
19. Shikimoto R, Nozaki S, Sawada N, et al. Coping in mid- to late life and risk of mild cognitive impairment subtypes and dementia: a JPHC Saku Mental Health Study. *J Alzheimers Dis*. 2022;90(3):1085-1101. doi:10.3233/JAD-215712/SUPPL_FILE/SJ-PDF-1-ALZ-10.3233_JAD-215712.PDF
20. Anson K, Ponsford J. Evaluation of a coping skills group following traumatic brain injury. *Brain Inj*. 2006;20(2):167-178. doi:10.1080/02699050500442956
21. Bridgland VME, Moeck EK, Green DM, et al. Why the COVID-19 pandemic is a traumatic stressor. *PLoS One*. 2021;16(1). doi:10.1371/JOURNAL.PONE.0240146
22. Santomauro DF, Mantilla Herrera AM, Shadid J, et al. Global prevalence and burden of depressive and anxiety disorders in 204 countries and territories in 2020 due to the COVID-19 pandemic. *Lancet*. 2021;398(10312):1700-1712. doi:10.1016/S0140-6736(21)02143-7
23. Dagley A, LaPoint M, Huijbers W, et al. Harvard Aging Brain Study: dataset and accessibility. *Neuroimage*. 2017;144(Pt B):255-258. doi:10.1016/J.NEUROIMAGE.2015.03.069
24. Vannini P, Gagliardi GP, Kuppe M, et al. Stress, resilience, and coping strategies in a sample of community-dwelling older adults during COVID-19. *J Psychiatr Res*. 2021;138:176-185. doi:10.1016/J.JPSYCHIRES.2021.03.050
25. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—A metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377-381. doi:10.1016/J.JBI.2008.08.010
26. COVID-19 State of Emergency | Mass.gov. Accessed May 6, 2025. https://www.mass.gov/info-details/covid-19-state-of-emergency
27. Papp KV, Rentz DM, Orlovsky I, Sperling RA, Mormino EC. Optimizing the preclinical Alzheimer's cognitive composite with semantic processing: the PACC5. *Alzheimer's Dement (New York, N Y)*. 2017;3(4):668-677. doi:10.1016/J.TRCI.2017.10.004
28. Carver CS, Brief COPE Inventory. PsycTESTS Dataset. Published online June 11, 2012. doi:10.1037/T04102-000
29. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. *J Health Soc Behav*. 1983;24(4):385-396. doi:10.2307/2136404
30. Klunk WE, Engler H, Nordberg A, et al. Imaging brain amyloid in Alzheimer's disease with Pittsburgh Compound-B. *Ann Neurol*. 2004;55(3):306-319. doi:10.1002/ANA.20009
31. Becker JA, Hedden T, Carmasin J, et al. Amyloid-β associated cortical thinning in clinically normal elderly. *Ann Neurol*. 2011;69(6):1032. doi:10.1002/ANA.22333
32. Raji CA, Becker JT, Tsopelas ND, et al. Characterizing regional correlation, laterality and symmetry of amyloid deposition in mild cognitive impairment and Alzheimer's disease with Pittsburgh Compound B. *J Neurosci Methods*. 2008;172(2):277-282. doi:10.1016/J.JNEUMETH.2008.05.005
33. Shoup TM, Yokell DL, Rice PA, et al. A concise radiosynthesis of the tau radiopharmaceutical, [(18) F]T807. *J Labelled Comp Radiopharm*. 2013;56(14):736-740. doi:10.1002/JLCR.3098
34. Johnson KA, Schultz A, Betensky RA, et al. Tau positron emission tomographic imaging in aging and early Alzheimer disease. *Ann Neurol*. 2016;79(1):110-119. doi:10.1002/ANA.24546
35. Jack CR, Wiste HJ, Weigand SD, et al. Defining imaging biomarker cut points for brain aging and Alzheimer's disease. *Alzheimer's Dement*. 2017;13(3):205-216. doi:10.1016/J.JALZ.2016.08.005
36. Rousseeuw PJ. Silhouettes: a graphical aid to the interpretation and validation of cluster analysis. *J Comput Appl Math*. 1987;20(C):53-65. doi:10.1016/0377-0427(87)90125-7
37. Thorndike RL. Who Belongs in the Family?. *Psychometrika*. 1953;18(4):267-276. doi:10.1007/BF02289263

38. Charrad M, Ghazzali N, Boiteau V, Niknafs A. NbClust: an R Package for determining the relevant number of clusters in a data set. *J Stat Softw*. 2014;61(6):1-36. doi:10.18637/JSS.V061.I06
39. Bonanno GA, Burton CL. Regulatory Flexibility. *Perspect Psychol Sci*. 2013;8(6):591-612. doi:10.1177/1745691613504116
40. Bejanin A, Schonhaut DR, La Joie R, et al. Tau pathology and neurodegeneration contribute to cognitive impairment in Alzheimer's disease. *Brain*. 2017;140(12):3286-3300. doi:10.1093/BRAIN/AWX243
41. Lupien SJ, McEwen BS, Gunnar MR, Heim C. Effects of stress throughout the lifespan on the brain, behaviour and cognition. *Nat Rev Neurosci*. 2009;10(6):434-445. doi:10.1038/nrn2639
42. Palpatzis E, Akinci M, Aguilar-Dominguez P, et al. Lifetime stressful events associated with Alzheimer's pathologies, neuroinflammation and brain structure in a risk enriched cohort. *Ann Neurol*. 2024;95:1058-1068.
43. Sotiropoulos I, Catania C, Pinto LG, et al. Stress acts cumulatively to precipitate Alzheimer's disease-like tau pathology and cognitive deficits. *J Neurosci*. 2011;31(21):7840-7847. doi:10.1523/JNEUROSCI.0730-11.2011
44. Satz P. Brain reserve capacity on symptom onset after brain injury: a formulation and review of evidence for threshold theory. *Neuropsychology*. 1993;7(3):273-295. doi:10.1037/0894-4105.7.3.273
45. Stern Y, Arenaza-Urquijo EM, Bartrés-Faz D, et al. Whitepaper: defining and investigating cognitive reserve, brain reserve, and brain maintenance. *Alzheimers Dement*. 2020;16(9):1305-1311. doi:10.1016/J.JALZ.2018.07.219
46. Stern Y. Cognitive reserve. *Neuropsychologia*. 2009;47(10):2015-2028. doi:10.1016/J.NEUROPSYCHOLOGIA.2009.03.004
47. Boyle R, Klinger HM, Shirzadi Z, et al. Left frontoparietal control network connectivity moderates the effect of amyloid on cognitive decline in preclinical Alzheimer's disease: the A4 Study. *J Prev Alzheimer's Dis*. 2024;11(4):881-888. doi:10.14283/JPAD.2024.140
48. Zhukovsky P, Coughlan G, Buckley R, Grady C, Voineskos AN. Connectivity between default mode and frontoparietal networks mediates the association between global amyloid-β and episodic memory. *Hum Brain Mapp*. 2023;44(3):1147-1157. doi:10.1002/HBM.26148
49. Liu X, Zhao Y, Suo X, et al. Psychological resilience mediates the protective role of default-mode network functional connectivity against COVID-19 vicarious traumatization. *Transl Psychiatry*. 2023;13(1). doi:10.1038/S41398-023-02525-Z
50. Guo Y, Pan N, Zou Y, et al. Neuroimaging insights into the psychosocial impact of the COVID-19 pandemic: a systematic review. *Transl Psychiatry*. 2025;15(1):1-18. doi:10.1038/s41398-025-03423-2
51. Cabello-Toscano M, Vaqué-Alcázar L, Cattaneo G, et al. Functional brain connectivity prior to the COVID-19 outbreak moderates the effects of coping and perceived stress on mental health changes: a first year of COVID-19 pandemic follow-up study. *Biol Psychiatry Cogn Neurosci Neuroimaging*. 2023;8(2):200-209. doi:10.1016/J.BPSC.2022.08.005
52. Stern Y. Cognitive reserve in ageing and Alzheimer's disease. *Lancet Neurol*. 2012;11(11):1006-1012. doi:10.1016/S1474-4422(12)70191-6
53. Khalsa DS. Stress, meditation, and Alzheimer's disease prevention: where the evidence stands. *J Alzheimers Dis*. 2015;48(1):1. doi:10.3233/JAD-142766
54. Luchetti M, Terracciano A, Stephan Y, Sutin AR. Personality and cognitive decline in older adults: data from a longitudinal sample and meta-analysis. *J Gerontol B Psychol Sci Soc Sci*. 2016;71(4):591-601. doi:10.1093/GERONB/GBU184

SUPPORTING INFORMATION

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

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