Journal of Affective Disorders 399 (2026) 121101

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research paper

Cognitive sequala of loneliness in long COVID: Differential associations by loneliness subtypes☆

Leah H. Rubin[a,b,c,d,*], Alba Azola[e,f], Moka Yoo-Jeong[g], Raha M. Dastgheyb[a], Rebecca Easter[b], Ana Ehrenspeck[b], Jennifer M. Coughlin[b,h], Tracy D. Vannorsdall[a,b], Rebecca T. Veenhuis[a,c], Tracey E. Wilson[i]

[a] Department of Neurology, Johns Hopkins University, Baltimore, MD, United States of America
[b] Department of Psychiatry and Behavioral Sciences, Johns Hopkins University, Baltimore, MD, United States of America
[c] Department of Molecular and Comparative Pathobiology, Johns Hopkins University, Baltimore, MD, United States of America
[d] Department of Epidemiology, Johns Hopkins University, Baltimore, MD, United States of America
[e] Department of Pediatrics, Johns Hopkins University, Baltimore, MD, United States of America
[f] Department of Physical Medicine and Rehabilitation, Johns Hopkins University, Baltimore, MD, United States of America
[g] School of Nursing, Bouvé College of Health Sciences, Northeastern University, Boston, MA, United States of America
[h] Department of Psychiatry, University of Texas Southwestern Medical Center, Dallas, TX, United States of America
[i] Department of Community Health Sciences, Downstate Health Sciences University, Brooklyn, NY, United States of America

ARTICLE INFO

Keywords:
Loneliness
Emotional loneliness
Social Loneliness
Cognition
Long COVID

ABSTRACT

Background/Objective: Loneliness is a risk factor for cognitive decline in aging and other clinical populations, but its role in long COVID (LC) remains poorly understood. Individuals with LC may be particularly vulnerable to loneliness due to debilitating, persistent symptoms and reduced functioning. We examined associations between overall loneliness and cognition in LC versus recovered controls, and whether loneliness subtypes (social, emotional) differentially relate to cognitive function.

Methods: Individuals meeting 2024 National Academy of Science, Engineering and Medicine criteria (NASEM) for LC and reporting at least one neuropsychiatric symptom ($n = 120$), along with recovered controls ($n = 51$), completed the 6-item De Jong Gierveld Loneliness Scale and a cognitive test battery. Correlation analyses, corrected for false discovery rate, identified bivariate loneliness-cognition associations. Significant correlations were followed by age-adjusted regressions using residualized loneliness scores, which excluded variance shared with depression and social isolation.

Results: LC participants reported higher overall, emotional, and social loneliness than controls. In bivariate analyses, greater overall and emotional loneliness were associated with more subjective cognitive complaints and poorer verbal fluency in the full sample and LC group, and with cognitive complaints and poorer verbal memory in controls. In adjusted models, residual overall and emotional loneliness remained significantly associated with fluency in LC and the full sample, and with memory in controls. Associations with cognitive complaints did not persist. Social loneliness showed weaker and inconsistent associations.

Conclusion: Overall and emotional loneliness are independently linked to objective cognitive difficulties. Findings highlight emotional loneliness as a potential target for cognitive intervention in LC and recovered individuals.

1. Introduction

Loneliness is increasingly recognized as a modifiable psychosocial risk factor for brain health disorders, including cognitive impairment and mental health conditions, particularly in aging and medically complex populations. Defined as a subjective sense of social

☆ Statistical analyses conducted by LHR

The data used in this study were obtained from RF1MH133411 (Rubin, Veenhuis). These data were deposited into the NIMH National Data Archive (NDA) and will be available upon completion of the grant.

* Corresponding author at: 600 N. Wolfe Street, Carnegie 303, Baltimore, MD, 21287, United States of America.
E-mail address: lrubin@jhu.edu (L.H. Rubin).

https://doi.org/10.1016/j.jad.2025.121101
Received 3 November 2025; Received in revised form 26 December 2025; Accepted 29 December 2025
Available online 4 January 2026
0165-0327/

disconnection due to perceived deficits in relationship quality or quantity (Hawkley and Cacioppo, 2010), loneliness is a transdiagnostic construct that exacerbates mental, physical, and cognitive symptoms (Kall et al., 2020). It is distinct from social isolation, an objective state of isolation indicated by lack of social contact or interactions (Hawkley and Cacioppo, 2010), and from depression, which encompasses a broader constellation of affective symptoms (Cacioppo et al., 2006). Importantly, loneliness is often conceptualized as comprising two distinct subtypes (Manoli et al., 2022; Weiss, 1973), emotional (absence of close, intimate ties) and social loneliness (lack of broader belonging), which may differentially relate to health outcomes (Park et al., 2020).

The COVID-19 pandemic significantly exacerbated both loneliness and social isolation, particularly among individuals with chronic illness and those affected by persistent symptoms of SARS-CoV-2 infection. Rates of severe loneliness nearly tripled during the pandemic, and were associated with elevated depressive symptoms, anxiety, and poorer cognitive function in post-COVID samples (Killgore et al., 2020; Palgi et al., 2020). These effects are thought to arise from a combination of pandemic-related disruptions in social routines, fear of infection, and symptom-related disability.

People with long COVID (LC) frequently experience persistent physical, psychological (e.g., mood and anxiety), and cognitive symptoms (O'Mahoney et al., 2025; Elboraay et al., 2025) that interfere with social functioning and increase vulnerability to loneliness. For example, the UK-based CLoCK study found that adolescents and young adults with LC were over three times more likely to report frequent loneliness compared to those who recovered (Stephenson et al., 2021). Lingering symptoms such as fatigue, brain fog, and mobility issues have also been associated with unemployment, social withdrawal, and reduced quality of life (Nasserie et al., 2021), all key correlates of loneliness.

In aging and medically complex populations, loneliness has been linked to poorer global and domain-specific cognitive performance (executive function [including fluency], psychomotor speed, memory, and motor function) as well as increased subjective cognitive concerns and elevated risk of mild cognitive impairment and dementia (Lee et al., 2025; Cachon-Alonso et al., 2023; Sutin et al., 2020; Sundstrom et al., 2020; Salinas et al., 2022; Harris et al., 2020; Luchetti et al., 2025; Huang et al., 2024; Harb et al., 2025; Kassam and McMillan, 2023; Yin et al., 2019; Yoo-Jeong et al., 2024; O'Luanaigh et al., 2012; Donovan et al., 2017). Meta-analyses estimate that loneliness is associated with a 40 % increased risk of incident dementia, independent of depression and other confounders (Ng et al., 2025; Kuiper et al., 2015).

Although most prior studies have relied on unidimensional loneliness measures, emerging work highlights the importance of distinguishing between emotional and social loneliness. In people with HIV, emotional, but not social, loneliness has been linked to poorer executive functioning (e.g., verbal fluency, behavioral inhibition, attention/working memory) and psychomotor speed (e.g., Digit Symbols, Trail Making Test)(Yoo-Jeong et al., 2024). Conversely, among individuals with mild to moderate dementia, social, but not emotional, loneliness was associated with discourse-level language skills (Carbone et al., 2022). A longitudinal study using the Health and Retirement Survey further showed that older adults with cognitive impairment experience higher levels of overall, emotional, and social loneliness compared to those without impairment, even after controlling for depressive symptoms, physical health, and marital status (Lee et al., 2022).

In this study, we examined whether overall, emotional, and social loneliness were associated with cognitive function in individuals with LC compared to recovered controls. Cognitive function was assessed using both self-report (subjective cognition) and a comprehensive battery of performance-based tasks (objective cognition) across multiple domains implicated in LC and loneliness including executive function, psychomotor speed, memory, and motor function. To empirically capture these constructs, we applied a data-driven approach (principal components analysis) to derive distinct cognitive factors from the full battery. This method groups outcomes according to shared variance, allowing higher-order constructs (e.g., executive function) to be decomposed into specific processes such as inhibitory control, fluency, and attention/working memory. Based on prior studies, we hypothesized that people with LC would report more loneliness than recovered controls and that higher loneliness would be associated with poorer cognition. Specifically, emotional loneliness may relate more strongly to executive function, psychomotor speed, and motor function. In contrast, loneliness may show weaker or non-significant associations with these domains. These relationships were expected to be more pronounced in people with LC compared to controls. Although both loneliness and cognitive difficulties are common in LC, their interrelationship, including potential subtype-specific associations, remains poorly understood. Addressing this gap may facilitate the identification of psychosocial targets to improve cognitive and mental health in this vulnerable population.

2. Methods

2.1. Study participants

Participants included individuals who met the 2024 National Academies of Sciences, Engineering, and Medicine (NASEM) criteria for LC and endorsed at least one persistent neuropsychiatric symptom (e.g., brain fog, headache), as well as individuals who had recovered from SARS-CoV-2 infection without lingering symptoms (controls). Recruitment was conducted through multiple channels including (1) targeted outreach via MyChart to eligible individuals within the Johns Hopkins Health System (JHHS) who had agreed to be contacted for research, (2) flyers posted in clinical and community locations, (3) referrals from enrolled participants, and (4) the Johns Hopkins (JH) HOPE Registry, a centralized database of individuals interested in COVID-19 related studies. MyChart eligibility was determined using a pre-defined algorithm developed in partnership with the JHHS recruitment team, which flagged adults aged 18–80 with documented prior SARS-CoV-2 infection based on either positive PCR/antigen test results or relevant ICD-10 codes (e.g., U09.9 or Z86.16). Both LC and control participants were recruited via these shared mechanisms, although the majority of LC participants were drawn from specialized post-COVID clinics, including the JH Post-Acute COVID-19 Team and the Long COVID Myalgic Encephalomyelitis/Chronic Fatigue Syndrome Clinic at JH.

To confirm cohort assignment, all participants completed a structured symptom inventory administered by trained clinicians (Rubin et al., 2025). This screener queried new or worsening post-COVID symptoms across multiple domains, including fatigue, cognitive complaints, post-exertional malaise [PEM], sleep disruption, orthostatic intolerance, pain, and sensory hypersensitivities. Additional items captured features of dysautonomia and mast cell activation (e.g., vasomotor instability, secretomotor changes, food-related gastrointestinal [GI] symptoms). Participants were classified as LC if they met NASEM criteria and endorsed at least one persistent symptom consistent with LC. Controls were required to report full recovery and denial of all ongoing or recurrent post-COVID symptoms, including neuropsychiatric complaints.

Eligibility criteria included age between 18 and 80, capacity to provide informed consent, and ability to attend in-person study visits. A positive SARS-CoV-2 infection history could be self-reported and included results from at-home tests. Participants were required to be at least eight weeks post–acute infection. Exclusion criteria included: inability to speak or read English, recent or active substance misuse (within the past three months, verified by clinical interview and toxicology screen; cannabis/nicotine use permitted), presence of primary psychotic disorders, and any contraindications for MRI.

2.2. Procedures

This cross-sectional study involved two in person visits conducted between July 2023 and June 2025. After initial telephone screening, eligible participants were invited for an in-person screening visit at Johns Hopkins, during which they provided written informed consent. At this visit, participants completed the Structured Clinical Interview for DSM-IV Disorders (SCID), a toxicology screen, blood draw, and a battery of questionnaires related to COVID-19 history, cognitive symptoms, and mental health (described in detail below). Eligible participants returned for a second visit that included administration of a comprehensive cognitive test battery. All study procedures were approved by the Johns Hopkins University School of Medicine Institutional Review Board (IRB00375493).

2.3. Measures

2.3.1. Loneliness

Loneliness was assessed using the 6-item De Jong Gierveld Loneliness Scale, which yields scores for overall, emotional, and social loneliness (Gierveld and Tilburg, 2006). The scale includes three items each for emotional (e.g., "I often feel rejected") and social (e.g., "There are many people I can trust completely") loneliness. Responses ("Yes," "More or less," "No") were scored per standard guidelines, with subscale scores ranging from 0 to 3 and higher scores indicating greater loneliness. Overall loneliness was calculated by summing all six items (range: 0–6). Internal consistency in this sample was good (α = 0.82 overall; emotional: 0.72; social: 0.84), consistent with previous studies (De Jong Gierveld and Van Tilburg, 2010; Gierveld and Tilburg, 2006).

2.3.2. Cognitive test battery

Cognitive function was assessed using a combination of standard neuropsychological measures, tablet-based tasks via the BrainBaseline platform (Clinical Ink), and self-report questionnaires. Paper-based tests included the Hopkins Verbal Learning Test–Revised, Controlled Oral Word Association Test, the Grooved Pegboard, and the Global Neuropsychological Assessment (Olson et al., 2022), which evaluates story memory, perceptual comparison, verbal fluency (animal fluency, category switching), and digit/spatial span forward and backward. Tablet-based measures included Stroop (color and interference conditions), Symbol Substitution, Trail Making Test Parts 1 and 2, Flanker, and finger tapping tasks (Rubin et al., 2021; Lee et al., 2012). Subjective cognitive difficulties were assessed with the Cognitive Failures Questionnaire (Broadbent et al., 1982; Rast et al., 2009) and subscales from the Behavior Rating Inventory of Executive Function–Adult Version (Roth, 2005).

To reduce dimensionality and align the cognitive outcomes with established constructs, we conducted a principal components analysis with varimax rotation on all cognitive variables. This data-driven approach grouped variables based on shared variance which enabled the identification of separate cognitive constructs. Ten factors were extracted (in order of variance explained) and interpreted based on the strongest loading variables aligning with traditional cognitive processes: (1) *self-reported cognitive complaints*—subjective cognition, (2) *psychomotor speed*—processing speed and motor actions, (3) *motor function*—motor skills (finger tapping), (4) *spatial attention and working memory*—nonverbal executive function, (5) *category-cued fluency*—language, verbal fluency, executive function (animal fluency, category switching), (6) *verbal attention and working memory*—verbal executive function, (7) *narrative verbal episodic memory*—memory (story recall), (8) *list-based verbal episodic memory*—memory (word list recall), (9) *letter-cued fluency*—language, verbal fluency, executive function, and (10) *inhibitory control*—executive function (Flanker). These empirically derived domains capture distinct facets of cognitive function while aligning with established neuropsychological constructs. Factor scores were winsorized to ±3 to minimize the impact of extreme outliers while preserving the full sample. See **Supplemental Materials,** Table S1 for full factor loadings.

2.3.3. Clinical and psychosocial characterization

To characterize clinical and psychosocial features, participants completed validated assessments of physical health, COVID-19 history, and current symptoms. COVID-related features including comorbidities, acute and ongoing symptoms, vaccination status, estimated SARS-CoV-2 variant, and disability, were characterized using the RADx® Underserved Populations (RADx-UP) Tier 1 and Tier 2 measures and the Yale COVID-19 Review of Systems, version 10. To harmonize with the National Institutes of Health (NIH) Researching COVID to Enhance Recovery (RECOVER) study (Thaweethai et al., 2023), we derived a post-acute sequelae of SARS-CoV-2 infection (PASC+) or intermediate classification using a composite symptom burden score based on the Neuro-QoL Short Form v2.0 (Cella et al., 2012), Seattle Angina Questionnaire (Spertus et al., 1995), PROMIS Fatigue Short Form (Cella et al., 2007), and a targeted checklist of PASC symptoms (e.g., post-exertional malaise, anosmia, gastrointestinal, cardiovascular, and autonomic symptoms). Psychiatric symptoms and risk factors were assessed via the SCID-IV and validated scales, including the Patient Health Questionnaire-9, Generalized Anxiety Disorder-7, and the PTSD Checklist–Civilian Version. Social isolation was measured using an adapted Berkman-Syme Social Network Index (Pantell et al., 2013).

2.4. Statistical analyses

Descriptive statistics were used to summarize demographic and clinical characteristics, with means and standard deviations reported for normally distributed continuous variables, medians and interquartile ranges for non-normally distributed continuous variables, and frequencies and percentages for categorical variables. Pearson correlation coefficients were calculated to examine unadjusted associations between loneliness dimensions (overall, emotional, and social) and cognitive factor scores. To control the false discovery rate (FDR), the Benjamini-Hochberg procedure was applied. FDR thresholds were set at 0.05 for the overall sample ($N = 171$) and LC group ($n = 120$). Given that the control group ($n = 51$) was approximately half the size of the LC group, an FDR threshold of 0.10 was used for controls.

For associations that survived FDR correction, multivariable linear regressions were used to evaluate loneliness-cognition relationships after accounting for social isolation and depressive symptoms. To address multicollinearity and isolate the unique contributions on loneliness dimensions, we used a residualization approach (García-García et al., 2024; Garcia et al., 2020). Overall, emotional, and social loneliness were each separately regressed on social isolation and depressive symptoms. The resulting residuals—representing the unique variance in each loneliness variable not explained by either depression or social isolation—were used as predictors in age-adjusted regression models. This approach allowed us to examine the independent associations between each loneliness dimension and cognition, free from the confounding effects of depression and social isolation. Other psychiatric variables (e.g., anxiety, PTSD, alcohol use) were considered but ultimately not included as confounders due to concerns about multicollinearity, limited variability within subgroups, and risk of overadjustment in stratified models. All analyses were conducted using SPSS version 31, with statistical significance for regression models set at $P < 0.05$.

3. Results

3.1. Study population

The final analytic sample included 120 individuals with LC and 51 recovered controls, aged 19–77 years (Table 1). Groups were demographically similar. Most participants were White, female, and highly

Table 1
Characteristics of patients with Long COVID (LC, NAM 2024) versus controls (SARS CoV 2 infected, fully recovered).

	N	LC (n = 120) n (%)	Controls (*n* = 51) n (%)	*P*-value
Demographics				
Age, median (IQR)	171	46.5 (39.2, 57.7)	40 (30, 59)	0.06
Years of education, M (SD)	171	16.9 (2.7)	17.5 (2.8)	0.16
Female sex	171	91 (76.5)	35 (68.6)	0.35
Race	171			0.13
White		98 (81.7)	35 (68.6)	
Black		13 (10.8)	6 (11.58)	
Asian		6 (5.0)	6 (11.8)	
Other		3 (2.5)	4 (7.8)	
Ethnicity	171			0.65
Hispanic or Latino		8 (6.7)	2 (3.9)	
Not Hispanic or Latino		111 (92.5)	48 (94.1)	
Unknown		1 (0.8)	1 (2)	
Employment status	171			<0.001
Currently employed full-time		50 (41.7)	41 (80.4)	
Currently employed part-time		8 (6.7)	2 (3.9)	
Not currently employed, but employed in past year		3 (2.5)	0 (0)	
Disabled		26 (21.7)	0 (0)	
Unemployment supported by savings/other or retired		33 (27.5)	8 (15.7)	
Mental Health and Substance Use				
Lifetime SCID diagnosis	171			
Post-traumatic stress disorder		40 (33.3)	5 (9.8)	0.001
Major depressive disorder		65 (54.2)	18 (35.3)	0.03
Generalized anxiety disorder		33 (27.5)	8 (15.7)	0.12
Panic disorder		16 (13.3)	0 (0)	0.003
Alcohol use disorder		14 (11.7)	7 (13.7)	0.80
Nicotine use				0.49
Never		84 (70)	40 (78.4)	
Past		27 (22.5)	10 (19.6)	
Active in past year		9 (7.5)	1 (2.0)	
Patient Health Questionnaire (PHQ)-9 total score, median (IQR)	171	10.5 (6, 15)	1 (0,3)	<0.001
Generalized Anxiety Disorder (GAD)-7 total score, median (IQR)	171	6 (3,12)	1 (0, 4)	<0.001
PTSD Civilian Scale (PCLC) total score, median (IQR)	171	37 (27.2, 48.7)	19 (18, 24)	<0.001
RADx® Underserved Populations (RADx-UP)				
Pre-existing conditions				
Immunocompromised condition	171	25 (20.8)	1 (2)	<0.001
Autoimmune disease	171	30 (25)	3 (5.9)	0.003
Hypertension	171	40 (33.3)	9 (17.6)	0.04
Diabetes	171	10 (8.3)	2 (3.9)	0.51
Chronic kidney disease	171	5 (4.2)	1 (2)	0.67
Cancer diagnosis and/or treatment in the past 12 months	169	4 (3.4)	1 (2)	1.00
Cardiovascular disease	170	5 (4.2)	0 (0)	0.32
Asthma	171	39 (32.5)	5 (9.8)	0.002
Chronic obstructive pulmonary disease	171	4 (3.3)	0 (0)	0.32
Self-reported disability and of those with disability,	169	54 (45.8)	3 (5.9)	<0.001
Difficulty concentrating, remembering, or making decisions		38 (70.3)	2 (66.7)	
Serious difficulty walking or climbing stairs		37 (68.5)	1 (33.3)	
Difficulty dressing or bathing		24 (44.4)	0 (0)	
Difficulty doing errands alone (i.e., shopping)		34 (62.9)	0 (0)	
Ever received a COVID-19 vaccine	171	115 (95.8)	49 (96.1)	1.00
COVID-19 index variant	119			
Pre-delta		42 (35)		
Delta		33 (27.5)		
Omicron		35 (29.2)		
Post-Omicron		9 (7.5)		
Unknown		1 (0.8)		
Months since first COVID-19 infection, median (IQR)	169	36 (26, 45)	35 (25, 43)	0.52
Months since index COVID-19 infection, median (IQR)	119	35 (25, 44)		
COVID-19 Care: Highest level of care for <u>any</u> COVID-19 infection?	168			<0.001
Hospital intensive care unit (ICU)		7 (5.9)	0 (0)	
Hospital inpatient		10 (8.5)	0 (0)	
Outpatient/Acute Care		64 (54.2)	12 (24)	
Home-based or no care		37 (31.4)	38 (76)	
Yale COVID-19 Review of Symptoms-version 10				
Symptoms during acute COVID-19	170			
Fever		88 (73.3)	36 (70.6)	0.85
Cough or shortness of breath		100 (83.3)	35 (68.6)	0.06
Upper respiratory (sore throat, congestion)		102 (85)	37 (72.5)	0.13
Nausea or vomiting		42 (35)	8 (15.7)	0.02
Diarrhea		40 (33.3)	8 (15.7)	0.03
Loss or altered sense of smell		52 (43.3)	16 (31.4)	0.23
Loss or altered sense of taste		57 (47.5)	14 (27.5)	0.03
Seizure		2 (1.7)	0 (0)	1.00
Headache		101 (84.2)	33 (66)	0.01
Confusion		54 (45)	6 (11.8)	<0.001
PASC score items				
Smell/taste	171	42 (35)	2 (3.9)	<0.001
Postexertional malaise	171	101 (84.2)	2 (3.9)	<0.001
Chronic cough	171	25 (20.8)	1 (2)	<0.001
Brain fog[a]	171	76 (63.3)	0 (0)	<0.001
Thirst	171	51 (42.5)	1 (2)	<0.001
Palpitations	171	81 (67.5)	3 (5.9)	<0.001
Chest pain[a]	169	74 (61.7)	8 (15.7)	<0.001
Fatigue[a]	171	83 (69.2)	4 (7.8)	<0.001
Sexual desire or capacity	171	52 (43.3)	2 (3.9)	<0.001
Dizziness	171	42 (35)	16 (31.4)	0.72
Gastrointestinal	171	102 (85)	15 (29.4)	<0.001
Abnormal movements	171	36 (30)	2 (3.8)	<0.001
Hair loss	171	51 (42.5)	1 (2)	<0.001
PASC total score, median (IQR)	169	17 (13, 24)	1 (0,2)	<0.001
PASC+	170	96 (80)	1 (2.0)	<0.001
Loneliness*†*, median (IQR)	171			
Overall		2 (1, 5)	0 (0, 2)	<0.001
Social		1 (0, 3)	0 (0, 1.7)	<0.001
Emotional		2 (1,3)	0 (0,1)	<0.001
High loneliness	171			
Overall		60 (50)	11 (21.6)	0.001
Social		51 (42.5)	12 (23.5)	0.02
Emotional		66 (55)	9 (17.6)	<0.001
Social isolation*†*, M (SD)	171			
Total score		1.9 (0.75)	2.3 (0.68)	0.002
Cognitive factor scores, M (SD)	171			
Factor 1: Self-reported cognitive complaints†		0.38 (0.94)	−0.87 (0.59)	<0.001
Factor 2: Psychomotor speed		−0.03 (1.04)	0.18 (0.79)	0.20
Factor 3: Motor function		−0.03 (1.01)	−0.02 (0.92)	0.95
Factor 4: Spatial attention and working memory		−0.15 (0.99)	0.33 (0.92)	0.004
Factor 5: Category-cued verbal fluency		−0.03 (1.02)	0.06 (0.94)	0.62
Factor 6: Verbal attention and working memory		0.08 (0.99)	−0.17 (1.04)	0.13
Factor 7: Narrative verbal episodic memory		−0.04 (1.06)	0.10 (0.87)	0.38

(*continued on next page*)

Table 1 (*continued*)

	N	LC (n = 120) n (%)	Controls (*n* = 51) n (%)	*P*-value
Factor 8: List-based verbal episodic memory		0.00 (1.05)	0.03 (0.87)	0.85
Factor 9: Letter-cued verbal fluency		−0.04 (1.01)	0.13 (0.90)	0.31
Factor 10: Inhibitory control		−0.17 (0.99)	0.17 (0.84)	0.03

Outpatient/Acute Care = Hospital emergency department, urgent care/walk-in clinic, primary doctor, health care center.
PASC score is calculated by adding up the scores for each symptom an individual has (Table 2 in RECOVER(Thaweethai et al., 2023)). Score < 12 = PASC-intermediate; ≥12 = PASC+; [a] Additional severity criteria required (see eTables 1 and 2 in Supplemental 3 in RECOVER).
SCID-V=Structured Clinical Interview for making diagnoses according to the American Psychiatric Association's Diagnostic and Statistical Manual for Mental Disorders (DSM).
Group differences were conducted using Independent *t*-tests/Mann-Whitney *U* test for continuous variables and Chi-square/Fisher's Exact Test for categorical variables.
[†] higher = more self-reported cognitive complaints, more loneliness, or less isolated.

educated. Compared to controls, LC participants endorsed higher rates of current mental health symptoms, lifetime psychiatric diagnoses, and medical comorbidities such as autoimmune disease, asthma, hypertension. LC participants also endorsed more severe acute COVID-19 symptoms (e.g., cough/shortness of breath, GI symptoms, headache, confusion, and altered taste). Nearly all participants had received COVID-19 vaccination. Among those with LC, the most common persistent symptoms were GI issues, post-exertional malaise, fatigue, palpitations, brain fog, and chest pain. Fourteen percent of LC participants had been hospitalized, defined as any report of inpatient or ICU care in accordance with WHO COVID-19 severity classification guidelines.

Compared to controls, LC participants reported significantly higher levels of overall, emotional, and social loneliness, greater social isolation, and more subjective cognitive complaints (*P*'s < 0.01). They also demonstrated significantly worse performance in spatial attention and working memory (*P* = 0.004) and inhibitory control (*P* = 0.03).

3.2. Overall loneliness and cognition

In unadjusted analyses, greater overall loneliness was associated with more severe self-reported cognitive complaints (*P* < 0.001) and poorer category-cued fluency (*P* = 0.001) across the full sample (Table 2). Associations with cognitive complaints were evident in both the LC (*P* < 0.001) and control groups (*P* < 0.001), while the category-cued fluency association was specific to the LC group (*P* = 0.001). Among controls, loneliness was instead associated with poorer narrative verbal episodic memory (*P* = 0.004). No other cognitive domains showed significant associations with overall loneliness.

In age-adjusted regression models using residualized loneliness scores, residual loneliness was no longer associated with subjective cognitive complaints in any group (*P*'s > 0.14). However, residual loneliness remained significantly associated with poorer category-cued fluency in the full sample (β = −0.20, *P* = 0.011) and the LC group (β = −0.21, *P* = 0.024). Among controls, residual loneliness continued to relate to poorer narrative verbal episodic memory (β = −0.41, *P* = 0.003).

3.3. Loneliness subtypes and cognition

In unadjusted analyses, both emotional and social loneliness were associated with greater subjective cognitive complaints across the full sample (*P*'s < 0.001). After FDR correction, only emotional loneliness remained significantly associated with poorer category-cued fluency (*P* < 0.001)(Table 3). Among LC participants, both loneliness subtypes were associated with cognitive complaints (*P*'s < 0.001), whereas in controls, only emotional loneliness was linked to greater cognitive complaints (*P* < 0.001).

Subtype-specific patterns emerged for objective cognition. In the LC group, emotional loneliness was significantly associated with poorer category-cued fluency (*P* < 0.001), whereas social loneliness, although statistically significant (*P* = 0.048), did not survive FDR correction. Among controls, emotional (*P* = 0.033) and social loneliness (*P* = 0.018) were associated with poorer narrative verbal episodic memory, but neither survived FDR correction. No other cognitive domains were significantly related to either subtype.

Age-adjusted regression models using residualized loneliness scores showed that while neither loneliness subtype was associated with subjective cognitive complaints in the full sample or LC group, residual emotional loneliness remained significantly associated with subjective cognitive complaints in the controls (β = 0.292, *P* = 0.039). For objective cognition, residual emotional loneliness remained significantly associated with poorer category-cued fluency in the full sample (β = −0.24, *P* = 0.002) and the LC group (β = −0.24, *P* = 0.009). Among controls, both residual emotional (β = −0.36, *P* = 0.001) and residual social loneliness (β = −0.37, *P* = 0.008) continued to be associated with poorer narrative verbal episodic memory.

4. Discussion

This study is among the first to examine associations between

Table 2
Pearson correlations (r) between overall loneliness and cognitive function in the total sample and by Group (patients with Long COVID [LC, NAM 2024], controls [SARS CoV 2 infected, fully recovered]).

	Total Sample		LC		Control	
Factor	r	*P*-value	r	*P*-value	r	*P*-value
1: Self-reported cognitive complaints†	**0.523****	**<0.001**	**0.411****	**<0.001**	**0.455****	**<0.001**
2: Psychomotor speed	−0.087	0.257	−0.084	0.364	0.040	0.781
3: Motor function	0.038	0.618	−0.008	0.928	0.189	0.183
4: Spatial attention and working memory	−0.015	0.846	−0.010	0.901	**0.304***	**0.03**
5: Category-cued verbal fluency	**−0.244****	**0.001**	**−0.290****	**0.001**	−0.126	0.379
6: Verbal attention and working memory	0.035	0.651	0.006	0.947	−0.043	0.764
7: Narrative verbal episodic memory	−0.042	0.587	0.086	0.352	**−0.348***	**0.004**
8: List-based verbal episodic memory	−0.073	0.344	−0.156	0.088	0.189	0.183
9: Letter-cued verbal fluency	−0.092	0.233	−0.062	0.503	−0.088	0.539
10: Inhibitory control	−0.158*	0.039	−0.108	0.242	−0.106	0.457

[†] higher = more self-reported cognitive complaints.
[**] *P* < 0.01
[*] *P* < 0.05 prior to false discovery rate (FDR) correction; Bolded correlation coefficients remained significant after FDR correction.

Table 3
Pearson correlations (r) between loneliness subtypes (emotional, social) and cognitive function in the total sample and by Group (patients with Long COVID [LC, NAM 2024], controls [SARS CoV 2 infected, fully recovered]).

	Total Sample		LC		Control	
Factor	r	*P*-value	r	*P*-value	r	*P*-value
Emotional						
1: Self-reported cognitive complaints†	**0.519****	**<0.001**	**0.360****	**<0.001**	**0.559****	**<0.001**
2: Psychomotor speed	−0.059	0.440	−0.035	0.700	0.024	0.869
3: Motor function	0.074	0.334	0.054	0.556	0.170	0.232
4: Spatial attention and working memory	−0.030	0.698	−0.016	0.861	**0.302***	**0.031**
5: Category-cued verbal fluency	**−0.269****	**<0.001**	**−0.318****	**<0.001**	−0.150	0.292
6: Verbal attention and working memory	0.108	0.161	0.097	0.290	−0.009	0.950
v7: Narrative verbal episodic memory	−0.041	0.596	0.068	0.461	**−0.299***	**0.033**
8: List-based verbal episodic memory	−0.026	0.738	−0.084	0.361	0.187	0.189
9: Letter-cued verbal fluency	−0.047	0.540	0.009	0.924	−0.103	0.470
10: Inhibitory control	**−0.198****	**0.009**	−0.154	0.093	−0.122	0.394
Social						
1: Self-reported cognitive complaints†	**0.398****	**<0.001**	**0.337****	**<0.001**	**0.282***	**0.045**
2: Psychomotor speed	−0.092	0.233	−0.102	0.267	0.047	0.743
3: Motor function	−0.005	0.953	−0.062	0.504	0.172	0.226
4: Spatial attention and working memory	0.003	0.973	−0.004	0.966	0.251	0.075
5: Category-cued verbal fluency	**−0.160***	**0.036**	**−0.181***	**0.048**	−0.082	0.568
6: Verbal attention and working memory	−0.042	0.588	−0.077	0.405	−0.065	0.649
7: Narrative verbal episodic memory	−0.033	0.673	0.077	0.406	**−0.330***	**0.018**
8: List-based verbal episodic memory	−0.099	0.199	−0.175	0.056	0.158	0.268
9: Letter-cued verbal fluency	−0.111	0.149	−0.106	0.247	−0.059	0.681
10: Inhibitory control	−0.083	0.283	−0.035	0.705	−0.074	0.607

† higher = more self-reported cognitive complaints.
** $P < 0.01$
* $P < 0.05$ prior to false discovery rate (FDR) correction; Bolded correlation coefficients remained significant after FDR correction.

loneliness and cognition in individuals with LC, with specific attention to emotional and social loneliness subtypes. We found that greater loneliness, particularly emotional loneliness, was associated with multiple indicators of poorer objective cognitive performance, after accounting for age, depressive symptoms, and social isolation. Although we hypothesized that emotional loneliness would broadly relate to executive function, psychomotor speed, and motor function in LC, the observed associations were more selective. Specifically, residualized emotional loneliness was independently associated with poorer category-cued fluency. This factor was primarily driven by performance on Animal Fluency and category switching, tasks that rely on executive control (e.g., strategic search and clustering, monitoring and inhibition, cognitive flexibility, etc) and semantic memory processes supported by frontal-temporal circuitry (Arrigo et al., 2024; Paschoal et al., 2021). Although fluency is recognized as a component of executive function, our finding suggests that emotional loneliness may selectively relate to certain executive subprocesses rather than executive functioning more broadly.

Among recovered controls, residualized emotional loneliness was associated with verbal episodic memory although we did not hypothesize this relationship. However, this finding is consistent with prior evidence linking loneliness to memory (O'Luanaigh et al., 2012) and increased risk of dementia including Alzheimers's disease (Sundstrom et al., 2020). Social loneliness also showed an association with verbal memory in controls which may reflect broader social disconnection impairing cognitive reserve in memory-related systems. These findings suggest that loneliness is not a generalized risk factor for cognitive difficulties. Rather, loneliness seems to vary depending on the subtype and illness status. In LC, loneliness may exacerbate dysfunction in executive networks already compromised by persistent symptoms whereas in recovered individuals loneliness may more strongly affect medial temporal systems supporting memory.

Associations between loneliness and subjective cognitive complaints did not remain in the LC group or full sample, only recovered individuals, after adjusting for depressive symptoms and social isolation. This pattern suggests that in individuals with greater psychiatric symptom burden, emotional distress, and social isolation may more strongly drive self-perceived cognitive difficulties rather than loneliness. These findings are consistent with prior studies demonstrating that subjective cognitive complaints often relate to affective states in older adults (Reid and Maclullich, 2006; Hill et al., 2016). Conversely, among recovered individuals, residualized emotional loneliness was still associated with subjective complaints. One possibility is that loneliness may independently shape cognitive self-appraisal when mood and medical symptoms are low.

Our findings align with prior research in aging and other clinical populations (e.g., HIV, dementia), where emotional loneliness has been linked to poorer cognitive performance, particularly in domains dependent on frontal and temporal lobe function (Yoo-Jeong et al., 2024; Kuiper et al., 2015; O'Luanaigh et al., 2012; Harb et al., 2025; Wu et al., 2024). Several mechanisms that may underlie these associations include alterations in autonomic and hypothalamic-pituitary-adrenal axis function, sleep fragmentation, disruptions in fronto-limbic circuitry, endothelial dysfunction, heightened inflammation, and reduced immune efficiency (Doane and Adam, 2010; Mwilambwe-Tshilobo et al., 2023; Cacioppo et al., 2000; Adam et al., 2006; Smith et al., 2020; Cacioppo et al., 2002; Hawkley and Cacioppo, 2010). These mechanisms are also relevant to LC, where evidence suggests dysregulation across neuroendocrine, immune, and vascular systems. Thus, emotional loneliness may amplify cognitive vulnerabilities in LC particularly in circuits supporting category switching and fluency.

Strengths of the study include a well-characterized LC sample, the use of both subjective and objective cognitive assessments, and a loneliness measure that distinguishes emotional and social components. The use of residualized loneliness scores also enhances interpretability by controlling for depressive symptoms and social isolation. However, limitations include the cross-sectional design, which precludes causal inferences, and the demographically homogenous sample, which may limit generalizability. The relatively small control group also reduces power for detecting group-specific effects. However, sample sizes for the LC and control groups ($n = 120$ and $n = 51$, respectively) exceed those in our prior work ($n = 42$) where we demonstrated significant loneliness-cognition associations (Yoo-Jeong et al., 2024). In addition, although analytic decisions were guided by prior literature and pre-specified to the extent possible, the study was not preregistered which introduces the potential for hindsight bias or analytic flexibility. Finally, while we adjusted for depressive symptoms and social isolation to isolate loneliness-specific effects, we did not adjust for other psychiatric factors (e.g., anxiety, PTSD, alcohol use). These variables may also contribute to cognitive outcomes but were excluded due to concerns about multicollinearity and over-adjustment.

In sum, this study provides novel evidence that emotional loneliness is independently associated with cognitive difficulties in LC. These associations are domain-specific with emotional loneliness linked more strongly to specific executive processes. Addressing loneliness, particularly its emotional dimension, may be a critical psychosocial intervention target in LC cognitive rehabilitation. Although evidence-based interventions for emotional loneliness remain limited, strategies emerging from the broader loneliness literature could be adapted to LC and include improving social skills and social support, increasing opportunities for social contact, and targeting maladaptive social cognitions (Masi et al., 2011). Future research should replicate these findings in larger, more diverse samples and examine longitudinal trajectories of loneliness and cognition in LC. Investigating biological and psychological mechanisms that mediate these relationships will be critical, as will testing whether interventions targeting emotional loneliness in can improve cognitive outcomes in this population.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jad.2025.121101.

CRediT authorship contribution statement

Leah H. Rubin: Writing – review & editing, Writing – original draft, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Alba Azola:** Writing – review & editing, Supervision, Project administration, Conceptualization. **Moka Yoo-Jeong:** Writing – review & editing, Conceptualization. **Raha M. Dastgheyb:** Writing – review & editing, Supervision, Software, Data curation. **Rebecca Easter:** Writing – review & editing. **Ana Ehrenspeck:** Writing – review & editing, Supervision, Project administration, Conceptualization. **Jennifer M. Coughlin:** Writing – review & editing. **Tracy D. Vannorsdall:** Writing – review & editing. **Rebecca T. Veenhuis:** Writing – review & editing, Funding acquisition. **Tracey E. Wilson:** Writing – review & editing, Conceptualization.

Funding

The work was supported by RF1 MH133411 (Rubin, Veenhuis) and K01AG090135 (Yoo-Jeong).

Declaration of competing interest

All authors declare no conflicts of interest, including relevant financial interests, activities, relationships, and affiliations.

Acknowledgements

The authors would like to first thank the research coordinators who were instrumental in facilitating participant recruitment, scheduling, and data collection. Their dedication and attention to detail were essential to the successful completion of this study. We are especially grateful to Sam Bronkers, Sofia Karras, Hannah Parker, Christina Della Penna, Isabel Santiuste, Holly Shultz, for their invaluable contributions. We would also like to thank Drs. Serena Spudich and Shelli Farhadian for generously sharing their tool: Yale COVID-19 Review of Systems—Version 10. Special thanks go to **Joan Severson**, current CEO of HumanTrue and former president of Digital Artefacts, the original developer of the BrainBaseline platform prior to its acquisition by Clinical Ink, Inc. We further thank the following individuals for their contributions to the development of the iPad-based cognitive assessment platform, **BrainBaseline Assessment of Cognition and Everyday Functioning (BRACE, Clinical Ink, Inc.): Isabel Bagheri** (BRACE design), **Katelyn McDonald** (multimedia design), and **Yefei He, PhD, Dan Amato, Michael Merickel, Allen Best,** and **Jared Sanderfeld** (software engineering and design). Finally, we gratefully acknowledge the study participants, without whom this research would not have been possible.

Data availability

This work described has not been published previously and is not under consideration for publication elsewhere. The manuscript is approved by all authors. If the manuscript is accepted, the article will not be published elsewhere in the same form, in English or in any other language, including electronically, without the written consent of the copyright-holder.

References

Adam, E.K., Hawkley, L.C., Kudielka, B.M., Cacioppo, J.T., 2006. Day-to-day dynamics of experience–cortisol associations in a population-based sample of older adults. Proc. Natl. Acad. Sci. USA 103, 17058–17063.

Arrigo, I.V., Da Silva, P.H.R., Leoni, R.F., 2024. Functional and Effective Connectivity Underlying Semantic Verbal Fluency. Brain Topogr. 37, 1043–1054.

Broadbent, D.E., Cooper, P.F., Fitzgerald, P., Parkes, K.R., 1982. The Cognitive Failures Questionnaire (CFQ) and its correlates. Br. J. Clin. Psychol. 21 (Pt 1), 1–16.

Cachon-Alonso, L., Hakulinen, C., Jokela, M., Komulainen, K., Elovainio, M., 2023. Loneliness and cognitive function in older adults: Longitudinal analysis in 15 countries. Psychol. Aging 38, 778–789.

Cacioppo, J.T., Ernst, J.M., Burleson, M.H., McClintock, M.K., Malarkey, W.B., Hawkley, L.C., Kowalewski, R.B., Paulsen, A., Hobson, J.A., Hugdahl, K., Spiegel, D., Berntson, G.G., 2000. Lonely traits and concomitant physiological processes: the MacArthur social neuroscience studies. Int. J. Psychophysiol. 35, 143–154.

Cacioppo, J.T., Hawkley, L.C., Berntson, G.G., Ernst, J.M., Gibbs, A.C., Stickgold, R., Hobson, J.A., 2002. Do lonely days invade the nights? Potential social modulation of sleep efficiency. Psychol. Sci. 13, 384–387.

Cacioppo, J.T., Hughes, M.E., Waite, L.J., Hawkley, L.C., Thisted, R.A., 2006. Loneliness as a specific risk factor for depressive symptoms: cross-sectional and longitudinal analyses. Psychol. Aging 21, 140–151.

Carbone, E., Piras, F., Pellegrini, F.F., Caffarra, P., Borella, E., 2022. Individual differences among older adults with mild and moderate dementia in social and emotional loneliness and their associations with cognitive and psychological functioning. BMC Geriatr. 22, 859.

Cella, D., Lai, J.S., Nowinski, C.J., Victorson, D., Peterman, A., Miller, D., Bethoux, F., Heinemann, A., Rubin, S., Cavazos, J.E., Reder, A.T., Sufit, R., Simuni, T., Holmes, G. L., Siderowf, A., Wojna, V., Bode, R., McKinney, N., Podrabsky, T., Wortman, K., Choi, S., Gershon, R., Rothrock, N., Moy, C., 2012. Neuro-QOL: brief measures of health-related quality of life for clinical research in neurology. Neurology 78, 1860–1867.

Cella, D., Yount, S., Rothrock, N., Gershon, R., Cook, K., Reeve, B., Ader, D., Fries, J.F., Bruce, B., Rose, M., GROUP, P. C, 2007. The Patient-Reported Outcomes Measurement Information System (PROMIS): progress of an NIH Roadmap cooperative group during its first two years. Med. Care 45, S3–S11.

De Jong Gierveld, J., Van Tilburg, T., 2010. The De Jong Gierveld short scales for emotional and social loneliness: tested on data from 7 countries in the UN generations and gender surveys. Eur. J. Ageing 7, 121–130.

Doane, L.D., Adam, E.K., 2010. Loneliness and cortisol: momentary, day-to-day, and trait associations. Psychoneuroendocrinology 35, 430–441.

Donovan, N.J., Wu, Q., Rentz, D.M., Sperling, R.A., Marshall, G.A., Glymour, M.M., 2017. Loneliness, depression and cognitive function in older U.S. adults. Int. J. Geriatr. Psychiatry 32, 564–573.

Elboraay, T., Ebada, M.A., Elsayed, M., Aboeldahab, H.A., Salamah, H.M., rageh, O., Elmallahy, M., Aboelfarh, H. E., Mansour, L. S., Nabil, Y., Eltawab, A. K. A., Atwan, H. & Alkanj, S., 2025. Long-term neurological and cognitive impact of COVID-19: a systematic review and meta-analysis in over 4 million patients. BMC Neurol. 25, 250.

Garcia, C.B., Salmeron, R., Garcia, C., Garcia, J., 2020. Residualization: justification, properties and application. J. Appl. Stat. 47, 1990–2010.

García-García, C., Salmerón, R., García-García, C., 2024. Unraveling Residualization: enhancing its application and exposing its relationship with the FWL theorem.

Gierveld, J.D.J., Tilburg, T.V., 2006. A 6-Item Scale for Overall, Emotional, and Social Loneliness: Confirmatory Tests on Survey Data. Res. Aging 28, 582–598.

Harb, A., Souza-Talarico, J.N., Willey, G., Da Silva, F.C., De Jesus, M.C.F., Deberg, J., 2025. Loneliness during the COVID-19 pandemic: A potential risk factor for post-pandemic cognitive decline in older adults without dementia. Dement Neuropsychol 19, e20240256.

Harris, M., Brouillette, M.J., Scott, S.C., Smaill, F., Smith, G., Thomas, R., Fellows, L.K., Mayo, N.E., 2020. Impact of Loneliness on Brain Health and Quality of Life Among Adults Living With HIV in Canada. J. Acquir. Immune Defic. Syndr. 84, 336–344.

Hawkley, L.C., Cacioppo, J.T., 2010. Loneliness matters: a theoretical and empirical review of consequences and mechanisms. Ann. Behav. Med. 40, 218–227.

Hill, N.L., Mogle, J., Wion, R., Munoz, E., Depasquale, N., Yevchak, A.M., Parisi, J.M., 2016. Subjective Cognitive Impairment and Affective Symptoms: A Systematic Review. Gerontologist 56, e109–e127.

Huang, Q.M., Zhang, P.D., Shen, D., Gao, J., Li, Z.H., LV, Y. B., Shi, X. M. & Mao, C., 2024. Analysis of changes in social isolation, loneliness, or both, and subsequent cognitive function among older adults: Findings from a nationwide cohort study. Alzheimers Dement. 20, 5674–5683.

Kall, A., Shafran, R., Lindegaard, T., Bennett, S., Cooper, Z., Coughtrey, A., Andersson, G., 2020. A common elements approach to the development of a modular cognitive behavioral theory for chronic loneliness. J. Consult. Clin. Psychol. 88, 269–282.

Kassam, K., McMillan, J.M., 2023. The impact of loneliness and social isolation during COVID-19 on cognition in older adults: a scoping review. Front. Psychol. 14, 1287391.

Killgore, W.D.S., Cloonan, S.A., Taylor, E.C., Dailey, N.S., 2020. Loneliness: A signature mental health concern in the era of COVID-19. Psychiatry Res. 290, 113117.

Kuiper, J.S., Zuidersma, M., Oude Voshaar, R.C., Zuidema, S.U., Van Den Heuvel, E.R., Stolk, R.P., Smidt, N., 2015. Social relationships and risk of dementia: A systematic review and meta-analysis of longitudinal cohort studies. Ageing Res. Rev. 22, 39–57.

Lee, H., Baniqued, P.L., Cosman, J., Mullen, S., McAuley, E., Severson, J., Kramer, A.F., 2012. Examining cognitive function across the lifespan using a mobile application. Comput. Hum. Behav. 28, 1934–1946.

Lee, J.H., Luchetti, M., Aschwanden, D., Sesker, A.A., Strickhouser, J.E., Terracciano, A., Sutin, A.R., 2022. Cognitive Impairment and the Trajectory of Loneliness in Older Adulthood: Evidence from the Health and Retirement Study. J. Aging Health 34, 3–13.

Lee, J.H., Sutin, A.R., Hajek, A., Karakose, S., Aschwanden, D., O'Suilleabhain, P.S., Stephan, Y., Terracciano, A., Luchetti, M., 2025. Loneliness and cognition in older adults: A meta-analysis of harmonized studies from the United States, England, India, China, South Africa, Mexico, and Chile. Psychol. Med. 55, e58.

Luchetti, M., Aschwanden, D., Stephan, Y., Karakose, S., Milad, E., Miller, A.A., zavala, D., Hajek, A., Terracciano, A. & Sutin, A. R., 2025. Loneliness and subjective cognitive concerns in daily life. Aging Ment Health, pp. 1–9.

Manoli, A., McCarthy, J., Ramsey, R., 2022. Estimating the prevalence of social and emotional loneliness across the adult lifespan. Sci. Rep. 12, 21045.

Masi, C.M., Chen, H.Y., Hawkley, L.C., Cacioppo, J.T., 2011. A meta-analysis of interventions to reduce loneliness. Personal. Soc. Psychol. Rev. 15, 219–266.

Mwilambwe-Tshilobo, L., Setton, R., Bzdok, D., Turner, G.R., Spreng, R.N., 2023. Age differences in functional brain networks associated with loneliness and empathy. Netw Neurosci 7, 496–521.

Nasserie, T., Hittle, M., Goodman, S.N., 2021. Assessment of the Frequency and Variety of Persistent Symptoms Among Patients With COVID-19: A Systematic Review. JAMA Netw. Open 4, e2111417.

Ng, T.K.S., Beck, T., Dennis, K.R., Desai, P., Krueger, K., Dhana, K., Wilson, R.S., Evans, D.A., Rajan, K.B., 2025. Social isolation, loneliness, and their joint effects on cognitive decline and incident Alzheimer's disease: Findings from the Chicago health and aging project. J. Prev Alzheimers Dis. 12, 100046.

Olson, L.T., Smerbeck, A., Figueroa, C.M., Raines, J.M., Szigeti, K., Schretlen, D.J., Benedict, R.H.B., 2022. Preliminary Validation of the Global Neuropsychological Assessment in Alzheimer's Disease and Healthy Volunteers. Assessment 29, 817–825.

O'Luanaigh, C., O'Connell, H., Chin, A.V., Hamilton, F., Coen, R., Walsh, C., Walsh, J.B., Caokley, D., Cunningham, C., Lawlor, B.A., 2012. Loneliness and cognition in older people: the Dublin Healthy Ageing study. Aging Ment. Health 16, 347–352.

O'Mahoney, L.L., Routen, A., Gillies, C., Jenkins, S.A., Almaqhawi, A., Ayoubkhani, D., Banerjee, A., Brightling, C., Calvert, M., Cassambai, S., Ekezie, W., Funnell, M.P., Welford, A., Peace, A., Evans, R.A., Jeffers, S., Kingsnorth, A.P., Pareek, M., Seidu, S., Wilkinson, T.J., Willis, A., Shafran, R., Stephenson, T., Sterne, J., Ward, H., Ward, T., Khunti, K., 2025. The risk of Long Covid symptoms: a systematic review and meta-analysis of controlled studies. Nat. Commun. 16, 4249.

Palgi, Y., Shrira, A., Ring, L., Bodner, E., Avidor, S., Bergman, Y., Cohen-Fridel, S., Keisari, S., Hoffman, Y., 2020. The loneliness pandemic: Loneliness and other concomitants of depression, anxiety and their comorbidity during the COVID-19 outbreak. J. Affect. Disord. 275, 109–111.

Pantell, M., Rehkopf, D., Jutte, D., Syme, S.L., Balmes, J., Adler, N., 2013. Social isolation: a predictor of mortality comparable to traditional clinical risk factors. Am. J. Public Health 103, 2056–2062.

Park, C., Majeed, A., Gill, H., Tamura, J., Ho, R.C., Mansur, R.B., Nasri, F., LEE, Y., Rosenblat, J. D., Wong, E. & McIntyre, R. S., 2020. The Effect of Loneliness on Distinct Health Outcomes: A Comprehensive Review and Meta-Analysis. Psychiatry Res. 294, 113514.

Paschoal, A.M., Da Silva, P.H.R., Rondinoni, C., Arrigo, I.V., Paiva, F.F., Leoni, R.F., 2021. Semantic verbal fluency brain network: delineating a physiological basis for the functional hubs using dual-echo ASL and graph theory approach. J. Neural Eng. 18.

Rast, P., Zimprich, D., Van Boxtel, M., Jolles, J., 2009. Factor structure and measurement invariance of the cognitive failures questionnaire across the adult life span. Assessment 16, 145–158.

Reid, L.M., Maclullich, A.M., 2006. Subjective memory complaints and cognitive impairment in older people. Dement. Geriatr. Cogn. Disord. 22, 471–485.

Roth, R.M., 2005. BRIEF-A: Behavior Rating Inventory of Executive Function–adult Version. Professional Manual, Psychological Assessment Resources.

Rubin, L.H., Severson, J., Marcotte, T.D., Savin, M.J., Best, A., Johnson, S., Cosman, J., Merickel, M., Buchholz, A., Del Bene, V.A., Eldred, L., Sacktor, N.C., Fuchs, J.B., Althoff, K.N., Moore, R.D., 2021. Tablet-Based Cognitive Impairment Screening for Adults With HIV Seeking Clinical Care: Observational Study. JMIR Ment Health 8, e25660.

Rubin, L.H., Shi, W., Azola, A., Bhattacharyya, A., Dastgheyb, R.M., Wu, J., Penna, C.D., Parker, H., Santiuste, I., Ehrenspeck, A., Coughlin, J.M., Vannorsdall, T.D., Lu, H., Veenhuis, R., 2025. Blood-Brain barrier disruption in long COVID and cognitive correlates: A cross-sectional MRI study. Brain Behav. Immun. 129, 989–999.

Salinas, J., Beiser, A.S., Samra, J.K., O'Donnell, A., Decarli, C.S., Gonzales, M.M., Aparicio, H.J., Seshadri, S., 2022. Association of Loneliness With 10-Year Dementia Risk and Early Markers of Vulnerability for Neurocognitive Decline. Neurology 98, e1337–e1348.

Smith, K.J., Gavey, S., Ne, R.I., Kontari, P., Victor, C., 2020. The association between loneliness, social isolation and inflammation: A systematic review and meta-analysis. Neurosci. Biobehav. Rev. 112, 519–541.

Spertus, J.A., Winder, J.A., Dewhurst, T.A., Deyo, R.A., Prodzinski, J., McDonell, M., Fihn, S.D., 1995. Development and evaluation of the Seattle Angina Questionnaire: a new functional status measure for coronary artery disease. J. Am. Coll. Cardiol. 25, 333–341.

Stephenson, T., Shafran, R., De Stavola, B., Rojas, N., Aiano, F., Amin-Chowdhury, Z., McOwat, K., Simmons, R., Zavala, M., Consortium, C., Ladhani, S. N. & MEMBERS, C. L. C, 2021. Long COVID and the mental and physical health of children and young people: national matched cohort study protocol (the CLoCk study). BMJ Open 11, e052838.

Sundstrom, A., Adolfsson, A.N., Nordin, M., Adolfsson, R., 2020. Loneliness Increases the Risk of All-Cause Dementia and Alzheimer's Disease. J. Gerontol. B Psychol. Sci. Soc. Sci. 75, 919–926.

Sutin, A.R., Stephan, Y., Luchetti, M., Terracciano, A., 2020. Loneliness and Risk of Dementia. J. Gerontol. B Psychol. Sci. Soc. Sci. 75, 1414–1422.

Thaweethai, T., Jolley, S.E., Karlson, E.W., Levitan, E.B., Levy, B., McComsey, G.A., McCorkell, L., Nadkarni, G.N., Parthasarathy, S., Singh, U., Walker, T.A., Selvaggi, C. A., Shinnick, D.J., Schulte, C.C.M., Atchley-Challenner, R., Alba, G.A., Alicic, R., Altman, N., Anglin, K., Argueta, U., Ashktorab, H., Baslet, G., Bassett, I.V., Bateman, L., Bedi, B., Bhattacharyya, S., Bind, M.A., Blomkalns, A.L., Bonilla, H., Brim, H., Bush, P.A., Castro, M., Chan, J., Charney, A.W., Chen, P., Chibnik, L.B., Chu, H.Y., Clifton, R.G., Costantine, M.M., Cribbs, S.K., Davila Nieves, S.I., Deeks, S. G., Duven, A., Emery, I.F., Erdmann, N., Erlandson, K.M., Ernst, K.C., Farah-Abraham, R., Farner, C.E., Feuerriegel, E.M., Fleurimont, J., Fonseca, V., Franko, N., Gainer, V., Gander, J.C., Gardner, E.M., Geng, L.N., Gibson, K.S., Go, M., Goldman, J. D., Grebe, H., Greenway, F.L., Habli, M., Hafner, J., Han, J.E., Hanson, K.A., Heath, J., Hernandez, C., Hess, R., Hodder, S.L., Hoffman, M.K., Hoover, S.E., Huang, B., Hughes, B.L., Jagannathan, P., John, J., Jordan, M.R., Katz, S.D., Kaufman, E.S., Kelly, J.D., Kelly, S.W., Kemp, M.M., Kirwan, J.P., Klein, J.D., Knox, K.S., Krishnan, J.A., Kumar, A., Laiyemo, A.O., Lambert, A.A., Lanca, M., Lee-Iannotti, J.K., Logarbo, B.P., Longo, M.T., Luciano, C.A., Lutrick, K., Maley, J.H., Marathe, J.G., Marconi, V., Marshall, G.D., Martin, C.F., et al., 2023. Development of a Definition of Postacute Sequelae of SARS-CoV-2 Infection. JAMA 329, 1934–1946.

Weiss, R.S., 1973. Loneliness: The experience of emotional and social isolation. The MIT Press.

Wu, X., Xiang, M., Jing, H., Wang, C., Novakovic, V.A., Shi, J., 2024. Damage to endothelial barriers and its contribution to long COVID. Angiogenesis 27, 5–22.

Yin, J., Lassale, C., Steptoe, A., Cadar, D., 2019. Exploring the bidirectional associations between loneliness and cognitive functioning over 10 years: the English longitudinal study of ageing. Int. J. Epidemiol. 48, 1937–1948.

Yoo-Jeong, M., Dastgheyb, R.M., Shorer, E.F., Demsky, C., Fox, O., Inaganti, D., Kanner, S., Neijna, A.G., Buchholz, A., Wilson, T.E., Rubin, L.H., 2024. Emotional Loneliness Is Related to Objective Cognitive Function in Older People With HIV in the Washington-Baltimore Area: A Cross-sectional Study. J. Assoc. Nurses AIDS Care 35, 519–529.