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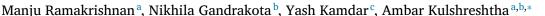
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# **Brief Report**

# Association of psychological stress and subjective cognitive decline



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#### ABSTRACT

Psychological stress is associated with several long-term consequences, including cognitive decline. Our study examined the relationship between psychological stress levels and subjective cognitive decline (SCD) using cross-sectional data from CDC's Behavioral Risk Factor Surveillance System (BRFSS 2020–2022) for participants aged 45 years and older. Among 881,479 participants, 7.5 % were African American, and 10.7 % reported high psychological stress, with 29 % experiencing SCD. High psychological stress had a 3-fold risk of SCD compared to low psychological stress (OR: 3.3; 95 % CI: 2.8, 4.0). A significant interaction between psychological stress and BMI was found in their association with SCD (p = 0.013). Individuals with high psychological stress and a BMI  $\geq$  25 had 4.3 times higher SCD risk (OR: 4.3; 95 % CI: 3.9, 4.7) compared to those with low psychological stress and a BMI  $\leq$  25 (OR: 0.23, 95 % CI: 0.2, 0.3). These results highlight the importance of addressing stress to prevent cognitive decline.

# 1. Introduction

Subjective cognitive decline (SCD) is a potential precursor to dementia, characterized by self-reported confusion or memory loss [1]. The Centers for Disease Control and Prevention (CDC) reports a SCD prevalence of 11.7 % in adults aged 65+ and 10.8 % in those aged 45–64, which affects quality of life and leads to increased healthcare utilization [2]

A recent American Psychological Association survey found that 37 % of US adults reported daily symptoms of stress, with 21 % noting increased forgetfulness [3]. Research links acute and chronic stress to impaired mental health and cognition, suggesting a prominent role in SCD [4]. However, this relationship is likely bidirectional, as stress can worsen perceptions of cognitive decline, while cognitive impairment can increase stress [5].

Prior studies show that psychological stress and poor mental health impair cognition by affecting key brain regions involved in cognition and emotional regulation (e.g., hippocampus, amygdala, prefrontal cortex) [5,6]. However, major reviews like the Lancet Commission have not discussed stress as a dementia risk factor, possibly due to limited large-scale evidence, emphasizing the necessity for further research in this area [7,8]. The relationship between psychological stress and SCD is complex and can be influenced by numerous factors, including but not limited to age, sex, and lifestyle [4]. Our study examined the association

between psychological stress and SCD in a large nationally representative sample, hypothesizing that higher psychological stress correlates with greater SCD.

# 2. Methods

# 2.1. Study data

The CDC's Behavioral Risk Factor Surveillance System (BRFSS) is a national monthly telephone survey collecting data regarding healthrelated behaviors and chronic health conditions from US residents [9]. The dataset is de-identified, publicly available, and exempted from IRB review. Our study utilized the data from 2020 to 2022, including participants aged 45 years and older. Psychological stress levels were categorized based on participants' self-reported number of poor mental health days in the past 30 days. Individuals reporting 0–13 days of poor mental health and 14-30 days were categorized into high psychological stress and low psychological stress groups, respectively [10]. SCD was assessed based on whether they experienced confusion or memory loss during the past 12 months. Respondents who answered "yes" were classified as having SCD. Sociodemographic characteristics that were assessed include age (categorized into 45-64 years, 65-79 years, and 80 years and above), sex (male, female), race (White, African American, and other), education (high school or below, and college or above), and income (<

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 Table 1

 Demographic characteristics based on the level of psychological stress.

Characteristic	Overall	Low psychological stress	High psychological stress*	p-value
Psychological Stress	881,479	787,515¹ (89.3 %)	93,9641 (10.7 %)	
Subjective Cognitive Decline	16,253 (10.1 %)	11,326 (7.9 %)	4927 (28.9 %)	< 0.001
Age (Years)				< 0.001
45–64	416,228 (48.6 %)	359,697 (47.1 %)	56,531 (61.8 %)	
65–79	340,811 (39.8 %)	311,957 (40.8 %)	28,854 (31.5 %)	
80+	98,776 (11.5 %)	92,625 (12.1 %)	6151 (6.7 %)	
Sex				< 0.001
Female	486,409 (55.2 %)	425,944 (54.1 %)	60,465 (64.3 %)	
Male	395,070 (44.8 %)	361,571 (45.9 %)	33,499 (35.7 %)	
Race				< 0.001
White	686,653 (80.1 %)	617,157 (80.6 %)	69,496 (76.4 %)	
African American	64,586 (7.5 %)	56,816 (7.4 %)	7770 (8.5 %)	
Other	105,738 (12.3 %)	92,024 (12 %)	13,714 (15.1 %)	
Education				< 0.001
College or above	603,707 (68.9 %)	545,955 (69.7 %)	57,752 (61.8 %)	
High school or below	272,848 (31.1 %)	237,133 (30.3 %)	35,715 (38.2 %)	
Income				< 0.001
≥50,000	572,633 (65.0 %)	526,876 (66.9 %)	45,757 (48.7 %)	
<50,000	308,846 (35.0 %)	260,639 (33.1 %)	48,207 (51.3 %)	
Smoking Status				< 0.001
Never	465,481 (56.3 %)	427,224 (57.8 %)	38,257 (43.2 %)	
Former	261,148 (31.6 %)	232,336 (31.5 %)	28,812 (32.6 %)	
Current	100,429 (12.1 %)	79,037 (10.7 %)	21,392 (24.2 %)	
BMI				< 0.001
<25	232,071 (29.3 %)	209,124 (29.6 %)	22,947 (27.1 %)	
≥25	559,275 (70.7 %)	497,433 (70.4 %)	61,842 (72.9 %)	
Diabetes	159,773 (18.2 %)	136,481 (17.4 %)	23,292 (24.9 %)	< 0.001
CVD	64,786 (7.4 %)	54,389 (7.0 %)	10,397 (11.2 %)	< 0.001

<sup>&</sup>lt;sup>1</sup>n ( %).

\$50,000,  $\geq $50,000$  per year). Lifestyle factors included smoking status (never, former, and current smokers) and BMI (< 25,  $\geq$  25). Cardiovascular factors were assessed based on self-reported diabetes and cardiovascular disease (CVD).

#### 2.2. Statistical analysis

Participant characteristics were summarized as proportions with chisquare tests comparing groups. Univariate and multivariate logistic regression assessed the association between psychological stress and SCD while controlling for sociodemographic, lifestyle, and CVD factors. Covariates were sequentially added to the models: Model 1 adjusted for sociodemographic (age, sex, education, race, income); Model 2 additionally adjusted for lifestyle (BMI, smoking, alcohol); Model 3 added CVD factors (diabetes, CVD). Potential interactions with age, race, gender, education, and body mass index (BMI) were explored. Analyses were performed using R (version 4.2.2).

#### 3. Results

A total of 881,479 participants were included in the pooled data. 55.2 % of the respondents were females, and 44.8 % were males. 80.1 % were White, 7.5 % were African American, and 12.3 % identified as Other. Additionally, 31 % of participants had a high school diploma or less, and 35 % reported earning less than \$50,000. 56.3 % of individuals never smoked, 31.6 % were former smokers, and 12.1 % currently smoked. 70.7 % of participants had a BMI > 25, 18.2 % reported having diabetes, and 7.4 % had CVD. Among those with high psychological stress (10.7 %), 29 % reported SCD. The high psychological stress group had a greater proportion of participants aged 45–64 (61.8 %), predominantly female (64.3 %), and White (76.4 %). Participants with high psychological stress were more likely to have a lower income (<\$50,000), with 51.3 % earning less, 72.9 % being overweight/obese, 24.9 % reporting diabetes, 11.2 % having CVD, and 24.2 % being cur-

Table 2
Association of psychological stress and subjective cognitive de-

OR <sup>a</sup>	95 % CI <sup>a</sup>	p-value
4.7	4.3, 5.1	< 0.001
4.5	4.1, 4.9	< 0.001
4.2	3.8, 4.6	< 0.001
3.3	2.8, 4.0	< 0.001
	4.7 4.5 4.2	4.7 4.3, 5.1 4.5 4.1, 4.9 4.2 3.8, 4.6

<sup>&</sup>lt;sup>a</sup> OR = Odds Ratio, CI = Confidence Interval.

rent smokers. (Table 1) Older age, lower education, and lower income levels were statistically significant, demonstrating the association with SCD. Smoking status and the presence of CVD factors were also statistically significant, with current smokers and individuals with these health conditions showing increased risk (p < 0.001).

Logistic regression analysis demonstrated a strong association between psychological stress and SCD (Table 2). In the unadjusted model, the high psychological stress group was more than four times as likely to experience SCD compared to the low psychological stress group (OR: 4.7 (95 % CI: 4.3, 5.1) p < 0.001). This strong association persisted even after sequentially adjusting for covariates in subsequent models: sociodemographic (Model 1: OR 4.5, 95 % CI: 4.1, 4.9, p < 0.001), lifestyle (Model 2: OR 4.2, 95 % CI: 3.8, 4.6, p < 0.001), and CVD factors (Model 3: OR 3.3, 95 % CI: 2.8, 4.0, p < 0.001).

A significant interaction between psychological stress and BMI was observed (p < 0.01), suggesting that the impact of psychological stress on SCD varies by BMI category. On further analysis, among individuals

<sup>&</sup>lt;sup>2</sup>Pearson's Chi-squared test.

<sup>\*</sup>Low psychological stress: 0-13 days; High psychological stress:14-30 days.

<sup>&</sup>lt;sup>b</sup> Model 1: Adjusted for sociodemographic factors, including age, sex, race, education, income.

 $<sup>^{\</sup>rm c}$  Model 2: Further adjusted for lifestyle factors, including BMI and smoking status.

<sup>&</sup>lt;sup>d</sup> Model 3: Further adjusted for cardiovascular factors, including diabetes and CVD.

with high psychological stress and BMI  $\geq$  25, the odds of SCD were 4.3 times compared to low psychological stress and BMI < 25 (95 % CI: 3.9, 4.7). In contrast, for individuals with low psychological stress and BMI < 25, the odds of SCD compared to high psychological stress and BMI  $\geq$  25 were 0.23 (95 % CI: 0.2, 0.3). The effects of age, race, gender, and smoking were not statistically significant.

#### 4. Discussion

Subjective cognitive decline can be an early manifestation of dementia, a leading cause of disability and dependence among older adults [2]. Our study demonstrates a significant association between high psychological stress and SCD after adjusting for demographic, lifestyle, and cardiovascular factors, with a statistically significant interaction between psychological stress and BMI.

Psychological stress activates the sympathetic nervous system and HPA axis, increasing catecholamines and cortisol levels, which can cause structural changes and neuronal degeneration, impacting cognition [11]. Prolonged activation of these pathways can disrupt efficient memory encoding, consolidation, and retrieval of memories [12]. These mechanisms may explain our findings and highlight the need for stress management strategies to mitigate cognitive decline.

Our analysis revealed a significant interaction between high psychological stress and high BMI, suggesting that the effects of psychological stress may vary by BMI levels. A higher BMI has been associated with lower cognitive scores, and prior studies have shown that a higher BMI is associated with a greater negative effect of stress, particularly in women [13]. Furthermore, studies have also demonstrated that individuals with chronic exposure to stress combined with a high waist-hip ratio demonstrated poorer memory performance [14]. Several pathophysiological mechanisms have been reported in the development of obesity-associated neuroinflammation, a known precursor to dementia [15]. Insulin resistance, disruption of gut microbes, and chronic systemic inflammation are believed to affect brain parenchyma and lead to cognitive decline [15]. Since higher BMI has been associated with cognitive decline, we hypothesize that stress may contribute to cognitive decline, at least in part, through its impact on BMI. Further research is needed to elucidate the mechanisms by which BMI influences the association between stress and cognitive decline.

Our findings align with prior research linking SCD to several known risk factors, including older age, lower education, income, smoking, CVD, and diabetes [16]. Additionally, our study reinforces that psychological stress is associated with an increased risk of self-reported SCD, after adjusting for these established risk factors. Previous evidence has shown that psychological distress, characterized by anxiety, depression, and somatic symptoms, is linked with increased self-reported SCD and poorer cognitive performance compared to informant-reported SCD [17]. The REGARDS study identified that high perceived stress is significantly associated with cognitive impairment across diverse demographics, including age, sex, and race, further supporting the role of stressrelated pathways in cognitive decline [18]. Chapman S et al. found that individuals who developed mild cognitive impairment had previously self-reported SCD, suggesting a strong association between SCD and early cognitive dysfunction [19]. The current study and previous literature together bring attention to the complex relationship between stress, SCD, and progression to cognitive dysfunction.

While our study offers additional evidence regarding sociodemographic, lifestyle, and CVD factors, further studies are warranted to determine the direction of the association and the underlying mechanisms to understand the effect of psychological stress on cognitive symptoms. The dynamic interplay between endogenous factors (e.g., genetic predispositions, metabolic disruptions) and exogenous stressors (e.g., environmental, social stress) adds complexity to the stress-cognition relationship with emerging evidence suggesting that stress influences cognitive outcomes through its impact on metabolomic, inflammatory, and neuronal signaling pathways which can compromise neuronal health and

contribute to cognitive decline [20,21]. Disruption of these pathways may impair cellular energy processes, promote inflammation, and alter neurotransmitter balance, all of which can influence the progression of cognitive dysfunction or the maintenance of cognitive well-being [22].

Our study has several strengths, including a large and nationally representative sample and good response rates for a survey study (approximately 45 %). However, our study has a few limitations. The data is self-reported, with the potential for recall bias. The study's cross-sectional design limits our ability to infer any causality. Additionally, hypertension, a key risk factor for cognitive decline, was not available in the 2020 BRFSS data, limiting our assessment of all CVD factors linked to psychological stress and SCD. Continued research using comprehensive data and longitudinal studies is essential to determine the direction of the association and the underlying mechanisms to understand the effect of the complex relationship between psychological stress and cognitive decline.

#### 5. Conclusion

Our study demonstrated a strong and independent association between high psychological stress and SCD and highlights the importance of recognizing psychological stress as a modifiable factor for cognitive health. Further understanding the association between stress and cognitive decline can lead to more comprehensive public health interventions to improve well-being and enhance brain health. Future investigations could gain valuable insights by incorporating advanced computational techniques to examine the complex and evolving interplay of stress-related cognitive changes across multiple domains. Fostering collaboration among experts in neuroscience, biology, and data science may enhance our understanding of these mechanisms and support the development of targeted strategies to promote cognitive resilience.

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# Disclosures

None.

## Data statement

This study uses publicly available data from the BRFSS, a national health-related survey conducted by the Centers for Disease Control and Prevention (CDC).

# Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used Grammarly to improve language and readability. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

# **Declaration of competing interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## CRediT authorship contribution statement

**Manju Ramakrishnan:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis. **Nikhila Gandrakota:** Writing – review & editing, Formal analysis. **Yash Kamdar:** Writing – review & editing, Writing – original draft. **Ambar Kulshreshtha:** Writing – review & editing, Supervision, Methodology, Conceptualization.

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