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Lifespan Stress effect on brain cognitive function

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Abstract

This study examined the influence of chronic stress on cognitive functions over the lifespan, drawing on a large, richly characterized pool of participants in the UK Biobank. Participants were grouped according to their own reported stress levels during childhood and adulthood and were categorized into one of four groups: low childhood, high to middle adulthood stress; low stress in both childhood and adulthood; high to middle stress in both childhood and adulthood; high to middle childhood and low adulthood stress. Cognitive performance was assessed with measures of memory, problem-solving, and fluid intelligence, among other indices. A one-way ANOVA with a Tukey post hoc honest significance difference test was used to determine the differential effect of stress on cognitive outcome. Statistically significant differences were found between the high stress group and the low stress group in regard to their cognitive performance, with those who had high stress during both childhood and adulthood faring the worst. Conversely, drops in stress across time from childhood to adulthood seemed to buffer some of the deleterious cognitive effects but not to the level of individuals with consistently low stress. The results provide a critical piece of information on the role of timing and intensity of exposure to stress on cognitive functions and suggest that timely and sensitive interventions might be of critical importance in buffering against the long-term adverse impact of stress. The study will extend knowledge on how chronic stress affects cognitive resilience and inform strategies to promote cognitive health across the lifespan.

Key Words: Stress, Cognitive Function, Lifespan Psychology, Neurobiology, UK Biobank, Chronic Stress, Cognitive Resilience, Mental Health

1. INTRODUCTION

Chronic stress is a key public health challenge and affects several features of human health across the lifespan. This study aims to leverage a large epidemiological data set available through the Biobank to clarify the nuanced implications of stress on cognitive performance and mental health. In addition, this study will address the gap in existing research on possibly sex-specific reactions to stress and the possibly mediating impact of neurobiological changes in response to stress. Previously, chronic stress had been linked to several conditions, including mental health, cardiovascular disorders, and a decrease in cognitive function [1][2]. Its detrimental impact has been well elaborated in most of the life stages on subjects of both sexes, except in the case of cognitive and neurological outcomes, where its effects were found to be different according to some studies, proposing that gender may be a factor influencing the physiological and psychological responses to stress [3][4]. Studies from neuroimaging have also shown that stress may facilitate changes in brain structure and functioning that underlie the observed differences in cognitive performance across life stages [5][6].

1.1 Importance of Studying Lifespan Stress

Understanding the effects of stress across different stages of life is critical, primarily due to the profound and varied impacts stress can have on brain health and cognitive functions. Stress experienced during critical developmental periods, such as childhood or adolescence, can influence the trajectory of brain development and have lasting effects on neural structures and functions. These changes can, in turn, affect cognitive abilities, mental health, and overall quality of life.

1.2 Data and Methods Overview

The methodology of this study involved a comprehensive analysis using data sourced from the UK Biobank, which is a large-scale biomedical database and research resource containing in-depth genetic and health information from approximately 500,000 participants across the United Kingdom. The data includes a wide range of biomarkers, health outcomes, and self-reported information, which allows for a robust examination of the links between stress, brain health, and cognitive functions.

2. METHODS

2.1 Data Source and Participant Categorization

Participants from the UK Biobank were categorized based on self-reported stress levels during childhood and adulthood into four groups: Low Childhood, High to Middle Adulthood Stress; Low Stress in Both Childhood and Adulthood; High to Middle Stress in Both Childhood and Adulthood; High to Middle Childhood, Low Adulthood Stress. These categorizations facilitate an analysis of stress

impacts over different life stages on cognitive and mental health outcomes.

Participants were categorized into four groups based on their self-reported stress levels during two pivotal life stages—childhood and adulthood. The categorization is as follows:

Low Childhood, High to Middle Adulthood Stress: Participants who reported low stress levels during childhood and high to middle stress levels during adulthood.

Low Stress in Both Childhood and Adulthood: Participants with low reported stress levels during both stages.

High to Middle Stress in Both Childhood and Adulthood: Participants experiencing high to middle stress levels during both childhood and adulthood.

High to Middle Childhood, Low Adulthood Stress: Participants with high to middle stress levels during childhood followed by low stress during adulthood.

These groups provide a framework for analyzing the differential impacts of stress timing on cognitive and mental health outcomes, highlighting the critical periods that may influence long-term health trajectories.

2.2 Assessment of Cognitive Performance

Cognitive performance was evaluated using metrics such as Maximum Digits Remembered Correctly, Number of Puzzles Solved, Fluid Intelligence Score, Number of Word Pairs Correctly Associated, and Number of Symbol Digit Matches Made Correctly. These assessments cover a range of cognitive functions including memory, problem-solving, and processing speed.

2.3 Statistical Analysis Methodology

Data Preprocessing

The initial step in the statistical analysis involved comprehensive data cleaning and preprocessing. This process addressed the handling of missing values and outliers and ensured data normalization where necessary. Proper data preparation is essential to ensure the integrity and robustness of the subsequent statistical analyses.

Adjustment for Confounders

To accurately assess the impact of stress on cognitive and mental health outcomes, linear regression models were employed to adjust for potential confounding variables. These variables included age, sex, and other socio-demographic factors that could influence the outcomes. This adjustment is crucial for isolating the effects of stress from other potentially influential factors, thereby enhancing the validity of the findings.

Analysis of Variance (ANOVA)

ANOVA was utilized to determine if there were statistically significant differences in cognitive and mental health outcomes across the four defined stress groups. This analysis method is particularly useful for comparing multiple groups simultaneously and can help identify whether the mean differences among groups are greater than would be expected by chance. The results from the ANOVA also informed the need for further post-hoc analyses to explore specific group differences in detail.

Multiple Regression Analysis

Multiple regression analysis was conducted to delve deeper into the relationships between lifespan stress (categorized by childhood and adulthood stress levels) and cognitive scores, with separate analyses for male and female participants. In these models, stress levels were treated as categorical predictors. This approach allowed for the exploration of how different levels and timing of stress impact cognitive function within each gender group. The categorization of stress levels enabled the examination of nuanced effects and provided insights into how varying stress exposures might influence cognitive and mental health outcomes differently for males and females.

3. Result

3.1 Impact of Age and Sex on Cognitive Scores

Our analysis began with regression models for each cognitive metric across the four stress groups, controlling for age and sex. The results consistently indicated significant effects from both factors across most cognitive scores, highlighting their substantial influence on cognitive outcomes. This necessitated adjustments of cognitive scores to isolate the impact of stress levels from these confounding effects.

3.2 Impact of Stress on Cognitive Scores

The analysis of variance (ANOVA) was conducted to investigate differences in cognitive scores across the four stress groups, revealing significant disparities. This result underscores the critical roles that both the intensity and timing of stress play in influencing cognitive functions. Notably, the findings remained statistically significant even after implementing False Discovery Rate (FDR) corrections for multiple comparisons, highlighting the robust and substantial influence of stress on cognitive performance.

Subsequent post-hoc analysis employing Tukey's Honest Significant Difference (HSD) test provided further insights into specific pairwise differences among the stress groups,

delineating the differential impacts of stress based on its timing and intensity:

High Stress in Both Childhood and Adulthood (HH Group): This group consistently exhibited the lowest performance across all assessed cognitive metrics, including fluid intelligence, memory, and problem-solving abilities. The pronounced disparities in performance between the HH group and the Low Stress in Both Life Stages (LL) group accentuate the severe and enduring negative impacts of sustained high stress across different life stages on cognitive functions.

Transitional Stress Effects:

High Childhood, Low Adulthood Stress (HL Group): Participants in this group generally demonstrated better cognitive outcomes compared to those in the Low Childhood, High Adulthood Stress (LH) group. This observation suggests that a reduction in stress levels during adulthood may partially alleviate the detrimental effects of high stress experienced during childhood. Nonetheless, the cognitive performance of the HL group did not attain the levels observed in the LL group, indicating some persistent effects of early life stress.

Low Childhood, High Adulthood Stress (LH Group): The cognitive scores for this group reveal that the onset of high stress during adulthood can significantly impair cognitive functions, despite less stressful conditions during childhood. This finding highlights the potential vulnerability of adult cognitive functions to new or increasing stress levels.

Multiple Regression Analyses on the Impact of Stress

Influence of Childhood Stress on Cognitive Performance
The impact of childhood stress on cognitive functions was found to be generally negative across both genders, particularly affecting memory-related tasks:

•Males: Notable declines were observed in the scores for Digits Remembered and Word Pairs, suggesting that early life stress significantly impairs memory functions. However, an intriguing pattern emerged in Fluid Intelligence, where males showed a slight positive effect. This unexpected result could indicate a form of cognitive compensation or resilience, where increased cognitive flexibility and problem-solving abilities develop as adaptive responses to early stress.

•Females: Similar to males, females showed detrimental effects of childhood stress on Digits Remembered. Unlike males, the positive effect on Fluid Intelligence in females was more pronounced. This stronger positive response may reflect more robust compensatory mechanisms in females, potentially facilitating better resilience in cognitive flexibility and problem-solving under the pressures of early life stress.

Impact of Adulthood Stress on Cognitive Functions
Adulthood stress appeared to have more uniformly negative effects on complex cognitive tasks, with some nuanced differences between genders:

•Males: The adverse impacts were especially pronounced in tasks requiring complex cognitive processing, such as Puzzles Solved, Puzzles Correct, and Symbol Matches. These findings suggest that stress encountered in adulthood may disrupt cognitive functions that involve problem-solving, abstract reasoning, and attentional processes.

•Females: Similar to males, females experienced negative effects of adulthood stress on Puzzles Solved and Fluid Intelligence, indicating difficulties in problem-solving and reasoning. Interestingly, a small positive effect was observed in Digits Remembered, which might suggest an adaptive enhancement in specific types of memory tasks under stress. This could be an indication of selective cognitive resilience, where certain memory processes are strengthened as a coping mechanism in response to stress.

Table-1:comprehensive view of the demographic composition across the different stress groups.

Group	Count of Participants	Sex Ratio (F:M)	Mean Age (SD)
High-High	176	5.52	62.35 (7.25)
High-Low	683	1.58	62.60 (7.03)
Low-High	939	3.65	63.06 (6.67)
Low-Low	9397	1.18	64.38 7.10)

4. DISCUSSION

This study underscores the profound impact of stress on cognitive functions, emphasizing the importance of the timing of stress exposure. Findings suggest that early interventions might be crucial in mitigating the long-term cognitive detriments associated with chronic stress. Furthermore, gender-specific analyses indicate differing resilience or vulnerability to stress, which could guide tailored preventative and therapeutic strategies.

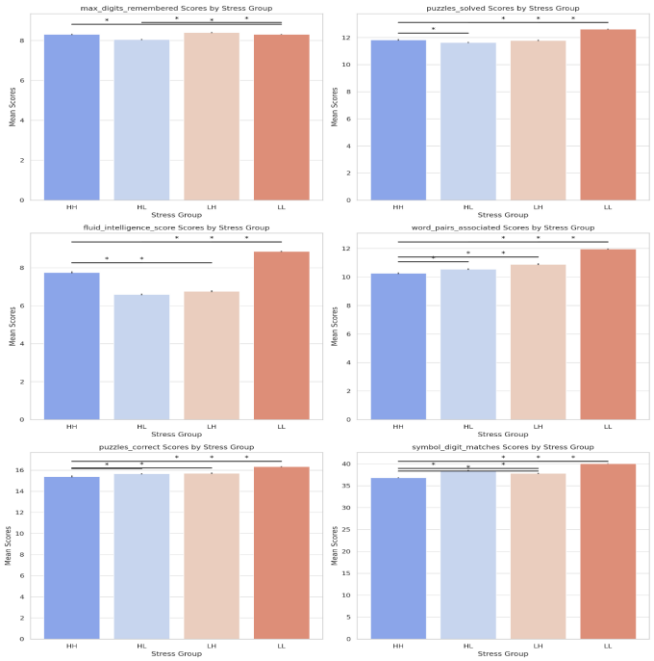

Chart -1: compares the four stress groups the mean scores and standard deviations for each significant cognitive test

Table 2 Impact of Stress on Cognitive Functions by Gender

Gender	Cognitive Function	Stress Period	Coefficient	P-Value	Impact
Male	Digits Remembered	Childhood	-0.272	<0.00001	Negative
	Fluid Intelligence	Childhood	0.239	0.018	Positive
	Word Pairs	Childhood	-0.433	0.0003	Negative
	Puzzles Solved	Adulthood	-0.820	<0.0001	Negative
	Symbol Matches	Adulthood	-2.623	<0.0001	Negative
Female	Digits Remembered	Childhood	-0.213	<0.000001	Negative
	Fluid Intelligence	Childhood	0.452	<0.0001	Positive
	Digits Remembered	Adulthood	0.091	0.034	Positive
	Puzzles Solved	Adulthood	-0.820	<0.0001	Negative
	Fluid Intelligence	Adulthood	-2.104	<0.0001	Negative

5 . CONCLUSIONS

The findings contribute significantly to understanding the complex relationships between stress, brain structure, and cognitive health. Insights into how chronic stress influences cognitive resilience and mental health could lead to improved clinical practices and health policy strategies, aimed at enhancing individual and community health outcomes

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