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What Are the Key Biological Pathways Through Which Lifestyle Factors Influence Neurodegeneration?

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Abstract. Neurodegenerative diseases (NDs), such as Alzheimer's and Parkinson's, pose significant health challenges globally, with current treatments offering limited efficacy. Preventive strategies targeting modifiable lifestyle factors are therefore of increasing importance. This study synthesizes evidence on four key biological pathways involved in neurodegeneration: (1) chronic inflammation and immune dysregulation, (2) circadian rhythm disruption, (3) oxidative stress and mitochondrial dysfunction, and (4) gut-brain axis signaling. Diet, sleep, and physical activity are highlighted as modulators of these pathways. To contextualize these mechanisms within public understanding and behavior, a cross-sectional survey was conducted to assess awareness, beliefs, and lifestyle practices related to brain health. Results indicated gaps between awareness and action, with education, diet, and sleep linked to prevention beliefs, but fatigue and stress limiting engagement in preventive behaviors. By integrating biological insights with real-world perceptions, this study offers guidance for both clinical prevention strategies and public health interventions aimed at reducing ND risk.

Keywords: Neurodegenerative diseases, prevention, lifestyle

1. Introduction

Neurodegenerative diseases (NDs), including Alzheimer's disease (AD), Parkinson's disease (PD), and amyotrophic lateral sclerosis (ALS), represent a growing global health burden. Characterized by progressive neuronal loss and dysfunction, these conditions impair cognition, memory, and motor function, with profound personal and socioeconomic consequences. As of 2023, over 55 million people are living with dementia worldwide—a figure projected to rise to 139 million by 2050, underscoring the urgent need for preventive strategies [1].

While aging remains the primary non-modifiable risk factor, accumulating evidence highlights the role of modifiable lifestyle factors—such as physical activity, diet, sleep, and social engagement—in influencing neurodegeneration risk [2,3]. These behaviors interact with core biological pathways implicated in neurodegeneration, including chronic inflammation, circadian disruption, oxidative stress, and gut-brain axis signaling, presenting opportunities for early intervention.

Chronic low-grade inflammation contributes to both the onset and progression of AD and PD through microglial activation and pro-inflammatory cytokine release, accelerating neuronal injury [4]. Circadian rhythm disruption, often resulting from irregular sleep-wake cycles, impairs

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glymphatic clearance of neurotoxic metabolites like amyloid-β, exacerbating cognitive decline [5]. Oxidative stress from mitochondrial dysfunction and reactive oxygen species (ROS) accumulation further heightens neuronal vulnerability [6]. Emerging research on the gut-brain axis also suggests that microbiota imbalances modulate neuroinflammation and neural function via immune, endocrine, and neural pathways [7].

In addition to synthesizing biological evidence, this study incorporates a cross-sectional survey assessing public awareness, beliefs, and health behaviors related to neurodegenerative disease prevention. By juxtaposing mechanistic insights with real-world perceptions and practices, this study aims to provide an integrated understanding of how lifestyle factors influence neurodegeneration, informing both individual and public health strategies.

2. Methods

2.1. Survey design and objectives

A cross-sectional survey was designed to assess public awareness, beliefs, and self-reported lifestyle behaviors related to brain health and neurodegenerative disease prevention. The survey explored participants' familiarity with neurodegenerative conditions, perceived causes and preventability, health habits (diet, exercise, sleep, stress), and preferences regarding preventive strategies and educational resources. The goal was to identify knowledge gaps and psychosocial factors influencing engagement in preventive actions.

2.2. Participants and recruitment

Participants aged 15 years or older were recruited online via social media, email lists, and word-of-mouth. Inclusion criteria required the ability to read Chinese. Participation was voluntary and anonymous, with digital informed consent obtained prior to survey initiation. No identifying information was collected.

2.3. Survey instrument

The 19-item questionnaire combined multiple-choice and Likert-scale questions across five sections: demographics and educational background, disease familiarity, beliefs about causes and preventability, lifestyle habits, and learning preferences. Key variables included prior brain health education, number of diseases recognized, perceived causes, belief in preventability, perceived inevitability, and self-reported behaviors (diet, physical activity, sleep, sugar intake, stress, and fatigue). Motivations for preventive actions and preferred educational formats were also recorded. Survey content was reviewed by neuroscience and education specialists for clarity and content validity.

2.4. Data collection and analysis

Responses were collected via the Wenjuanxing platform over two weeks in May 2025 and analyzed in Python using Pandas, Matplotlib, Seaborn, and SciPy. Descriptive statistics summarized responses. Welch's t-test assessed differences in understanding levels between participants with and without prior brain health education. Linear regression examined associations between the number of diseases recognized and understanding scores. Relationships between belief in preventability and perceived inevitability were explored via cross-tabulation and heatmaps. Associations between

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lifestyle factors and both belief in prevention and engagement in preventive behaviors were analyzed using chi-square tests of independence. Statistical significance was set at $p < 0.05$.

3. Results

3.1. Educational exposure and understanding

Among all respondents, participants who had previously taken a brain health-related course (n = 16) reported significantly higher levels of self-rated understanding of neurodegenerative diseases than those without such exposure (n = 56). The mean understanding score was 2.31 (SD = 0.87) among course-takers versus 1.25 (SD = 0.81) among non-takers. This difference was statistically significant (Welch's t-test, $t(70) = 4.36$, $p < 0.001$), indicating a strong association between educational exposure and perceived understanding (Figure 1A).

Additionally, a regression analysis revealed a positive correlation between the number of neurodegenerative diseases participants had heard of and their self-rated understanding. While the effect size was modest, increased disease familiarity was associated with higher understanding scores (Figure 1B).

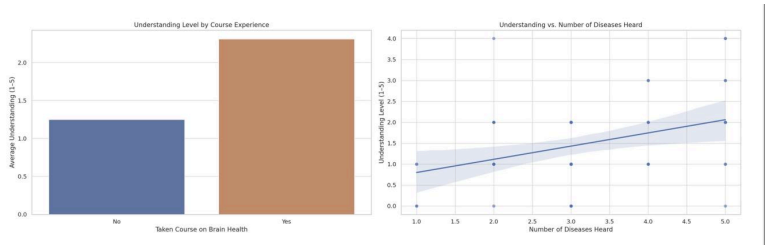


Figure 1. Educational exposure and understanding

(A) Self-rated understanding of neurodegenerative diseases among participants who had taken a brain health course versus those who had not. Participants with course experience reported significantly higher understanding levels ($p < 0.001$).

(B) Positive correlation between the number of neurodegenerative diseases participants had heard of and their self-rated understanding level. Shaded area represents 95% confidence interval.

3.2. Beliefs about preventability, prevention timing, and perceived causes

Belief in the preventability of neurodegenerative diseases was strongly associated with rejection of the notion that such diseases are inevitable with aging. Cross-tabulation indicated that participants endorsing the possibility of prevention were more likely to reject aging as an inevitable cause of brain disease (Figure 2A).

Regarding prevention timing, younger participants (≤18 and 19–35 age groups) tended to endorse a broader age range for initiating preventive actions, often selecting "<40" or "40–59" as appropriate starting points. In contrast, older respondents (36–59) typically chose a single prevention age bracket, most often "40–59," reflecting generational differences in perceived prevention timing (Figure 2B).

When asked about perceived causes of neurodegenerative diseases, respondents most commonly cited genetics (62 mentions), followed by aging (55 mentions) and lifestyle (54 mentions) (Figure 2C).

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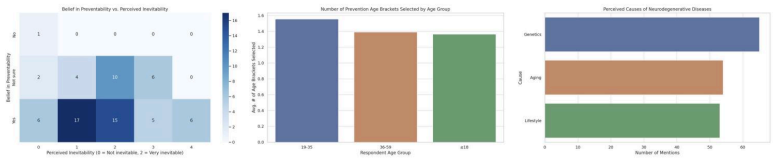


Figure 2. Beliefs, prevention timing, and perceived causes

(A) Heatmap showing the relationship between participants' belief in the preventability of neurodegenerative diseases and their perception of disease inevitability with aging.

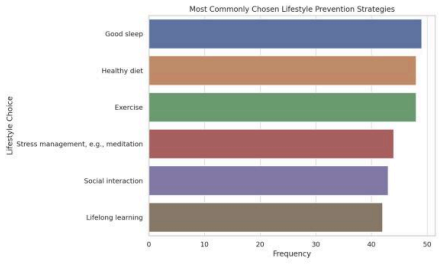
(B) Average number of prevention age brackets selected by different age groups, indicating younger participants tend to endorse earlier prevention.

(C) Frequency of mentions for perceived causes of neurodegenerative diseases, with genetics, aging, and lifestyle being the most commonly cited factors.

3.3. Lifestyle strategies and associations with prevention beliefs and behaviors

The most frequently selected lifestyle strategies believed to prevent neurodegenerative diseases included healthy diet (90.3%), regular exercise (88.9%), adequate sleep (81.9%), social interaction (75.0%), and lifelong learning (63.9%) (Figure 3A).

Chi-square tests were conducted to examine associations between lifestyle behaviors and both belief in preventability and actual engagement in preventive behaviors (Table 1, Figure 3B). Diet type (χ^2 = 79.89, p < 0.00001) and sleep hours (χ^2 = 25.64, p = 0.00026) showed significant associations with belief in prevention. Additionally, daytime fatigue was significantly associated with reported engagement in preventive behaviors (χ^2 = 122.15, p = 0.03707). No other lifestyle variables demonstrated statistically significant associations with either outcome.



Variable	Associated Outcome	χ^2	p-value	Significant?
Diet Type	Belief in Prevention	79.89	<0.00001	Yes
Sleep Hours	Belief in Prevention	25.64	0.00026	Yes
Physical Activity	Belief in Prevention	7.57	0.27131	No
Sugar Food Frequency	Belief in Prevention	6.43	0.37675	No
Daytime Fatigue	Belief in Prevention	12.94	0.11391	No
Stress Level	Belief in Prevention	10.44	0.23528	No
Physical Activity	Preventive Behaviors (Q18)	90.22	0.07199	No
Sugar Food Frequency	Preventive Behaviors (Q18)	56.04	0.91725	No
Diet Type	Preventive Behaviors (Q18)	94.39	0.52738	No
Sleep Hours	Preventive Behaviors (Q18)	50.19	0.97646	No
Daytime Fatigue	Preventive Behaviors (Q18)	122.15	0.03707	**Yes**
Stress Level	Preventive Behaviors (Q18)	75.63	0.93828	No

Figure 3. Lifestyle strategies and associations with beliefs and preventive behaviors

(A) Frequency of participants selecting various lifestyle strategies believed to prevent neurodegenerative diseases. Healthy diet, exercise, and sleep were the most frequently chosen strategies.

(B) Summary table of chi-square test results examining associations between lifestyle factors and both belief in prevention and engagement in preventive behaviors. Significant associations are indicated in bold.

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3.4. Psychosocial factors, motivations, and learning preferences

When asked about motivations for engaging in preventive actions, respondents most frequently cited personal or family medical history (48.0%), followed by doctor's advice (27.6%) and educational experiences (24.4%) (Figure 4A). Preferred educational formats included videos (30.8%), articles (28.1%), books (23.8%), and workshops (17.3%) (Figure 4B).

Finally, a large majority (94.4%) of respondents agreed or strongly agreed that schools should incorporate brain health education (Figure 4C), underscoring broad support for formal brain health education in school curricula.

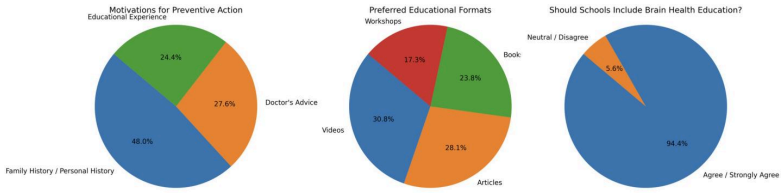


Figure 4. Psychosocial motivations and learning preferences

(A) Reported motivations for engaging in brain health preventive actions, with family or personal history being the most common motivator.

(B) Preferred educational formats for learning about brain health, with videos and articles favored over books and workshops.

(C) Participants' agreement regarding the inclusion of brain health education in school curricula, with 94.4% supporting school-based brain health education.

4. Discussion

This study examined how lifestyle factors relate to neurodegenerative disease (ND) risk via biological mechanisms and public beliefs. Integrating a cross-sectional survey with existing mechanistic research on inflammation, circadian disruption, oxidative stress, and gut-brain signaling, this work explores physiological pathways of neurodegeneration as well as how individuals perceive and act on these risks.

Survey findings revealed that educational exposure was significantly associated with higher self-rated ND understanding, consistent with evidence that health education improves awareness and perceived agency [2]. Notably, even passive exposure—measured by the number of ND types participants had heard of—was positively associated with perceived familiarity, emphasizing the importance of early, broad-based brain health education.

Belief in ND preventability was strongly linked to rejecting these diseases as inevitable consequences of aging. Younger participants favored early prevention and recognized lifestyle as a modifiable risk factor, suggesting generational shifts toward preventive mindsets.

Although most respondents endorsed protective behaviors (healthy diet, exercise, adequate sleep, etc.), only diet type and sleep duration were significantly associated with belief in disease preventability. This aligns with biological evidence highlighting the roles of diet and circadian regulation in modulating neuroinflammation and glymphatic clearance [4,5].

However, a notable gap emerged between belief and action. Mental fatigue and stress—linked to mitochondrial dysfunction and circadian disruption—were associated with reduced engagement in preventive behaviors. This suggests biological or psychological burdens hinder action despite recognition of prevention.

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Finally, strong support for school-based brain health education and preferences for multimedia formats offer guidance for future public health interventions. Tailoring educational strategies to preferred formats may enhance public engagement and translate knowledge into action.

Overall, these findings reinforce the biological relevance of lifestyle in modulating neurodegeneration risk while highlighting the behavioral barriers that limit preventive action. Bridging this gap between knowledge and practice through accessible, behaviorally-informed interventions represents a critical opportunity for public health.

5. Conclusion

This study highlights how lifestyle factors—diet, sleep, and physical activity—modulate neurodegeneration risk through inflammation, circadian disruption, oxidative stress, and gut-brain signaling. While public awareness of these risks exists, significant gaps remain between knowledge and preventive action. Educational exposure improves understanding and prevention beliefs, yet stress and fatigue limit engagement in healthy behaviors. Younger participants show greater openness to early prevention, and strong support for school-based brain health education offers a clear public health opportunity. Bridging the gap between knowledge and behavior through accessible, multimedia education could help reduce neurodegenerative disease risk and promote long-term brain health.

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