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Original Article

Effect of Healthy Lifestyle Behaviors on the Development of Alzheimer's Disease: Case–Control Study

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What is already known on this topic?

- *Aging is the biggest risk factor for AD.*
- *Healthy lifestyle habits can be protective.*
- *Physical diseases (HT, diabetes, and hypercholesterolemia) are associated with AD.*

What does this study add on this topic?

- *It is one of the rare case-control studies conducted in Türkiye.*
- *Contrary to expectations, the higher rate of physical illness in the control group is a new finding worthy of discussion.*
- *The strong association of sensory loss with AD was re-emphasized.*

ABSTRACT

Objective: Age is a major risk factor for Alzheimer's disease (AD), and the increasing population of elderly individuals highlights the importance of preventive measures for public health and economic resources. This study aimed to examine the effects of physical health and lifestyle on AD by comparing them with a healthy control group.

Methods: The case-control study included 118 individuals aged 65 and older, consisting of 59 patients diagnosed with AD per the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV), and 59 older adults serving as controls. Data collection occurred from September to December 2018 at the Geriatric Psychiatry Outpatient Clinic. Assessments included the Geriatric Depression Scale (GDS), Healthy Lifestyle Behaviors Scale (HLBS), and the Mini-Mental State Examination (MMSE).

Results: In contrast to the control group, the patient group exhibited lower levels of education and physical illness ($P = .016$ and $P = .000$, respectively), while exhibiting a significantly higher prevalence of hearing impairment or vision loss ($P = .000$). The patient group had lower total HLBS ($P = .000$) and subscale scores for physical activity ($P = .000$), nutrition ($P = .019$), health responsibility ($P = .000$), and stress management ($P = .000$).

Conclusion: This study investigated the effects of physical health and lifestyle on AD. Results suggested that increased education levels, intact sensory functions, such as hearing and vision, adoption of healthy lifestyle habits, such as consistent physical activity, a high level of health responsibility, healthy nutrition, and successful stress management may contribute to lowering the risk for the development of AD.

Keywords: Healthy lifestyle behaviors, older adults, the risk of factors, Alzheimer's disease, geriatric depression scale

Introduction

The most significant challenge among aging populations in the twenty-first century is anticipated to be clinical problems arising from neurodegenerative changes that naturally increase with advancing age.[1] According to the Alzheimer's Association's 2024 *Facts and Figures* report,[2] it is estimated that 6.9 million Americans ≥65 years of age are currently living with Alzheimer's dementia. In the absence of major medical breakthroughs to prevent or cure the disease, this figure is expected to rise to 13.8 million by 2060. The increasing proportion of elderly individuals in the general population is an important indicator that the demand for dementia-related services will increase in the future.

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Neurofibrillary tangles and neural plaques are the main neuropathological hallmarks and definitive diagnostic findings of Alzheimer's disease (AD).[3] It has been established that the disease becomes irreversible once neurons are filled with abnormal protein structures.[4] Because it is difficult to stop disease progression with pharmacological treatment(s) after onset, it is critically important to take appropriate measures before occurrence or at an early stage of the illness. Addressing risk factors may alter the course of cognitive impairment. As such, it is necessary to define risk factors for individuals diagnosed with cognitive impairment and functional loss who do not exhibit symptoms that fulfill the diagnostic criteria for AD, as well as their relatives.

In its 2017 report, the Lancet Commission on Dementia Prevention, Intervention, and Care outlined 9 modifiable risk factors for dementia. Risk factors for dementia that can potentially be modified—3 of which are currently in the "proposed" category—include education *in younger age*; obesity, traumatic brain injury, hypertension (HT), hearing loss, and alcohol abuse *in middle-age individuals*; and low social contact, smoking, physical inactivity, diabetes, depression, and exposure to air pollution in the later stages of life.[5] Among these factors, those currently in the "proposed" category include traumatic brain injury, alcohol abuse, and air pollution. These lifestyle-related risk factors contribute to an increased risk for dementia in advanced age.[6]

Conversely, despite the increasing prevalence of dementia, some studies have indicated that advances in education, nutrition, healthcare, and lifestyle modifications have contributed to a reduction in the incidence of age-specific dementia in some countries.[7,8] Accordingly, the present study aimed to investigate the impact of modifiable risk factors for dementia, including education level, sensory function (hearing and vision), physical activity, nutrition, health responsibility, and stress management, on the development of AD among elderly individuals. The main question of the research is as follows "Are healthy lifestyle behaviors effective in reducing the risk of developing Alzheimer's disease?" This case-control study involved 118 participants ≥65 years of age, including 59 diagnosed with AD, and 59 healthy controls. This study used assessment tools including the Geriatric Depression Scale (GDS), Healthy Lifestyle Behaviors Scale (HLBS), and Mini-Mental State Examination (MMSE) to analyze differences between the patient and control groups in relation to these risk factors.

Research Question

1 Are healthy lifestyle behaviors effective in reducing the risk of developing Alzheimer's disease?

Methods

Participants

This study included 118 participants ≥65 years of age, comprising 59 patients diagnosed with AD according to criteria from the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, and 59 healthy controls. The patients were recruited from the Geropsychiatry Clinic of Bakırköy, Professor Dr. Mazhar Osman Mental Health and Nervous Diseases Hospital Hospital, İstanbul, Türkiye. Data collection was conducted between September 2018 and December 2018. Informed consent was obtained from all participants and their relatives. Inclusion criteria were as follows: age ≥65 years, diagnosis of AD, and no advanced vision, hearing problems, or delirium. Individuals with early onset dementia, other central nervous system conditions, systemic diseases causing dementia, dementia due to substance use, delirium, severe sensory impairment, intellectual disability, or depression (in healthy controls) were excluded. Participants and their relatives provided informed written consent after receiving details of the study.

Protocol

Participants underwent a geropsychiatric evaluation of demographic characteristics, socioeconomic status, clinical features, and lifestyle. Both groups completed the Standardized Mini-Mental Test (SMMT), GDS, and HLBS. Patients diagnosed with AD and healthy controls were compared in terms of the specified characteristics. Ethics approval was granted by the Bakırköy Dr. Sadi Konuk Hospital (Approval No: 2018/168; Date: 30.04.2018) .

Measurements

Sociodemographic and clinical data form: Data used in the present study were by the geropsychiatry outpatient clinic, where demographic characteristics, socioeconomic conditions, clinical characteristics, physical illness, nutrition, and lifestyle are recorded. Age, sex, education level, profession, marital status, number of children, socioeconomic level, time of onset of the illness, treatment received, who they stayed with, where they lived, history of physical illness, and treatments used for physical illnesses were evaluated with this form.

Standardized Mini-Mental Test: The SMMT, developed by Folstein et al, is a brief standardized tool that assesses global cognitive levels. Administered in 10 minutes by trained professionals, the SMMT is scored out of 30 points and includes 11 items under 5 domains: attention, orientation, language, recall, and memory. Mini-mental test scores can be between 0 and 30. A score of less than 10 indicates severe impairment. Scores between 10 and 19 indicate moderate dementia. Scores between 19 and 24 indicate early dementia. Scores of 25 and above are considered normal. Güngen et al validated the Turkish version of the SMMT and found that a threshold of 23/24 was highly sensitive and specific for the diagnosis of mild dementia in elderly Turks. Inter-rater reliability demonstrated strong results, with $r = 0.99$ and kappa = 0.92.[9]

Geriatric Depression Scale: Developed by Yesavage to assess depression in the elderly, the GDS can be completed by the patients or their relatives. Its validity and reliability in a Turkish population were confirmed by Sağduyu,[11] with high test-retest reliability ($r = 0.87$) and adequate internal consistency (Cronbach's alpha = 0.72). Strongly correlated with the Hamilton Depression Scale, the GDS effectively identified depression, yielding a sensitivity of 0.90, and a specificity of 0.97 at a cut-off of 13-14 points. Scale scoring is done as the number of yeses. Total Depression Score is calculated from the sum of the scores. A score between 0 and 9 is considered "normal," between 10 and 19 is considered "mild depression" and between 20 and 30 is considered "severe depression."[10,11]

Healthy Lifestyle Behaviors Scale: Drawing on Pender's health promotion model, Walker et al,[12] developed the "Healthy Lifestyle Behaviors Scale." The initial version, the Health-Promoting Lifestyle Profile, consisted of 48 items categorized into 6 domains: self-actualization, nutrition, health responsibility, exercise, stress management, and interpersonal support. In 1996, the scale was revised and updated as the Health-Promoting Lifestyle Profile II, featuring 52 items and 6 refined domains: spiritual growth, interpersonal relations, nutrition, physical activity, health responsibility, and stress management. The scale is a 4-point Likert-type scale. The alpha reliability coefficient of the scale varies from 0.79 to 0.94. The lowest and highest scores were 52 and 192, respectively. Higher scores reflect a higher level of engagement in specific health behaviors.[12]

Statistical Analysis

Descriptive statistical data are expressed mean, SD, median, lowest and highest rate, and frequency. Data distribution (i.e., normality) was examined using the Kolmogorov–Smirnov test. Quantitative data were compared using the independent samples *t*-test and Mann–Whitney

U-test, whereas qualitative data were compared using the chi-squared test. Logistic regression was used in the effect-level analysis. Specifically, a logistic regression was conducted with AD diagnosis (AD vs. control) as the dependent variable, and independent variables including education level, physical illness, hearing/vision impairment, and total HLBS scores. Chain analysis was performed to determine the best explanatory power. Statistical analysis was performed using SPSS version 21.0 (IBM SPSS Corp.; Armonk, NY, USA).

Results

Mean age was significantly higher in the patient group than that in the control group ($P < .05$). Sex distribution, rate of social security, and rate of living with family did not differ significantly between the groups ($P > .05$). The control group exhibited a significantly longer duration of education than the patient group ($P < .05$).

The prevalence of sensory impairment was significantly greater in the patient group than that in the control group ($P < .05$), whereas the prevalence of physical illness was significantly lower ($P < .05$) (Table 1). Here, the latter may be explained by the low level of societal awareness of AD and the limited access to general health services of the patient population included in the study due to socioeconomic reasons. The patient group exhibited significantly higher Standardized Mini-Mental Test (SMMT) and GDS scores than the control group ($P < .05$) (Table 2).

The patient group exhibited significantly lower total HLBS scores and physical activity, health responsibility, nutrition, and stress management factor scores than the control group ($P < .05$) (Table 3, Figure 1).

Discussion

Results of the present study suggest that increased education levels, intact sensory functions—such as hearing and vision—and adopting healthy lifestyle habits, such as consistent physical activity, a high level of health responsibility, healthy nutrition, and successful stress management, may contribute to lowering the risk for the onset of AD. Lifestyle activities may enhance cognitive health by potentially fostering neurogenesis and mitigating the aging processes through protection against cerebrovascular and amyloid-beta pathologies, which are believed to contribute to the development of AD.[13]

In this study, the duration of education was significantly greater ($P < .05$) in the control group than that in the patient group. A previous study reported that high education level may be a protective factor against the development of AD.[14]

According to Evans et al,[15] each year devoted to education results in a risk reduction of approximately 17%. In the current study, the mean (± SD) years of education were 8.4 ± 5.4 and 2.2 ± 3.4 years in the control patient groups, respectively. A higher level of education—particularly during childhood—throughout the lifespan, is widely recognized to be a factor that reduces the risk for dementia. However, the potential benefits of education tend to be less significant after 20 years of age.[16] This implies that cognitive stimulation is particularly crucial during the earlier stages of life. In this study, education was defined as the period of schooling up to 20 years of age for both the control and patient groups.

While there is evidence that an increased risk for dementia and family history dementia is associated with lower educational attainment, the mechanism underlying this nexus remains unclear. For example, differentiating the impact of education from the influence of overall cognitive ability may not always be straightforward.[17] Although there are studies reporting contrary findings, a limited number of studies refer to the association of this relationship with lifestyle, which tends to vary depending on education level.[18,19] Therefore, when the findings of this study's Healthy Lifestyle Behaviours Scale are evaluated, it can be concluded that individuals with a higher level of education are more likely to adopt and practise health literacy, and therefore engage in healthier lifestyle behaviours. Furthermore, given that educational disparity is a modifiable risk factor for dementia, the authors did not observe educational parity between the patient and control groups. While the current study aligns with the existing literature—indicating that a lower level of education is a risk factor for AD—conducting similar studies with larger sample sizes would be advantageous.

Data from this study, consistent with the relevant literature, demonstrated that sensory loss was higher in individuals diagnosed with AD than in controls. Literature reports addressing sensory loss in those with AD indicate a greater loss in hearing and vision than in the general

Table 1. Distribution of Sociodemographic Data, Sensory Loss, and Physical Illness

Variables		Control Group		Case Group		
		Mean ± SD / n – %	Med (Min-Max)	Mean ± SD / n – %	Med (Min-Max)	*P*
Age		72.9 ± 6.8	72 (65-69)	79.5 ± 5.7	80 (65-92)	<.000
Gender	Female	31-52.5%		40-67.8%		.091
	Male	28-47.5%		19-32.2%		
Duration of Education		8.4 ± 5.4	8 0-15	2.2 ± 3.4	0 0-15	<.000
		Control Group		Case Group		
		n	%	n	%	*P*
**Physical illness	No	12	20.3	24	40.7	.016
	Yes	47	79.7	35	59.3	
	Hypertension	38	64.4	30	50.8	
	Hypercholesterolemia	21	35.6	9	15.3	
	Diabetes mellitus	13	22.0	11	18.6	
	Coronary artery dis.	1	1.7	1	1.7	
	Cerebrovascular dis.	1	1.7	0	0.0	
	Other	5	8.5	0	0.0	
**Sensory loss	No	49	83.1	30	50.8	<.000
	Yes	10	16.9	29	49.2	
	Hearing	6	10.2	14	23.7	
	Vision	5	8.5	20	33.9	

Table 2. Comparison of Mini-Mental State Examination and Geriatric Depression Scale Scores

		Control Group		Case Group		
		n	%	n	%	*P*
MMSE Score	Normal	59	100	0	0.0	<.000
	Mild (20-24)	0	0.0	7	11.9	
	Moderate (10-19)	0	0.0	30	50.8	
	Severe (<10)	0	0.0	22	37.3	
Geriatric depression	Yes	59	100	22	37.3	
	No	0	0.0	37	62.7	

elderly population.[20,21] Although the exact mechanism of hearing loss remains poorly understood, it may also be observed in mild cognitive disorders. Hearing loss has also been observed to develop in direct proportion to the loss of cognitive function.[22] Individuals with AD tend to become lost in even in known and familiar environments. Apart from its relationship with loss of cognitive function, it is also believed to be related to vision loss. The cause of vision loss has been reported to be retinal degeneration in AD.[23] Collectively, it is anticipated that the evaluation of sensory loss may attract further attention in the non-pharmacological management of dementia.[24]

In this study, 5 indicators of physical ailments were identified: diabetes mellitus (DM), HT, hypercholesterolemia, coronary artery disease, and cerebrovascular disease. Hypertension is associated with stroke and ischemic white matter lesions, DM with obesity and hypercholesterolemia, and atherosclerosis with vascular risk factors, all of which are risk factors for AD. Currently, it is believed that detecting and treating vascular risk factors, such as HT and DM in middle-age individuals, may reduce the risk for AD.[21] In this study, contrary to expectations, the rate of physical illness was found to be higher in the control group ($P < .016$). The fact that healthy controls have more regular medical follow-up and are diagnosed with an effort to keep conditions such as HT and DM under control may explain this situation. Another reason may be the challenges or neglect patients with AD experience in attempting to accessing healthcare services. In the authors' country, care for dementia symptoms is often delayed. In regions with a low socioeconomic status, the rate at which patients present to health institutions with dementia symptoms is lower than in more developed regions of Türkiye and in Western societies in general.[25] However, as the disease progresses, the emergence of psychotic symptoms, such as hallucinations, delusions, and agitation, forces families to seek treatment from a health organization.[26] Studies also indicate that caregivers of patients with AD, as well as home health care providers in Türkiye, experience multidimensional problems and cannot find professional support, necessitating institutional help.[27]

Table 3. Comparative Healthy Lifestyle Behaviors Scale Scores

	Control Group			Case Group			
	Mean ± SD	Med	(Min-Max)	Mean ± SD	Med	(Min-max)	*P*
Healthy lifestyle Beh. S.	136.0 ± 23.0	135	107-191	122.4 ± 15.4	122	78-158	**<.000**
Physical activity	16.9 ± 6.2	16	8-32	12.9 ± 3.1	12	8-26	**<.000**
Health responsibility	20.8 ± 5.2	20	11-31	16.1 ± 2.7	16	12-26	**<.000**
Nutrition	24.1 ± 4.6	24	13-35	22.4 ± 3.3	22	15-30	**.019**
Spiritual development	27.1 ± 4.4	27	17-38	26.8 ± 3.7	27	16-33	.734
Inter-individual relationships	26.1 ± 3.7	26	19-34	25.6 ± 4.0	25	13-33	.503
Stress management	21.3 ± 4.4	21	14-35	8.6 ± 2.8	18	12-29	**<.000**

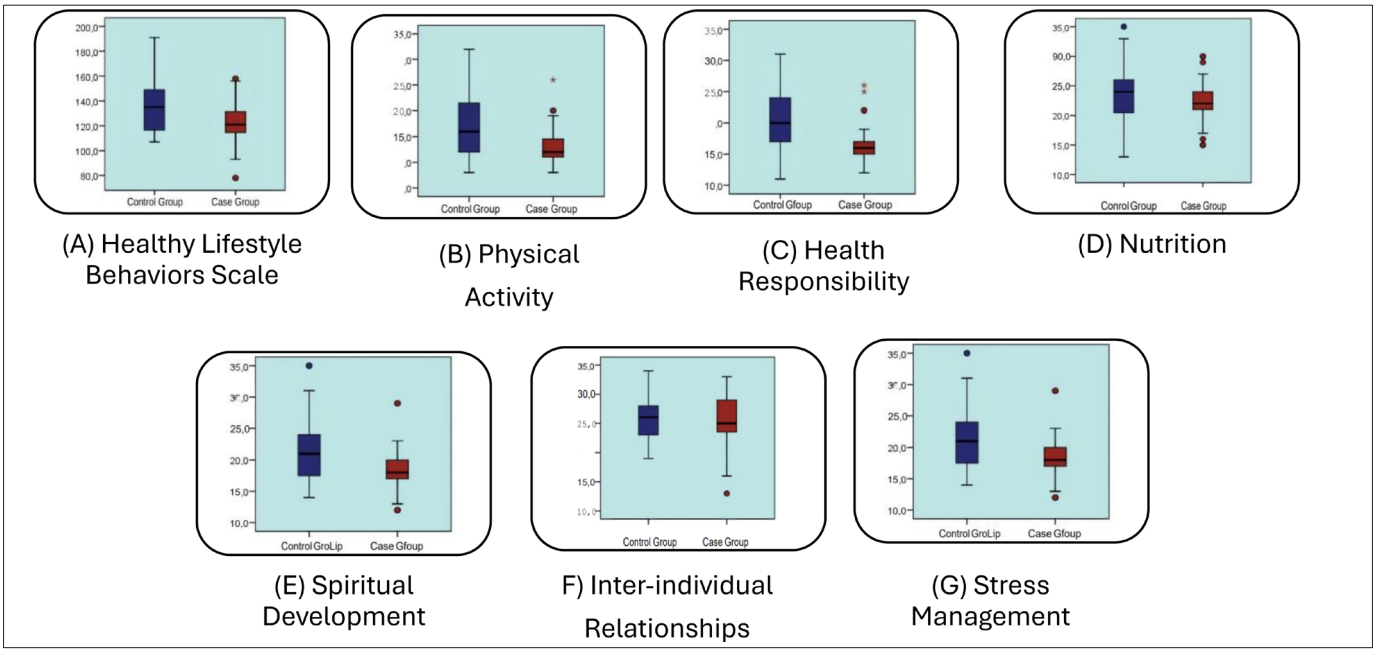

Figure 1. Comparative Healthy Lifestyle Behaviors Scale scores (A) Healthy Lifestyle Behaviors Scale, (B) Physical Activity, (C) Health Responsibility, (D) Nutrition, (E) Spiritual Development, (F) Inter-individual Relationships, (G) Stress Management.

While none of these can directly explain the higher rate of comorbidity in the control group, the difficulty experienced by Alzheimer's patients in accessing general health services may be a possible reason. Nevertheless, the authors believe that the generalizability of this finding is limited due to the small sample size and the potential influence of other risk factors that contribute to the development of the disease. Studies that address physical examinations and laboratory investigations, instead of being content with only focusing on the medical history of concomitant diseases, would provide more useful information in this regard.

In the patient group, the overall HLBS score, along with scores for physical activity, nutrition, health responsibility, and stress management were notably lower than those in the control group ($P < .05$). For example, when analyzed separately, studies examining the relationship between physical activity and AD appear to be complex. One of the related reasons is that the definition and type of physical activity vary with age, generation, and morbidities, as well as differences based on sex, social class, and culture. Evidence indicates that aerobic exercise and physical activity have a modest—but, nevertheless beneficial—effect on normal cognition in those with mild cognitive impairment (MCI).[28] Conversely, evidence regarding the impact of specific forms of exercise, such as progressive muscle resistance training, on the risk for dementia remains limited.[7] In a study investigating the effect of physical and cognitive activity on cognitive endurance in the latter years of life among the elderly who were not diagnosed with dementia, Casaletto et al[29] reported that both were associated with better brain structure and cognitive output. Physical activity in the HLBS used in this study was based on self-reports such as "I follow a regular exercise program," and the physical activity score in the patient group was found to be lower than that in the healthy control group. These data suggest that researchers should explore exercise by specifying it in future studies.

The mean nutritional factor score of the patient group in this study (22.4 ± 3.3) was lower than that the control group (24.1 ± 4.6). Gardener et al[30] reported that adherence to diet was the main predictor of AD or MCI, and healthy controls exhibited better adherence to diet than those with AD and/or MCI, based on the results of their 18-month follow-up study investigating the relationship between adherence to a "Mediterranean diet" and the risk for AD and MCI.

A systematic review of 361 studies that examined the effects of adding omega-3 fatty acids to the treatment regimen for AD reported that this intervention was effective in preserving cognitive function(s), especially in the early stages of the disease, although it is not possible to expect the same effect in the later stages.[31] Obesity has also been associated with dementia in advanced age, while this is not the case for being overweight (body mass index 25-30 kg/m^2).[32] These findings are consistent with the low nutrition factor score determined by HLBS in the patient group in this study. These results highlight the importance of acquiring healthy eating habits as healthy lifestyle behaviors, before or at an early stage of the disease.

In the current study, the health responsibility factor score was significantly lower in the patient group ($P < .05$) compared with that the control group. An accumulating body of literature has increasingly emphasized strategies for mitigating cognitive decline and fostering healthy cognitive aging. The primary recommendations include consistent physical activity and effective management of cardiovascular risk factors. Similarly, cognitively stimulating activities, healthy eating habits, smoking cessation, and combating metabolic syndrome are recommended. Among the risk factors identified by the Lancet Commission on Dementia Prevention, Intervention, and Care in 2017 (i.e., low education levels, obesity, hearing impairment, diabetes, smoking, HT, depression, physical inactivity, and limited social engagement), those potentially linked to both the HLBS total score and the health responsibility factor score include smoking, alcohol consumption, physical inactivity, and refusal to use hearing aids despite a clear need. Therefore, the control group with high health responsibility factor scores in this study were considered to be protected from defined risk factors for dementia.

In this study, the stress management factor score of the patient group was significantly lower ($P < .05$) than that of the control group. Studies have shown that regular social participation, stress management, and adequate sleep hygiene are associated with successful cognitive aging.[33,34] The results of this study addressing stress management obtained from the HLBS are consistent with the literature, suggesting that healthy lifestyle behaviors are protective against dementia.

Several studies have focused on the possible benefits of interventions that can be applied during the early stages of AD. For example, in a study by Guili et al,[35] healthy lifestyle programs were effective in improving memory and other abilities in elderly individuals with and without cognitive decline. That study revealed improved auditory and verbal short-term memory in participants with MCI together with a decrease in subjective memory complaints.

Not all cases of dementia are necessarily preventable; however, it has been shown that the incidence of all-cause dementia is lower in individuals born more recently, although methodological differences exist across studies. This may be explained by changes and improvements in education, socioeconomic aspects, healthcare services, and overall lifestyle over the years.[14] However, the increasing prevalence of obesity and diabetes, as well as decreasing physical activity, may reverse this course in the future. These data highlight that the nature of dementia may change with lifestyle. All these aspects are associated with healthy lifestyle behaviors, which suggests that the healthy control group in this study was protected from the risk factors defined for dementia, with significantly higher HLBS scores than the patient group. A major limitation of the present study was its relatively small sample size. As such, these findings need to be supported by larger multicenter studies that include more potential risk factors for AD.

Limitations and Strengths

A major limitation of the present study was its relatively small sample size. As such, these findings need to be supported by larger multicenter studies that include more potential risk factors for AD.

One of the strengths of this study is its focus on modifiable risk factors for Alzheimer's disease (AD). Focusing on modifiable factors such as education level, physical activity, healthy eating, health responsibility and stress management makes an important contribution to developing preventive health strategies. The comparison of AD patients and healthy control group in the study increased the significance and reliability of the findings. In addition, the use of different and validated measurement tools such as the Geriatric Depression Scale (GDS), the Healthy Lifestyle Behaviors Scale (HLBS) and the Mini-Mental State Examination (MMSE) provided a multidimensional assessment of both psychological, cognitive and lifestyle characteristics of the participants. Statistically significant results on concrete and measurable variables such as education level, sensory functioning (hearing and vision loss) and physical activity are instructive for health policies and individual intervention programs. The fact that the data were collected in a geriatric psychiatry outpatient clinic ensured that the findings were consistent with clinical reality and applicable. Finally, the fact that the study was conducted with individuals aged 65 years and older increased the

value of the study by making it possible to directly evaluate the target group for AD, a disease associated with the aging process.

Conclusion

The present study investigated the effects of physical health and lifestyle on the development of AD, suggesting that increased education levels, intact sensory functions such as hearing and vision, and the adoption of healthy lifestyle behaviors, such as a high level of health responsibility, healthy nutrition, regular physical activity, and successful stress management, may play a role in reducing the risk for developing the disease. There appears to be a need for multicenter, prospective epidemiological studies conducted with samples representing a larger proportion of the population, in which regular physical and cognitive follow-up of individuals starts from a younger age with medical monitoring across a wide range of risk factors to more precisely identify risk factors, establish preventive guidelines, and determine the appropriate preventive measures. To date, virtually all evidence in the relevant literature appears to be from studies conducted in high-income countries. Consequently, risk factors may vary across countries, and interventions may need to be adapted to suit diverse cultural contexts and settings. Despite these limitations, the authors believe that this study draws attention to this area, which we—as psychiatrists—tend to exhibit somewhat limited interest in the authors' country, and represents a step toward determining the risk factors and developing protective measures against this disease, which is associated with increasingly serious social and socioeconomic problems. This study highlighted some specific factors that may contribute to informing the design of more comprehensive epidemiological studies.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: Ethical approval was received from the Bakırköy Dr. Sadi Konuk Training and Research Hospital Ethics Committee (Date: Date: 30.04.2018; Approval no: 2018/168 and). .

Informed Consent: Informed consent was obtained from all participants and their relativeswho agreed to take part in the study.

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