



# Is There Any Relation with Chronic Headache Disorder and Dementia?

## Kronik Baş Ağrısı Sendromları ile Demans Arasında Bir İlişki Var mı?

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### ABSTRACT

**Objectives:** Headache disorders can be reasonably speculated to be associated with the increased risk of dementia. However, the current evidence from longitudinal studies linking headache disorders to dementia is scarce, and study populations are often too small to detect clinically relevant associations. In this study, we investigated the incidence of chronic headache history in the dementia population in comparison with the age-matched non-demented control group.

**Methods:** A total of 122 dementia patients and 114 age-matched non-demented people admitted to outpatient clinic for any complaints other than headache in dates between January 2022 and June 2022 included in this study. Dementia patients who were classified as Alzheimer disease, vascular dementia, mixed dementia, frontotemporal dementia, and Parkinson-related dementia were selected. Mini-mental test score (MMSE) was used to assess the severity of the cognitive impairment. Headache subtypes were classified as migraine headache, episodic tension type headache, and chronic tension-type headache according to International Headache Classification. We investigated and compare the frequency of chronic headache disorders in between two groups. We also aimed to investigate the types of the headaches in demented people and to search the difference from the general population.

**Results:** We could not find any difference statistically between the patient and control groups for the frequency of chronic headache disorder ( $p=0.568$ ) and between headache subtypes and MMSE ( $p=0.669$ ). We also examine the relationship between dementia type and subtypes of chronic headache in patient group and we could not find any relationship between this ( $p=0.070$ ).

**Conclusion:** In our small population retrospective study, we could not detect increased chronic headache history in demented people other than non-demented and could not find any relation between chronic headache disorders and dementia.

**Keywords:** Dementia; headache; mini-mental test score.

### ÖZET

**Amaç:** Kronik baş ağrısı sendromlarının demans riskinin artmasıyla ilişkili olduğu makul olarak öne sürülebilir. Bununla birlikte, baş ağrısını demansa bağlayan çalışmalardan elde edilen mevcut kanıtlar azdır ve çalışma popülasyonları genellikle klinik olarak ilgili ilişkileri tespit etmek için çok küçüktür. Bu çalışmada, demans popülasyonundaki kronik baş ağrısı öyküsü insidansı, aynı yaştaki demansı olmayan kontrol grubuyla karşılaştırmalı olarak araştırılmıştır.

**Yöntem:** Ocak 2022-Haziran 2022 tarihleri arasında baş ağrısı dışında herhangi bir şikayetle polikliniğe başvuran toplam 122 demans hastası ve benzer yaş grubundaki demansı olmayan 114 kişi çalışmaya dahil edildi. Demans hastaları Alzheimer hastalığı, vasküler demans, mikst demans, frontotemporal demans ve Parkinson ile ilişkili demans olarak sınıflandırılanlar arasından seçildi. Bilişsel bozulmanın şiddetini değerlendirmek için mini mental test skoru kullanıldı. Uluslararası baş ağrısı sınıflamasına göre baş ağrısı alt tipleri migren tipi baş ağrısı, epizodik gerilim tipi baş ağrısı ve kronik gerilim tipi baş ağrısı olarak sınıflandırıldı. Bu iki grup arasında kronik baş ağrısı bozukluk-

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larının sıklığı karşılaştırıldı. Ayrıca, demansı olan hastalarda baş ağrısı tipleri ve genel popülasyondan farkı araştırıldı.

**Bulgular:** Kronik baş ağrısı sıklığı açısından hasta ve kontrol grubu arasında istatistiksel bir farklılık tespit edilmedi ( $p=0,568$ ). Baş ağrısı alt tipleri mini mental test skorları arasında da istatistiksel olarak anlamlı ilişki yoktu ( $p=0,669$ ). Ayrıca demans türü ve baş ağrısı alt tipleri arasında da herhangi bir anlamlı ilişki tespit edilmedi ( $p=0,070$ ).

**Sonuç:** Bu küçük gruplu retrospektif çalışmada, kronik baş ağrısı öyküsü açısından demansı olan ve olmayan gruplar arasında anlamlı bir farklılık ve dolayısıyla kronik baş ağrısı sendromları ile demans arasında anlamlı bir ilişki tespit edilmedi.

**Anahtar sözcükler:** Baş ağrısı; demans; mini mental test.

Dementia is one of the most common neurological diseases in the elderly and giving rise to an important economic stress on the society. Over the past couple of decades, scientists have been working on finding a treatment for dementia, especially that associated with Alzheimer's disease (AD). At present, there are no any powerful drugs that can significantly slow the progression of dementia.<sup>[1]</sup> And also, researchers have also given attention on the study of the risk factors for dementia with the thought of that can still be reduced by controlling the risk factors. The identified risk factors that can be manipulated at present for dementia include obesity, diabetes, hypertension, lipid metabolism disorders, coronary heart disease, and heart failure.<sup>[2-5]</sup> A lot of studies also have shown that optimal control of hypertension, hyperlipidemia, and diabetes might reduce the risk of dementia.<sup>[6-8]</sup>

Approximately 40% of adults in the general population suffer from any type of headache disorders.<sup>[9]</sup> Some of these headache disorders are known to be risk factors for a couple of frequently seen diseases, such as stroke, coronary artery diseases, and depressive disorders.<sup>[10-12]</sup> A lot of studies have shown that chronic migraine disorders are significantly associated with cardiovascular and cerebrovascular diseases as well as asymptomatic brain white matter damage.<sup>[13-15]</sup> Chronic headaches other than migraine are also associated with some cerebrovascular risk factors.<sup>[16,17]</sup> These risk factors are thought to be related to increased cerebral white matter ischemic damage and this, in turn, may increase the risk of especially the vascular or mixed-type dementia. However, evidence from some studies investigating the relation of headache disorders to dementia is weak, and study populations are usually too small to detect significant associations between them. In this study, we investigated the incidence of chronic headache history in the dementia population in comparison with the age-matched non-demented control group. Furthermore, we tried to classify the subgroup of chronic headache in these patients with the aid of their relatives. Hence, we hope to find higher chronic headache inci-

dence in all subtypes in the dementia group compared with the controls, similar to the literature meta-analysis.<sup>[18,19]</sup>

## Methods

A total of 122 dementia patients (70 females and 52 males) and 114 age-matched non-demented people (62 females and 52 males) admitted to outpatient clinic for any complaints other than headache in dates between January 2022 and June 2022 included in this study. This study was designed as a retrospective study, a written informed consent was obtained from the patients or from their relatives on admission. The study was done appropriately to the Helsinki Declaration and Ethical Committee approval date and number was July 04, 2022/37. Dementia patients who were classified as Alzheimer disease (AD), vascular dementia, mixed dementia, frontotemporal dementia, and Parkinson-related dementia were selected. Mini-mental test score (MMSE) was used to assess the severity of the cognitive impairment. Headache history in demented patients was investigated by talking to his/her main relatives. Headache subtypes were classified as migraine headache, episodic tension-type headache, and chronic tension-type headache according to International Headache Classification. The classification was had to be restricted for three types of headache because of the difficulty to obtain detailed headache history, especially the demented patients. For avoiding making mistake in classification, we decided to restrict the types into the three forms. We investigated and compare the frequency of chronic headache disorders in dementia patients and non-demented controls. We also aimed to investigate the types of the headaches in demented people and to search the difference from the general population.

## Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 20. To deter-

mine whether the variables were normally distributed, the Kolmogorov–Smirnov test was used. Mean and standard deviation values were given for variables with normal distribution. For parametric variables with normal distribution, Student’s t-test was used. Chi-square test was used for non-parametric non-numeric data. Pearson’s test was used as the correlation test.  $P < 0.05$  were considered statistically significant.

## Results

A total of 122 dementia patients (70 females and 52 males) and 114 age-matched non-demented people (62 females and 52 males) were included in this study (Table 1). The mean age was not statistically different in the patient and demen-

Table 1. Gender distribution in the patient and control groups

Gender	Patient	Control
Female	70	62
Male	52	52

Table 2. Age distribution in the patient and control groups

Group	n	Mean	Median	SD	p=0.204
Control	114	74.009	75.500	7.7374	
Patient	122	75.352	77.000	8.4059	

n: Number, SD: Standard deviation.

Table 3. Distribution of dementia subtypes in the patient group

Type	Number	Percentage
Alzheimer	64	52.459
Vascular	20	16.393
Mixed	15	12.295
PD	10	8.197
FTD	13	10.656

PD: Parkinson Disease Dementia; FTD: Frontotemporal Dementia.

Table 4. The comparison of frequency of chronic headache in the patient and control groups

Type of headache	Migraine (MH)	ETTH	CTTH	Others	Total	p=0.568
Control	11 (9.649)	23 (20.175)	6 (5.263)	74 (64.912)	114 (100.00)	
Patient	12 (9.836)	33 (27.049)	8 (6.557)	69 (56.557)	122 (100.00)	
Total	23 (9.746)	56 (23.729)	14 (5.932)	143 (60.593)	236 (100.00)	

ETTH: Episodic Tension Type Headache; CTTH: Chronic Tension Type Headache.

tia groups (75.352 and 74.009, respectively,  $p=0.204$ ), (Table 2). The distribution of dementia subtypes in the patient group is shown in Table 3.

We could not find any difference statistically between the patient and control groups for the frequency of chronic headache disorder ( $p=0.568$ ) (Table 4) and between headache subtypes and MMSE score ( $p=0.669$ ) (Table 5). We also examine the relationship between dementia type and subtypes of chronic headache in the patient group and we could not find any relationship between this ( $p=0.070$ ) (Table 6).

## Discussion

The association between chronic headache disorders and de-

Table 5. The relationship between headache subtypes and MMSE scores

Headache type	n	Mean MMSE	SD	p=0.669
Migraine	12	15.167	2.8868	
ETTH	33	14.576	2.7842	
CTTH	8	14.500	2.9761	
Non	69	14.029	3.7175	

n: Number, SD: Standard deviation; ETTH: Episodic Tension Type Headache; CTTH: Chronic Tension Type Headache; MMSE: Mini-mental test score.

Table 6. The relationship between dementia type and subtypes of chronic headache in the patient group

Dementia	MH	ETTH	CTTH	Others	Total	p=0.070
AH	3	15	2	44	64	
VaD	1	8	3	8	20	
Mixed	3	5	2	5	15	
PD	1	4	0	5	10	
FTD	4	1	1	7	13	
Total	12	33	8	69	122	

AH: Alzheimer disease; MD: Mixt Dementia; ETTH: Episodic Tension Type Headache; CTTH: Chronic Tension Type Headache; VaD: Vascular Dementia; PD: Parkinson Disease Dementia; FTD: Frontotemporal Dementia.

mentia remains largely unknown, but a lot of mechanisms are put forward to be involved in pathogenesis. A previous study found that some of the brain structures such as the thalamus, insula, anterior cingulate, amygdalae, and temporal cortex involved in the pain network and some morphologic changes have been detected in these structures during the disease process.<sup>[20]</sup> Surprisingly, these anatomic cerebral regions also play critical and important roles in the memory network.<sup>[21]</sup> A detailed structural-neuroimaging study on chronic headache patients showed that the cerebral gray matter volume of memory network structures, including the cingulate cortex, insula, prefrontal area, and parahippocampal gyrus, decreased significantly compared with people who did not have any type of headache disorders.<sup>[22]</sup> These striking changes in the overlapping pain and memory networks explain the potential correlation between chronic pain and memory impairment in headache patients. Moreover, a previous meta-analysis found an association of cerebral white matter hyperintensity with an increased risk of dementia.<sup>[23]</sup> It is also well known from the literature, headache patients were reported to have an increased risk of cerebral white matter hyperintensity.<sup>[24]</sup> Therefore, subtle changes in the brain white matter might contribute to an increased risk of dementia in chronic headache patients. Chronic headache and especially chronic migraine are often closely related with depressive disorders.<sup>[25]</sup> And also, stress and anxiety have been identified as predictors of some kind of headache disorder.<sup>[26]</sup> A previous study found an association between stress and anxiety disorders with the development of AD type dementia, especially in the middle-aged women.<sup>[27]</sup> The underlying mechanism for this relation remained unclear, but the affected hypothalamopituitary-adrenal axis and the failed glucocorticoid regulation by this system on the brain are thought to be responsible with the association.<sup>[28]</sup>

There are a lot of meta-analysis which was the first to summarize the association between chronic headache disorders and the risk of dementia, and some of them also indicated that any type of chronic headache disorder is a risk factor for developing of all-cause dementia.<sup>[18,19,29,30]</sup> However, we could not find higher incidence of any type of chronic headache history in the patient group than the control group, different from the results of large meta-analysis reviews. This may be related to either the small population of the study group which is failed to give optimal statistical data, or the difficulty of obtaining objective true chronic headache history, especially in the patient group, or may be related to combination of both.

The association we found might aid in identifying people prone to dementia or cognitive decline. This emphasizes the need to reveal the mechanisms underlying the link between headache and dementia, which may become all the more evident while improving the quality of life of patients with headache disorder. The information is critical to finding new preventive and treatment strategies for dementia. It is also of crucial importance that we figure out whether treatment for headache disorder might intervene in the overlapping pathways and subsequently reduce the risk of dementia.

Despite the small number of person included in the study, our results also highlighted that population-based data on the association of headache with incident dementia remain limited and that further study into the underlying mechanism of the association is needed.

#### Disclosures

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** None declared.

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