



Original Article

Comparison of Brain Atrophic Changes in Dementia Patients with and Without Swallowing Dysfunction

Mansoureh Chegeni¹, MD; Shiva Ebrahimian Dehaghani^{2,3*}, PhD; Mehrzad Lotfi¹, MD; Zahra Salami⁴, MD

¹Department of Radiology, Shiraz University of Medical Sciences, Shiraz Iran

²Department of Speech Therapy, School of Rehabilitation Sciences, Shiraz University of Medical Sciences, Shiraz, Iran

³Rehabilitation Sciences Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

⁴Department of Neurology, Shiraz University of Medical science, Shiraz Iran

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ABSTRACT

Background: On the one hand, very limited studies were performed on identifying the active regions during swallowing among healthy individuals and those with dementia. On the other hand, to the best of our knowledge, no research has yet compared the injured areas in the brain of patients with dementia with and without dysphagia, such that damage to specific regions in dementia causes dysphagia may be found using this approach. The present study was performed to evaluate the atrophic changes in the internal temporal lobe (hippocampus), frontal (anterior cingulate cortex), and parietal (posterior cingulate cortex), and insula cortex in these patients.

Methods: The present study is a retrospective cross-sectional study. 54 patients with dementia were investigated. The data were collected using a checklist, including information related to the dysphagia, and the brain MRI findings to determine atrophy. The extent of atrophic changes was recorded in the checklist using the median temporal lobe atrophy (MTA) score, Koedem score scale, and the global cortical atrophy (GCA) scale. To present the results, descriptive statistics, and data comparison, chi-square tests were used.

Results: The mean age of the examined patients was 72.01 with a standard deviation of 10.64 years, and range of 50-95 years. Out of them, 32 (59.3%) were male, and 22 (40.7%) were female. The degree atrophy of hippocampus ($p=0.12$), frontal lobe ($P=0.46$), parietal lobe ($P=0.83$), and insular cortex ($P=0.91$) in the patients with and without dysphagia did not show significant differences. The frequency distribution of the degree of atrophy based on the site of the development of atrophy was significant in the patients with dysphagia ($P=0.033$).

Conclusion: In general, the findings showed that individuals with dementia who had dysphagia had more hippocampal and frontal lobe (and anterior cingulate) atrophy than dementia patients who did not have this impairment.

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Introduction

The prevalence of dementia doubles every 20 years; it is predicted that the 35.6 million population of individuals

with dementia in 2010 would reach 65.7 and 115 million people in 2030 and 2050, respectively [1].

People with dementia suffer from symptoms such as memory disorders, diminished oral and linguistic skills, decreased concentration, and inability in decision-making. In moderate to severe dementia, disorders including inability to control digestive functions, the incidence of respiratory and urinary infections, immobility, and

*Corresponding author: Shiva Ebrahimian Dehaghani, Department of Speech Therapy, School of Rehabilitation Sciences, Abiverdi 1st St., Chamran Blvd, Alam Square, Shiraz, Iran. Tel: +98 9133035770
Email: ebrahimsh@sums.ac.ir

swallowing dysfunction are added to the primary symptoms of dementia [2]. Researchers showed that swallowing disorders of people with dementia are in terms of the inability in the food preparation stage in the mouth as well as the entrance of the food to the respiratory system during the pharyngeal stage of swallowing [3]. Eating and swallowing require cognitive awareness, visual perception of food, physiological response, planning, motor implementation, as well as sensorimotor responses [4]. As patients' focus, coordination, executive function, decision-making, and apraxia deteriorate, eating and swallowing become more difficult. When individuals with dementia lose cognitive and functional skills, behavioral issues with their diet become more apparent, limiting their ability to eat and swallow. This is not unexpected given that people with Alzheimer's disease lose all five senses, which are necessary for eating [5]. Although dementia is a clinical diagnosis and the physician reaches the diagnosis based on history taking, examination, and clinical findings, performing graphy is important in the patient assessment to rule out causes that mimic dementia as well as diagnose part of its etiological causes [6]. In this regard, various studies have mentioned atrophy in various cortical regions in dementia. For example, Humbert stated that generally the brain matter volume of Alzheimer's disease (AD) patients is smaller in the left paracentral lobule, superior temporal pole, and mid frontal gyrus and the right pre-central gyrus and cerebellum compared to normal individuals [7]. Besides, Humbert compared active regions during swallowing among health individuals and those with dementia, and found that the insula/operculum regions are associated with the initiation of swallowing. Moreover, Humbert findings indicated that the left anterior insula in AD patients may be more active compared to healthy individuals, since in inhibitory tasks (once the patient is ordered not to swallow), these individuals require more time so that they could stop their planning for swallowing [8].

On the one hand, the usage of novel rehabilitation techniques for treating swallowing dysfunction, such as transcranial magnetic stimulation depends on our knowledge about special regions that support swallowing function in the motor cortex [9]. On the other hand, very limited studies were performed on identifying the active regions during swallowing in healthy individuals and those with dementia. To our knowledge, no research has examined the brain-damaged areas in individuals with dementia with and without swallowing difficulties, such that damage to specific regions in dementia leads to swallowing dysfunction may be found by this comparison. Since in previous studies, the brain cortex regions involved in normal swallowing and affected by Alzheimer's were found to be the inferior frontal lobe [10, 11] and anterior cingulate cortex [12, 13], and other studies have reported activity in the anterior- middle temporal lobe (a region of brain cortex which undergoes considerable atrophy and Alzheimer's) during normal swallowing [14, 15], thus in this study our goal is to evaluate atrophic changes in the medial temporal lobe (hippocampus), frontal and parietal (cingulate cortex), and insular cortex in patients suffering from dementia with and without swallowing dysfunction.

Methods

The present study is a cross-sectional retrospective study approved by the ethics committee of Shiraz University of medical sciences (IR.SUMS.MED.REC.1398.585). After the approval of research proposal by the research Deputy of Shiraz University of medical sciences, the necessary permission for data collection was received. Before participation in the study, written informed consent form was completed and signed by the care providers of all participants. The researcher then investigated the MRI of patients who met the inclusion criteria using information from Shiraz University of medical sciences' medical imaging archive system (PACS) as well as MRI clichés from the patients themselves, and the extent of atrophic changes was recorded in the checklist. Participants

The participants in this study included individuals with dementia referred to the radiologic Department of Namazi and Shahid Faghihi hospitals in Shiraz, whose disease had been diagnosed by a neurologist from 20/10/2020 to 20/3/2021. The sample size was determined 54 in the two groups using GPower software and based on previous studies at alpha level of 0.05, test power of 80%, and mean statistical difference tests. Then, 27 individuals were assigned to the group of patients with dementia with swallowing dysfunction and 27 to the group of dementia patients without swallowing dysfunction. All individuals with dementia, including Alzheimer's, vascular dementia, and frontotemporal dementia, who had their condition diagnosed by a neurologist met the inclusion criteria. Clients would be diagnosed with dementia if they exhibited memory deficits that were accompanied by speech difficulty, executive dysfunction, and apraxia and could not be explained by reversible issues. Besides, they should not be transient and should have impaired the function of client. The patients who suffered from reversible conditions, including metabolic disorders, infectious problems, hydrocephaly, HIV, and Jacob's Creutzfeldt were excluded from the study as these conditions are reversible. In addition, the participants whose MRI was not available were again excluded.

Instruments

The data were collected using researcher-made checklist and based on the information recorded in the medical file of participants. This checklist has two sections. The first section captures demographic characteristics of patients, including age, gender, and duration of disease, while the second section includes the information related to swallowing dysfunction as well as the brain MRI findings to determine atrophy in the participants. To determine the condition of swallowing dysfunction in individuals with dementia, Albertinen Dementia Dysphagia Screening (ADDS) test and report of patients themselves were used [16].

MRI images of the participants were used to determine the extent of atrophy. The changes in the atrophy of the medial temporal lobe were evaluated by medial temporal lobe atrophy (MTA) score scale [17]. MTA score is a scale to determine the medial temporal lobe atrophy graded on T1 coronal images. This scale is based on a

visual assessment of the choroid fissure width, temporal horn width, and hippocampus height. On this scale, a score of zero indicates no atrophy, a score of 1 indicates choroid fissure widening alone, a score of 2 indicates widening of the temporal horn of the lateral ventricle, a score of 3 indicates loss of average hippocampus volume (height reduction), and a score of 4 indicates severe loss of hippocampus volume. In this scale, score 1 for ages younger than 75 years, score 2 or more are abnormal. For ages above 75 years and score 3 or more is abnormal. The parietal lobe atrophy changes were evaluated by Koedam score scale. This scale was developed to allow visual assessment of parietal atrophy in MRI, and is useful to assess the patients with dementia especially atypical Alzheimer's or premature Alzheimer's. To obtain this score, the brain should be evaluated in three segments of sagittal plane, coronal plane, and axial plane. In this scale, scored zero means closed sulci, no gyral atrophy. Score 1 represents mild gyral atrophy, mild sulcal widening, score 2 indicates substantial gyral atrophy, substantial sulcal widening, and score 3 represents marked knife blade atrophy and sulcal widening [18]. Furthermore, to determine the atrophy in other parts of the brain, global cortical atrophy (GCA) scale was used. It is a qualitative ranking system developed for evaluating brain atrophy especially regarding neurodegenerative diseases. This investigation of atrophy is performed on 13 brain regions evaluated separately in each hemisphere, and the outcome is a final score which is the sum of score of all regions [17].

After data collection, the information were inputted into SPSS 23 software. Descriptive data were reported using descriptive statistics (mean and standard deviation), and for data analysis, chi-square test was used. The significance level was considered 0.05 in this study.

Results

Out of 54 patients examined in this study, 27 were in the swallowing dysfunction group and 27 in the swallowing dysfunction group. The mean age of the patients was 72.01 with standard deviation 10.64 years, and with the range of 50-95 years. Thirty-two (59.3%) were male and 22 (40.7%) were female. The mean age of the male patients was 73 with SD of 9.70 years, and that of female patients was 70.59 with SD of 11.98 years. The mean duration of disease was 2.20 years with the standard deviation of 1.27 years. The duration of disease among the participants ranged from 1 to 6 years.

Table 1 presents the frequency distribution of the gender and mean difference of age and duration of disease among patients with and without swallowing

dysfunction. The mean age of patients with swallowing problem was greater than that of patients without this dysfunction, according to the table's findings, and this difference was significant. Moreover, the duration of disease was significantly longer in patients with swallowing dysfunction compared to those without it. The frequency distribution of swallowing dysfunction was higher in male patients compared to women, but this difference was not significant.

Figure 1 shows the frequency distribution of degree of hippocampus atrophy in all patients. Based on the diagram, 7.4% of patients had no atrophy, 35.2% had score 1 (only widening of choroid fissure), 37 had score 2 (widening of temporal horn of lateral ventricle), 18.5% had moderate atrophy (score 3), and 1.9 had severe atrophy.

Table 2 reports the frequency distribution of the degree of hippocampus atrophy in patients with and without

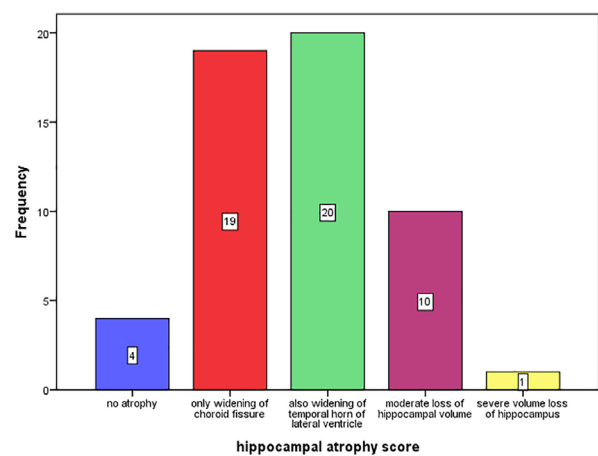


Figure 1: Frequency distribution of degree of hippocampus atrophy in all patients

swallowing dysfunction. According to the table, score 2 of hippocampal atrophy had the greatest incidence in patients with swallowing difficulty, whereas score 1 of hippocampus atrophy had the highest frequency in patients without this problem. The difference between the two groups was not statistically significant.

Figure 2 indicates the frontal lobe atrophy frequency distribution (and anterior cingulate) in all patients. Based on the diagram, 3.7% of patients had no atrophy, 46.3% had mild atrophy, 42.6% had moderate, and 7.4% had severe atrophy.

Table 3 lists the frequency distribution of the degree of frontal lobe atrophy (and anterior cingulate) in patients with and without swallowing dysfunction. According to the table's findings, patients with swallowing difficulties had the greatest frequency of score 2 frontal lobe atrophy

Table 1: Frequency distribution of the gender as well as the mean difference of age and duration of disease in patients with and without swallowing dysfunction

Swallowing dysfunction	Variable	Yes	No	P
Age		75.33±10.39	68.70±10.01	0.021
Gender	Male	18 (66.6%)	14 (43.8%)	0.26
	Female	9 (33.3%)	13 (59.1%)	
Duration of disease		2.62±1.57	1.77±0.69	0.014

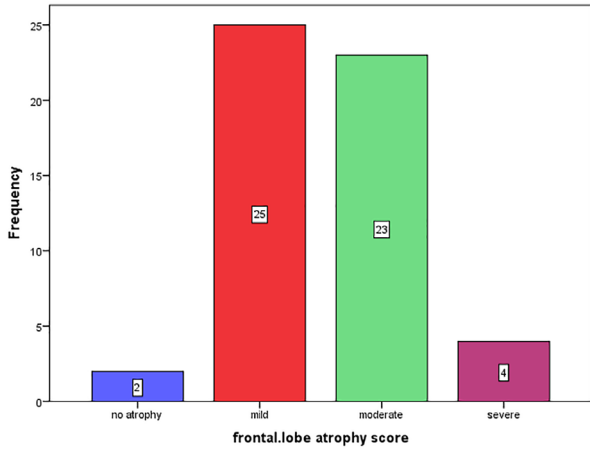


Figure 2: Depicts the frequency distribution of the frontal lobe atrophy (and anterior cingulate) in all patients.

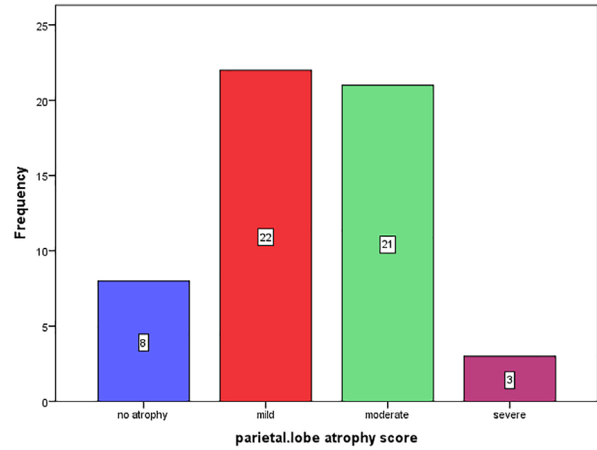


Figure 3: Frequency distribution of the degree of parietal lobe atrophy (and posterior cingulate) in all patients

Table 2: Frequency distribution of degree of hippocampus atrophy in the patients with and without swallowing dysfunction

Swallowing dysfunction	Yes	No	P
Degree of hippocampus atrophy			
Score 0	0	4 (14.8%)	0.12
Score 1	8 (29.6%)	11 (40.7%)	
Score 2	11 (40.7%)	9 (33.3%)	
Score 3	7 (25.9%)	3 (11.1%)	
Score 4	1 (3.7%)	0	

Table 3: Frequency distribution of the degree of frontal lobe atrophy (and anterior cingulate) in patients with and without swallowing dysfunction

Swallowing dysfunction	Yes	No	P
Degree of frontal lobe atrophy			
No atrophy	0	2 (7.4%)	0.46
Score 1 (mild atrophy)	12 (44.4%)	13 (48.1%)	
Score 2 (moderate atrophy)	13 (48.1%)	10 (37.0%)	
Score 3 (severe atrophy)	2 (7.4%)	2 (7.4%)	

Table 4: Frequency distribution of the degree of parietal lobe atrophy (and posterior cingulate) in patients with and without swallowing dysfunction

Swallowing dysfunction	Yes	No	P
Degree of parietal lobe atrophy			
No atrophy	5 (18.5%)	3 (11.1%)	0.83
Score 1 (mild atrophy)	11 (40.7%)	11 (40.7%)	
Score 2 (moderate atrophy)	10 (37.0%)	11 (40.7%)	
Score 3 (severe atrophy)	1 (3.7%)	2 (7.4%)	

(moderate atrophy), whereas patients without swallowing dysfunction had the highest frequency of score 1 frontal lobe atrophy (mild atrophy). The difference between the two groups was not statistically significant.

Figure 3 reveals the frequency distribution of the degree of parietal lobe atrophy (and posterior cingulate) in all patients. Based on the diagram, 14.8% of patients had no atrophy, 40.8% had mild atrophy (score 1), 38.9% showed moderate atrophy (score 2), and 5.6% suffered from severe atrophy (score 3).

The frequency distribution of parietal lobe atrophy (including posterior cingulate) in individuals with and without swallowing difficulties is shown in Table 4. According to the table, in patients with swallowing dysfunction, degree score 1 of parietal low atrophy (mild atrophy) had the highest frequency, and in patients without this dysfunction, score 1 and score 2 of parietal lobe atrophy

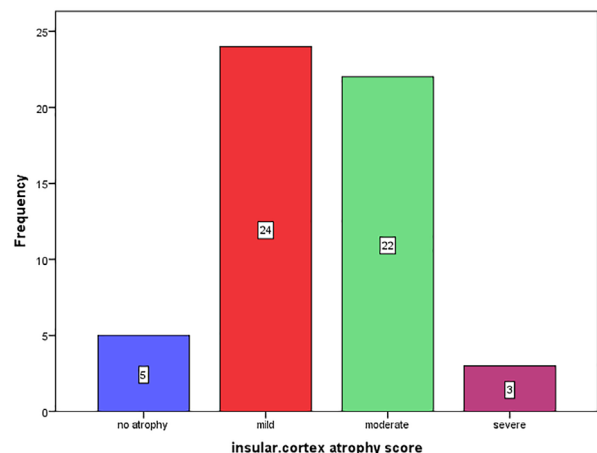


Figure 4: Frequency distribution of the degree of insular cortex atrophy in all patients

Table 5: The frequency distribution of the degree of insular cortex atrophy in patients with and without swallowing dysfunction

Swallowing dysfunction	Yes	No	P
Degree of insular cortex atrophy			
No atrophy	3 (11.1%)	2 (7.4%)	0.91
Score 1 (mild atrophy)	12 (44.4%)	12 (44.4%)	
Score 2 (moderate atrophy)	11 (40.7%)	11 (40.7%)	
Score 3 (severe atrophy)	1 (3.7%)	1 (7.4%)	

Table 6: Frequency distribution of the degree of atrophy based on site of development of atrophy in patients with swallowing dysfunction

Site of involvement	Hippocampal	frontal.lobe	parietal.lobe	insular.cortex	P
Degree of atrophy					
No atrophy	0	0	5 (18.5%)	3 (11.1%)	0.033
Score 1	8 (29.6%)	12 (44.4%)	11 (40.7%)	12 (44.4%)	
Score 2	11 (40.7%)	13 (48.1%)	10 (37.0%)	11 (40.7%)	
Score 3	7 (25.9%)	2 (7.4%)	1 (3.7%)	1 (3.7%)	
Score 4	1 (3.7%)	0	0	0	

Table 7: Frequency distribution of the degree of atrophy based on site of development of atrophy in patients without swallowing dysfunction

Site of involvement	Hippocampal	frontal.lobe	parietal.lobe	insular.cortex	P
Degree of atrophy					
No atrophy	4 (14.8%)	2 (7.4%)	3 (11.1%)	2 (7.4%)	0.99
Score 1	11 (40.7%)	13 (48.1%)	11 (40.7%)	12 (44.4%)	
Score 2	9 (33.3%)	10 (37.0%)	11 (40.7%)	11 (40.7%)	
Score 3	3 (11.1%)	2 (7.4%)	2 (7.4%)	1 (7.4%)	

(mild and moderate atrophy) had the maximum frequency, but this difference was not statistically significant.

Figure 4 indicates the frequency distribution of the degree of insular cortex atrophy in all patients. According to the diagram, 9.3% of patients had no atrophy, 44.4% showed mild atrophy (score 1), 40.7% indicated moderate atrophy (score 2), and 5.6% had severe atrophy (score 3).

Table 5 presents the frequency distribution of the degree of insular cortex atrophy in the patients with and without swallowing dysfunction. Based on the table's results, score 1 cortex atrophy (mild atrophy) had the highest frequency in both patients with and without swallowing dysfunction, but this difference was not statistically significant.

Table 6 shows the frequency distribution of the degree of atrophy in individuals with swallowing difficulties depending on the place of atrophy development. According to the table, score 2 atrophy had the greatest incidence in patients with hippocampal and frontal lobe involvement, whereas score 1 had the highest frequency in patients with parietal lobe and insular cortex involvement. The difference between the two groups was not statistically significant.

Table 7 lists the frequency distribution of the degree of atrophy based on the site of development of atrophy in patients without swallowing dysfunction. Based on the table, in patients with involvement of hippocampus, frontal lobe, parietal lobe, and insular cortex involvement, score 1 had the highest frequency. This difference was not statistically significant.

Discussion

The results of the present study indicated that most patients

with swallowing dysfunction had MTA=2 (40.7%), but MTA=1 (40.7%) showed the highest frequency in patients without swallowing dysfunction. This difference was not statistically significant. These results indicated that patients with swallowing dysfunction showed higher atrophy in the medial temporal lobe. Besides, most patients with swallowing dysfunction had moderate frontal lobe atrophy (score 2, 48.1%), and most patients without swallowing dysfunction had mild frontal lobe atrophy (48.1%), and this difference was not significant. In this regard, in patients with swallowing dysfunction, score 1 of parietal lobe atrophy (mild atrophy) had the highest frequency, and in patients without swallowing dysfunction, score 1 and score 2 of parietal lobe atrophy (mild and moderate) had the highest frequency. In addition, insular cortex atrophy did not differ significantly among dementia patients with and without swallowing dysfunction. The results showed that the mean age and disease duration were significantly higher in dementia patients with swallowing dysfunction than those without this dysfunction. With regards to the results related to the higher atrophy of the medial temporal lobe in patients with swallowing dysfunction, Humbert indicated that the hippocampus and para-hippocampus regions which are involved in cognitive demands of swallowing are smaller bilaterally in AD patients [7]. Besides, Humbert showed that the left parahippocampus region in elderly adults has shown greater activity compared to the youth in the "do not swallow" task. This task was designed for investigating ordered swallowing. The aim of this type of task was to investigate the differences of brain functioning in the off stage of intended swallowing in healthy elderly and those with Alzheimer's disease. Thus, it seems that the medial temporal lobe atrophy in dementia patients is

an important predictor in the incidence of swallowing dysfunction in these patients.

Furthermore, based on the results of the present study, most patients with swallowing dysfunction had moderate atrophy of the frontal lobe (48.1% score 2), and most patients without swallowing dysfunction had mild frontal lobe atrophy (48.14% score 1), and this difference was not significant. Previous studies have also shown that the lateral parts of the precentral gyrus, the posterior portion of the inferior frontal gyrus [19], and the anterior lateral frontal area [20] are involved in swallowing. Besides, Humbert showed that the anterior and posterior cortex of central gyrus and frontal-parietal operculum become activated in the “swallow your saliva” task [8]. The results of these studies in line with the present study show that the frontal lobe atrophy is an important predictor for the incidence of swallowing dysfunction in the patients with dementia.

In this regard, in the patients with swallowing dysfunction degree score 1 of parietal lobe atrophy (mild atrophy) had the highest frequency, and in the patients without swallowing dysfunction score 1 and score 2 of parietal lobe atrophy (mild and moderate atrophy) had the highest frequency. These results suggest that incidence of higher atrophy in the parietal lobe has not been an important predictor in incidence of swallowing dysfunction in dementia patients. Results of previous studies also show that during the “do not swallow” task, healthy elderly and patients with Alzheimer’s disease did not show the differences in their parietal lobe functioning [8].

Therefore, this study’s results showed that insular cortex atrophy did not differ significantly in dementia patients with and without swallowing dysfunction. The study by Humbert showed that insula is one of the few cortical regions which undergoes atrophy at the beginning of AD [8]. Since swallowing dysfunction belongs to the group of symptoms which are observed in the advanced stages of dementia [5], it can be concluded that the findings of the present study concur with the results of Humbert; involvement of insula is not different in dementia patients in the primary stages of disease and the patients who do not show swallowing dysfunction in the disease symptoms. Meanwhile, there are also studies that have noted the very important role of the right insula during swallowing in diseases such as stroke, which is not in line with the present study results [21]. It seems that further studies are required regarding the role of insula atrophy in the incidence of swallowing dysfunction in patients with dementia.

Conducting this type of study contributes to our knowledge about the regions involved in swallowing. Also, based on the results of this study, in patients with dementia, the atrophy of the medial temporal lobe and frontal lobe can be investigated and in case of the presence of atrophy in these portions, swallowing dysfunction screenings could be done thereby preventing the incidence of problems resulting from swallowing dysfunction in these people.

Finding individuals with dementia who could cooperate in swallowing dysfunction tests was time-consuming and caused the study to take a long time.

Conclusion

The results of this study showed that the atrophy of the medial temporal lobe and frontal lobe (and anterior cingulate) in dementia patients is an important predictor in the incidence of swallowing dysfunction in these patients.

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Conflict of Interest: None declared.

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