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Incidental findings of brain magnetic resonance imaging in patients with treatment-resistant depression

Tedaviye dirençli depresyon hastalarında beyin manyetik rezonans görüntülemenin tesadüfi bulguları

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Abstract

Aim: In this study, incidental findings of brain magnetic resonance imaging (MRI) of patients diagnosed with treatment-resistant depression (TRD) were compared with healthy controls (HC).

Materials and Methods: The study included 68 patients with TRD (42 females, 26 males) and 72 HC (35 females, 37 males). Global assessment scale (GAS) was administered.

Results: In the TRD group, those with general cerebral atrophy were found to have significantly lower global assessment scale (GAS) scores (p<0.001). In the TRD group, those with cavum veli interpositi (CVI) were found to have significantly lower GAS scores (p=0.001). In the TRD group, when the effect of age was controlled, a significant correlation was found between the GAS score and the duration of the disorder (r=-0.400; p=0.001).

Conclusion: CVI, a neurodevelopmental abnormality, has been shown to be more common in patients diagnosed with TRD.

Keywords: Treatment-resistant major depressive disorder; Magnetic resonance imaging; Incidental finding.

Öz

Amaç: Bu çalışmada, tedaviye dirençli depresyon (TDD) tanılı hastaların beyin manyetik rezonans görüntüleme (MRG)'nin tesadüfi bulguları sağlıklı kontrollerle (SK) karşılaştırıldı.

Gereç ve Yöntem: Çalışmaya TDD tanılı 68 hasta (42 kadın, 26 erkek) ve 72 SK (35 kadın, 37 erkek) dahil edildi. Global değerlendirme ölçeği (GDÖ) uygulandı.

Bulgular: TDD grubunda, genel serebral atrofisi olanların global değerlendirme ölçeği (GDÖ) skorlarının anlamlı derecede düşük olduğu bulundu (p<0,001). TDD grubunda, kavum veli interpositi (KVİ) saptananların GDÖ skorlarının anlamlı derecede düşük olduğu bulundu (p=0,001). TDD grubunda, yaşın etkisi kontrol edildiğinde, GDÖ skoru ile bozukluk süresi arasında anlamlı bir korelasyon bulundu (r=-0,400; p=0,001).

Sonuç: Nörogelişimsel bir anormallik olan KVİ'nin TDD tanılı hastalarda daha yaygın olduğu gösterilmiştir.

Anahtar Kelimeler: Tedaviye dirençli majör depresif bozukluk; Manyetik rezonans görüntüleme; Tesadüfi bulgu.

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Introduction

Major depressive disorder (MDD) is characterized by symptoms including a persistently low mood, diminished pleasure in activities, fatigue, psychomotor retardation, difficulty concentrating, and disruptions in sleep and appetite. This condition imposes a substantial burden on affected individuals and is linked to significant economic costs.[1] According to 2015 data from the World Health Organization, the global prevalence of depression ranges from 2.90% to 6.31%, with a prevalence rate of 4.4% in Turkey.[2] MDD is influenced by a combination of social, cultural, and biological factors and is typically diagnosed in women at twice the rate of men. Approximately 40% of individuals experience their first depressive episode before the age of 20, with onset most commonly occurring between mid-adolescence and the mid-40s.[3,4]

MDD often follows a recurrent, lifelong course with episodic patterns. Approximately 80% of individuals experience at least one subsequent episode of depression. The likelihood of future episodes increases with each recurrence, particularly when the onset occurs at an older age, which is associated with less favorable outcomes.[5] While approximately half of patients recover within a year, with episodes typically lasting three to six months, the other half do not achieve full remission.[6] Treatment-resistant depression (TRD) describes cases where individuals fail to achieve remission despite several therapeutic interventions.[7] There is no singular, universally recognized definition of treatment-resistant depression (TRD); however, it is typically characterized in patients who do not exhibit a sufficient response to at least two trials of appropriate antidepressant therapy. Prevalence estimates vary widely due to these differing definitions, with rates reported between 12% and 55%.[8] Studies indicate that patients with substantial treatment resistance often experience ongoing symptoms and impaired functioning, despite continuous treatment.[9]

The mechanisms driving TRD remain incompletely understood. While structural brain alterations in MDD have been widely studied, research on brain structure in TRD is more limited. MRI studies on TRD patients have primarily focused on white matter (WM) and gray matter (GM) variations.[10] Research demonstrates that both first-episode MDD and TRD patients exhibit diminished gray matter volume in the right middle temporal cortex when contrasted with healthy controls (HC), with a notable reduction in bilateral caudate volume specifically in TRD cases.[11] Additionally, patients with TRD display decreased GM density in the right putamen, right superior frontal gyrus, and diminished volumes in the right caudate nucleus and right prefrontal lobe compared to HCs and individuals recovered from recurrent MDD. Fronto-striatal atrophy patterns in TRD have been significantly linked to disorder severity, affecting regions like the rostral anterior cingulate cortex and the hippocampus.[12] In TRD patients, reduced GM volumes in the insula and parahippocampal gyrus have also been reported, and in comparison to first-episode MDD, patients with TRD show smaller right medial frontal gyrus and left insula volumes, correlated with the duration of illness.[13] One WM study found a notable decrease in fractional anisotropy among TRD patients, involving regions such as the corpus callosum, forceps minor, forceps major, and bilateral superior and inferior longitudinal fasciculi.[14] Besides these commonly noted structural changes in MDD, incidental anatomical differences also exist. This study aims to identify incidental MRI findings in TRD patients, hypothesizing a possible link between these incidental findings and TRD.

Materials and Methods

Type of the study

A cross-sectional study.

The sample of the study

This study was conducted in Adıyaman Training and Research Hospital psychiatry outpatient clinic. Sociodemographic and clinical data of the participants were obtained through the hospital record system and e-nabiz. The e-nabiz application serves as a database that provides access to comprehensive medical histories of patients, including details on surgeries, hospital stays, laboratory results, imaging studies, allergy information,

diagnoses, prescribed medications, vaccination history, cancer screening records, intensive care details, reports, and emergency documentation. The treatment processes of patients followed up with depression spectrum disorder are recorded by their physicians. Through the patient registration system, information on the duration of medication use, depression severity score, and treatment resistance status of the patients can be accessed. Individuals who were similar to the TRD group in terms of age and gender, who applied to the hospital where the study was conducted for any reason and had MRIs obtained but were not diagnosed with any disease, were accepted as the control group.

The criteria of TRD

The definition of TRD adopted by the US Food and Drug Administration and the European Medicines Agency is failure to respond to two or more antidepressant regimens despite adequate dose and duration and adherence to treatment.[15] This definition was also taken into account in this presented study.

The procedures of the study

Brain MRIs scanned for any purpose are evaluated by the same hospital's radiologist and the imaging report is also recorded in the e-nabiz. Atrophy, one of the parameters investigated in this study, refers to generalized cerebral atrophy.

The Fazekas scale is utilized to classify and assess the severity of white matter (WM) hyperintensities observed in brain imaging studies. These lesions may signal a range of neurological issues, particularly related to small vessel disease or cerebrovascular conditions. The scale generally includes two main categories: Fazekas Score 0 indicates no significant WM hyperintensities, while Scores 1, 2, and 3 denote progressively greater severity of hyperintensities. Higher scores on the Fazekas scale are frequently linked to an increased risk of cognitive decline.[16]

The septum pellucidum is a delicate, semi-transparent bilaminar structure comprised of both white and gray matter, located between the anterior horns of the lateral ventricles in the brain. Variations of the septum pellucidum include the cavum septum pellucidum (CSP), cavum vergae (CV), and cavum veli interpositi (CVI).[17]

There were 72,325 admissions to the Adıyaman Training and Research Hospital psychiatry outpatient clinic between the specified dates. Nineteen thousand one hundred and fifty-two of these admissions were for health board reports. Nine thousand eight hundred and seventy-four of the remaining admissions consisted of depression spectrum disorder diagnoses. Information indicating that 2,843 of these admissions met the TRD criteria was recorded in the patient registration system. One hundred seventy-six of these admissions had a brain MRI report after TRD record. Abnormal brain MRI findings were reported in 11 of these reports. The e-nabiz records of the subjects with non-abnormal brain MRIs were examined in detail. Twenty-three patients were excluded due to a lack of sufficient data confirming they met the TRD criteria. Thirty-six patients were excluded due to comorbid mental disorder. Seven patients were excluded due to comorbid neurological disease, two patients due to history of brain trauma, one patient were excluded due to history of brain tumour, one patient due to previous brain surgery, four patients due to history of electroconvulsive therapy, and ten patients due to chronic and/or systemic diseases. Thirteen patients with TRD were excluded from the study because they were not in remission. Consequently, a total of 68 individuals diagnosed with TRD were incorporated into the study. A flowchart depicting the study's sample is provided in Figure 1. All included patients were in remission and were receiving regular psychotropic medications. The HC group consisted of individuals who had undergone brain MRI examinations due to conditions like non-migraine headaches and vertigo, with findings reported as normal. These individuals had no active illnesses and were not on any medication.

Data collection tools

Sociodemographic information for all patients was collected using the patient registration system. The Global Assessment

Scale, created by Endicott and Spitzer in 1976, is a rapid assessment tool that evaluates various dimensions of changes in psychopathology, including psychological, social, and professional functioning. This scale has a scoring range from 0 to 100.[18]

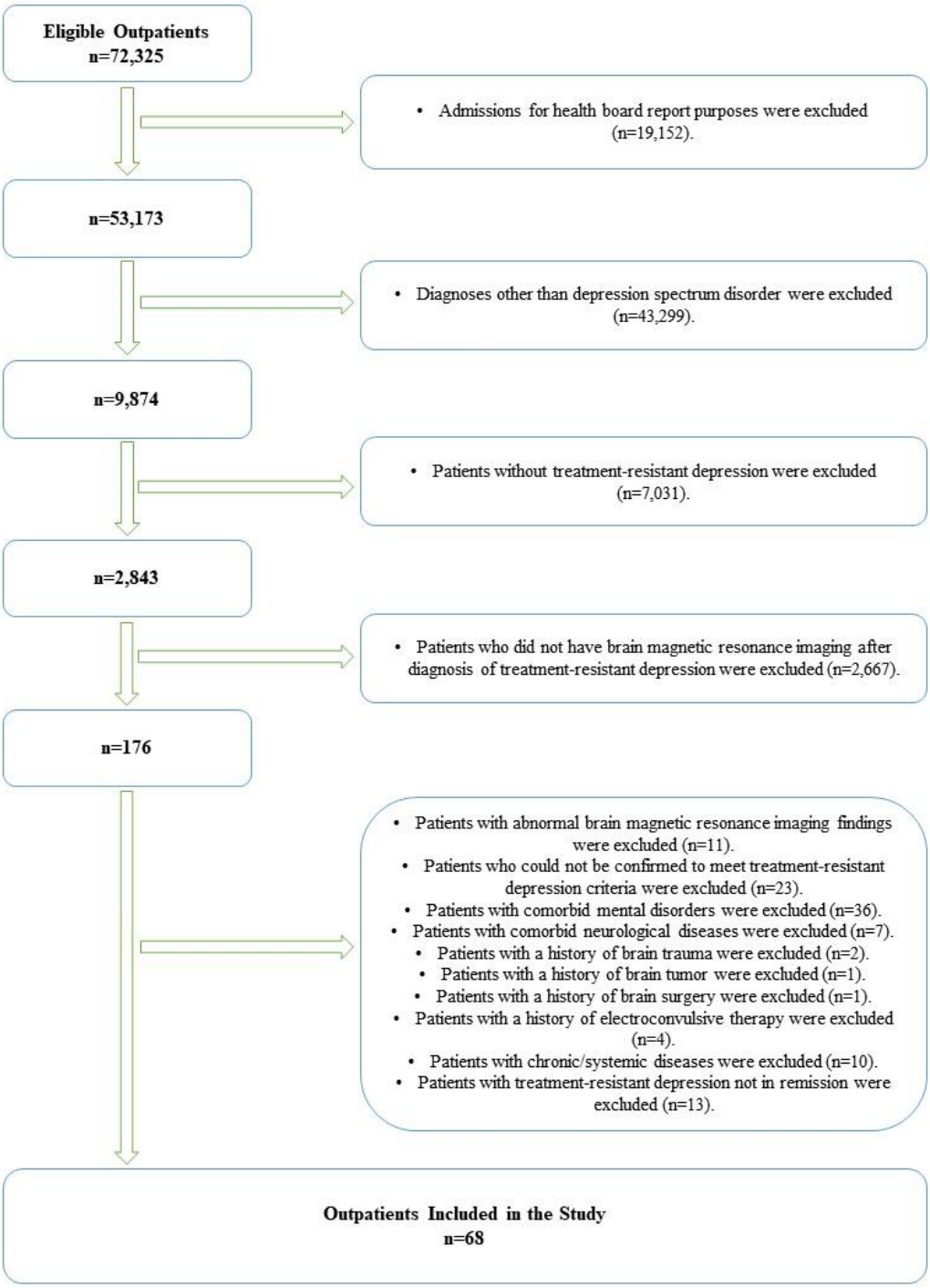

Figure 1. Flow-chart illustration of the study's sample

For brain MRI scans, we utilized a Philips Achieva MR machine (Philips Medical Systems, Best, Netherlands), applying a magnetic field intensity of 1.5 Tesla using a head coil. The mass intermedia was identified in cross-sectional images through the cranial midline, specifically from T1 FLAIR-weighted images in the sagittal plane. The MRI parameters included a repetition time (TR) of 1665 ms, echo time (TE) of 20 ms, a field of view (FOV) of 220×230, slice thickness of 5 mm, a matrix of 292×214, a number of acquisitions (NSA) of 1, a gap of 1 mm, voxel size of 0.75×1.07×5, and a total of 24 sections.

The images were evaluated using the PACS system at our facility and the Philips Achieva Rev R5 v30-rev.02 workstation. For the assessment, we employed T1-weighted axial, T2-weighted axial, FLAIR axial, T2-weighted coronal, and T1-weighted sagittal images. Patient data, including age, gender, and brain MRI findings, were recorded. The Fazekas scale was utilized to evaluate cognitive aging, following the guidelines for white matter hyperintensities (WMH). According to the Fazekas scale, grades 0–1 indicate spot foci, grade 2 signifies the initial formation of a foci group, and grade 3 refers to more extensively grouped areas.[19]

Data analysis

Statistical evaluations were conducted using IBM SPSS Statistics version 26.0 (IBM SPSS Inc., Chicago, IL, USA). Continuous variables were presented as averages with their standard deviations, and categorical variables were displayed as percentages. Kurtosis and skewness values were calculated and compliance with normal distribution was determined by the Kolmogorov-Smirnov test. For continuous data that met normality assumptions, an independent samples t-test was used for comparisons between independent binary groups; otherwise, the Mann-Whitney U test was applied. Categorical variables were evaluated using Chi-square tests and Fisher's Exact test. A p-value threshold of less than 0.05 was defined as statistically significant.

Ethics committee approval

Ethics committee approval was obtained from Adıyaman University for this study (Date of Decision: May 21, 2024; IRB Number: 2024/5-16). All methods followed the ethical guidelines outlined in the Declaration of Helsinki. Signed informed consent form was obtained from all participants.

Results

The TRD group included 68 participants (42 women and 26 men), whereas the HC group comprised 72 individuals (35 women and 37 men). The average age in the TRD group was 38.31 ± 9.30 years, compared to 37.28 ± 8.15 years in the HC group. There were no notable differences between the groups in terms of mean age (p=0.486) or gender distribution (p=0.118). Within the TRD group, the average duration of MDD was 13.98 ± 7.21 years.

All patients in the TRD group were using at least one antidepressant medication (venlafaxine 26, duloxetine 10, fluoxetine nine, bupropion seven, escitalopram seven, sertraline six, paroxetine two, and reboxetine one). Twenty-seven patients in the TRD group were using a second antidepressant medication (mirtazapine 10, clomipramine six, amitriptyline six, mianserin three, sertraline one, and escitalopram one). Four patients in the TRD group were using a third antidepressant medication (clomipramine three and amitriptyline one). As a result, 41 patients (60.30%) were using one antidepressant, 23 patients (33.80%) were using two antidepressants, and four patients (5.90%) were using three antidepressants. In the TRD group, 38 patients were using one of the antipsychotic medications other than quetiapine (olanzapine 13, aripiprazole 12, paliperidone five, risperidone four, sulpride two, and clozapine two). The number of patients using quetiapine for the treatment of insomnia in the TRD group was 18 (26.50%). In the TRD group, five patients (7.40%) were using lamotrigine as a mood stabilizer, while three patients (4.40%) were using lithium. In the TRD group, 16 patients (23.50%) were managed with single, 24 patients (35.30%) with double, 17 patients (25.00%) with triple, seven patients (10.30%) with quadruple and four patients (5.90%) with quintuple psychotropic medications (antidepressant, antipsychotic, or mood stabilizer). Three patients (4.40%) in the TRD group were on thyroid hormone replacement. There were no patients using benzodiazepines or psychostimulants.

The sociodemographic data and frequency of incidental MRI findings of the groups was shown in Table 1 and Table 2. The GAS score showing the level of functionality in the TRD group was significantly lower than in the HC group (p<0.001). Generalized cerebral atrophy (p=0.012), Fazekas grade (p=0.013), and CVI

(p=0.002) were significantly higher in the TRD group than in the HC group.

No remarkable differences were found between genders in terms of antidepressant type, antipsychotic type, thyroid replacement therapy, Fazekas grade, CVI, and generalized cerebral atrophy in patients with TRD (Table 2).

Table 1. Comparison of sociodemographic, clinical data, and incidental MRI findings between patients with TRD and HCs.

Variables	TRD (n=68) mean±SD & n (%)	HC (n=72) mean±SD & n (%)	*p*
Age (years)	38.31±9.30	37.28±8.15	0.486[a]
GAS score	64.55±8.43 (mean rank 34.50)	93.31±4.82 (mean rank 104.50)	<0.001*[b]
Gender (female/male)	42/26	35/37	0.118[c]
Atrophy (generalized atrophy)	6 (8.80)	0 (0.00)	0.012*[d]
Fazekas (grade 0/grade 1/grade 2/grade 3)	60/5/2/1	71/1/0/0	0.013*[d]
Cavum veli interpositi	8 (11.80)	0 (0.00)	0.002*[d]
Cavum septum pellucidum	4 (5.90)	0 (0.00)	0.053[d]
Cavum vergae	3 (4.40)	0 (0.00)	0.112[d]
Ethmoidal thickening	26 (38.20)	24 (33.30)	0.545[c]
Maxillary thickening	11 (16.20)	15 (20.80)	0.479[c]
Frontal thickening	1 (1.50)	4 (5.60)	0.193[d]
Sphenoid thickening	3 (4.40)	0 (0.00)	0.112[d]
Retention cyst	11 (16.20)	14 (19.40)	0.614[c]
Arachnoid cyst	4 (5.90)	0 (0.00)	0.053[d]
Adenoid hypertrophy	10 (14.70)	5 (6.90)	0.138[c]
Non-specific gliotic foci	4 (5.90)	2 (2.80)	0.365[d]
Demyelination plaque	1 (1.50)	0 (0.00)	0.486[d]
Mastoiditis	2 (2.90)	3 (4.20)	0.527[d]
Virchow-Robin spaces	2 (2.90)	0 (0.00)	0.234[d]
Pituitary macroadenoma	1 (1.50)	0 (0.00)	0.486[d]
Antrochoanal polyp	1 (1.50)	0 (0.00)	0.486[d]
Central neurocytoma	1 (1.50)	0 (0.00)	0.486[d]
Meningioma	0 (0.00)	1 (1.40)	0.514[d]
Hyperostosis frontalis interna	1 (1.50)	0 (0.00)	0.486[d]

*p<0.05; Independent Samples t-test (a), Mann-Whitney U test (b), Chi-square analysis (c) and Fisher's Exact test (d) were used in statistical analysis. Abbreviations: MRI=Magnetic resonance imaging, TRD=Treatment-resistant depression, HC=Healthy control, SD=Standard deviation, GAS=Global assessment scale

Table 2. Comparison of sociodemographic, clinical data, and incidental MRI findings of TRD group by gender.

Variables	Female (n=42) mean±SD & n (%)	Male (n=26) mean±SD & n (%)	*p*
Age (years)	39.17±9.10	36.92±9.64	0.338[a]
GAS score	62.88±8.56	66.30±8.45	0.112[a]
Duration MDD	15.23±7.15	11.96±6.98	0.069[a]
Atrophy (generalized atrophy)	4 (9.50)	2 (7.70)	0.582[c]
Fazekas (grade 0/grade 1/grade 2/grade 3)	38/1/2/1	22/4/0/0	0.359[c]
Cavum veli interpositi	6 (14.30)	2 (7.70)	0.341[c]
Cavum septum pellucidum	2 (4.80)	2 (7.70)	0.496[b]
Cavum vergae	1 (2.40)	2 (7.70)	0.324[c]
Ethmoidal thickening	15 (35.70)	11 (42.30)	0.587[b]
Maxillary thickening	7 (16.70)	4 (15.40)	0.889[b]
Frontal thickening	0 (0.00)	1 (3.80)	0.382[c]
Sphenoid thickening	1 (2.40)	2 (7.70)	0.324[c]
Retention cyst	6 (14.30)	5 (19.20)	0.590[b]
Arachnoid cyst	1 (2.40)	3 (11.50)	0.152[c]
Adenoid hypertrophy	5 (11.90)	5 (19.20)	0.407[b]
Non-specific gliotic foci	3 (7.10)	1 (3.80)	0.504[c]
Demyelination plaque	0 (0.00)	1 (3.80)	0.382[c]
Mastoiditis	0 (0.00)	1 (3.80)	0.382[c]
Virchow-Robin spaces	2 (4.80)	0 (0.00)	0.378[c]

Pituitary macroadenoma	0 (0.00)	2 (7.70)	0.143[c]
Antrochoanal polyp	0 (0.00)	1 (3.80)	0.382[c]
Central neurocytoma	0 (0.00)	1 (3.80)	0.382[c]
Hyperostosis frontalis interna	1 (2.40)	0 (0.00)	0.618[c]

Independent Samples t-test (a), Chi-square analysis (b) and Fisher's Exact test (c) were used in statistical analysis. Abbreviations: MRI=Magnetic resonance imaging, TRD=Treatment-resistant depression, SD=Standard deviation, GAS=Global assessment scale, MDD=Major depressive disorder

In the TRD group, GAS scores of those with generalized cerebral atrophy (mean ± standard deviation=49.50±3.93; mean rank=5.17) and those without (mean ± standard deviation=65.61±7.56; mean rank=37.34) were compared and it was found that those with generalized cerebral atrophy had significantly lower GAS scores (Mann-Whitney U test $p<0.001$).

In the TRD group, GAS scores of those with CVI (mean ± standard deviation=65.61±7.91; mean rank=12.06) and those without (mean ± standard deviation=53.50±6.00; mean rank=37.49) were compared and it was found that those with CVI had significantly lower GAS scores (Mann-Whitney U test $p=0.001$).

Correlation analysis conducted within the TRD group, while controlling for age, revealed a significant relationship between the GAS score and the duration of MDD ($p=0.001$, r=-0.400).

Discussion

This study compared the incidental findings obtained from MRI in patients with TRD with those in HC and the following findings were obtained: (i) Higher Fazekas grades were detected more frequently in the TRD group, (ii) Generalized cerebral atrophy was higher in the TRD group, (iii) CVI was higher in the TRD group, (iv) Incidental MRI findings in female and male patients were similar, (v) In the TRD group, the presence of CVI and generalized cerebral atrophy was associated with lower functionality.

On T2-weighted MRI sequences, WM hyperintensities are shown as lesions with increased signal intensity. Amount of WM T2 hyperintense lesions is measured using the Fazekas classification system.[16] Histopathological findings such as demyelination, axon loss, arteriosclerosis, dilated perivascular spaces, gliosis, lacunar infarcts, and spongiosis are detected in WM hyperintensities areas. WM hyperintensities can occur in healthy individuals,[20] studies have identified a correlation between these hyperintensities and cerebrovascular risk factors such as hypertension,[21] hypercholesterolemia,[22] and diabetes mellitus.[23] However, patients in this study did not exhibit these risk factors. WM hyperintensities have been extensively studied in depression,[24] particularly in late-life depression.[25] A meta-analysis by Wang et al.[26] found that deep WM hyperintensities were significantly linked to depression in their cross-sectional subgroup analyses. Numerous cross-sectional studies have also indicated an association between WM hyperintensities and TRD.[27] Furthermore, alterations in WM microstructure have been correlated with treatment resistance in MDD.[14] Patients with a greater burden of WM hyperintensities may require higher initial doses of antidepressants and may provide insights into the treatment response trajectory.[28] This study demonstrated that WM hyperintensities were significantly higher in TRD than in HC. This finding supports the literature that WM hyperintensities may be associated with treatment resistance.

In addition to genetic and developmental factors, stress also has a significant effect on the emergence of depression. Studies have shown that stress leads to changes in brain structure through mechanisms such as decreased brain derived neurotrophic factor, increased glucocorticoids, and decreased neurogenesis. These mechanisms may result in atrophy.[29] Brain atrophy in various regions is often observed in individuals with depression. Structural changes in MDD are primarily noted in areas such as the orbitofrontal cortex, caudate nucleus, putamen, and hippocampus, which play roles in emotion processing and stress regulation.[30] Research has indicated that these brain structural changes may correlate with factors like the severity of depression and treatment resistance, potentially aiding in differentiating TRD from MDD.[14] In a review

by Klok et al.[31], examining structural brain features in depression, it was found that reduced GM in the right cerebellum, anterior cingulate cortex, superior and medial frontal gyrus, hippocampus, and caudate nucleus did not effectively differentiate TRD from MDD. However, decreased GM in the precentral gyrus, inferior frontal gyrus, putamen, angular gyrus, and post-central gyri, alongside specific changes in parietal white matter tracts, may be indicative of TRD.[31] While a direct comparison of cerebral atrophy between TRD and MDD was not feasible due to the absence of MDD patients in this study, generalized cerebral atrophy was identified in some TRD patients, whereas it was absent in the HC group. In MDD patients, functionality may decline due to various factors.[32] TRD tends to be more closely linked to reduced functionality than MDD, and this study found a significant relationship between generalized cerebral atrophy and functionality levels in TRD patients.[33]

The CSP, a variant of the septum pellucidum, is more prevalent in schizophrenia and bipolar disorder, but studies indicate that its occurrence is comparable in MDD patients and HCs.[34] In this study, no significant differences were noted in CSP frequency between patients with TRD and HCs. Landin-Romero et al.[35] suggested that another variant of the septum pellucidum, the CV, may be a risk factor for severe mental disorders, with a frequency of 1.1% reported in individuals with mood and psychotic disorders, and none detected in HCs. Although the prevalence of CV in TRD has not been previously studied, the current research indicates that it may be more common in TRD patients than in HCs, although this difference was not statistically significant. The CVI, located within the double-layered tela choroidea of the third ventricle and surrounding the internal cerebral veins, has also not been thoroughly explored in relation to mental disorders.[36] The association of CVI with psychotic disorder has been reported through a limited number of cases.[37,38] Supprian et al.[37] reported CVI in a patient with a diagnosis of psychotic disorder but not in monozygotic twin. They suggested that the finding of the CVI in the psychotic twin could be incidental; however, it may indicate a dysgenic process in early brain development and, thus, play a significant role in the etiology of psychosis.[37] This study is the first to demonstrate that the frequency of CVI is significantly higher in TRD patients compared to HCs. Additionally, the presence of CVI is associated with lower functionality levels. CVI on brain MRI of one of the TRD patients is shown in Figure 2.

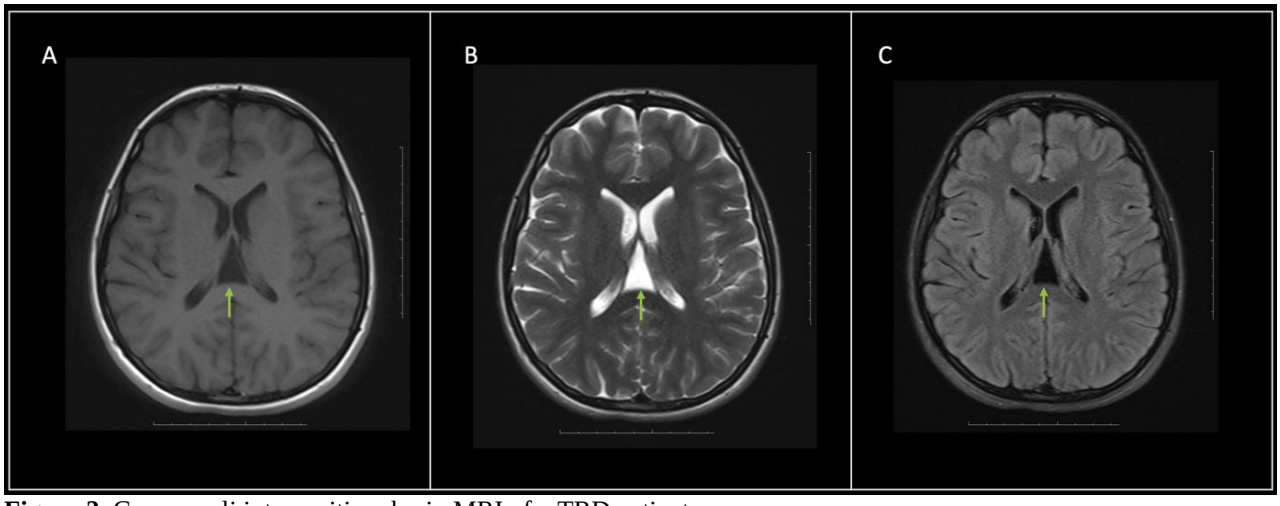

Figure 2. Cavum veli interpositi on brain MRI of a TRD patients

Notes: Cavum veli interpositi (green arrow) is shown in axial sections in T1-weighted sequence (A), T2-weighted sequence (B) and FLAIR-weighted sequence in a 37-year-old female patient.

This investigation scrutinized a variety of incidental findings extending beyond the previously mentioned variables, disclosing no substantial discrepancies between the TRD and HC cohorts. Although these variables did not show statistical significance, many were explored for the first time in the context of TRD. The paranasal sinuses, which include the

maxillary, frontal, ethmoid, and sphenoid sinuses, are air-filled spaces in the bones surrounding the nose.[39] This study is the inaugural investigation into the occurrence of mucosal thickening in the paranasal sinuses in individuals with TRD, revealing no notable differences between the two groups. Retention cysts occurring along the floor of the paranasal sinuses were also identified as similar between groups.[40] Arachnoid cysts, which are fluid-filled sac structures, were also found to be similar between the groups.[41] Adenoid hypertrophy is a natural reaction to increased immunological activity in early stages of development, and no evidence has been found to be associated with TRD.[42] Non-specific gliotic foci, demyelination plaque, mastoiditis, Virchow-Robin spaces, pituitary macroadenoma, antrochoanal polyp, central neurocytoma, meningioma, hyperostosis frontalis interna were observed at very low frequencies and did not help distinguish between the groups. It has been shown that MRI incidental findings in the TRD group did not vary according to gender.

Strengths and limitations

The striking feature of this study is the investigation of incidental MRI findings in patients diagnosed with TRD and the presentation of findings related to CVI. A control group is not needed in studies investigating incidental findings. However, the inclusion of a control group in this presented study can be considered as a contribution of the study to the literature. This study has several limitations. Its cross-sectional nature is the most important limitation. Another important limitation is that it did not include patients with MDD in addition to TRD and HC. The possible effects of psychotropic medications used in the treatment of TRD on MRI incidental findings are unknown. One limitation of this study is the absence of volumetric analysis, as it focuses solely on morphological characteristics.

Conclusion

This study shows that WM hyperintensities are more frequently detected in TRD, generalized cerebral atrophy is more common in TRD, and the level of functionality decreases as generalized cerebral atrophy increases. Evidence suggests that CVI, a neurodevelopmental anomaly, occurs more frequently in individuals with TRD. It was determined that TRD patients with CVI had lower levels of functionality. It may be useful to consider this information in the management of patients with TRD who are detected to have CVI on MRI examinations. Cerebral atrophy may be a parameter in the follow-up of patients with TRD and the Fazekas scale can be used for this purpose. Longitudinal studies are needed to reveal the relationship between incidental findings detected through MRI and TRD processes. Additional research could provide a deeper understanding of these findings in individuals with TRD.

Ethics Committee Approval

Ethics committee approval was obtained from Adıyaman University for this study (Date of Decision: May 21, 2024; IRB Number: 2024/5-16). All procedures were utilized in accordance with the Declaration of Helsinki.

Informed Consent

Signed informed consent form was obtained from all participants.

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None.

Conflict of Interest

There is no conflict of interest to declare.

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Peer-review

Externally peer-reviewed.

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