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Research Article

Investigation of the Network Made with the Complementary Motor of the Thalamus with the DTI Method in Individuals with Tinnitus

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Abstract

Objectives: This study aimed to investigate the differences in the networks between the thalamus and the supplementary motor area in brain MRI examinations of individuals with subjective chronic tinnitus and healthy control groups.

Methods: In the study, brain MRI imaging was performed on 47 patients suffering from bilateral tinnitus for two years or more and 42 healthy individuals. The tensor information obtained using the diffusion tensor imaging sequence data obtained from both groups was processed in the DSI Studio program. Brain connection maps were obtained from the data obtained. Quantitative information of the individual connecogram maps of each case was recorded and the groups were compared.

Results: In the tinnitus group, there is an increase in the pathways between the thalamus and the supplementary motor area. In addition, it was determined that the pathways of the thalamus with the hippocampus, superior and middle occipital area and frontal area increased, and the pathways with the hippocampus and cerebellum decreased.

Conclusion: Important functions of the supplementary motor area and thalamus; These are cognitive actions in which attention plays an important role, such as noticing the stimulus from the environment, planning and implementing the response action. It is thought that changes in the pathways between the thalamus and the supplementary motor area will especially affect attention-related functions.

Keywords: Tinnitus, DTI, Thalamus, Complementary Motor Area

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Tinnitus is the hearing of sounds that can also be described as buzzing in the ears of patients without any real sound stimulus. These noises sometimes cause such serious problems that sometimes they may even be suicidal in order to get rid of these voices. In cases of chronic bilateral tinnitus, the patient hears an unreal sound. This situation disturbs the patient very much and the patient's condition becomes a health problem and seeks treatment-solutions.

Most of these patients continue their lives. However, if the patient does dangerous work while working at work, tinnitus; Concentration disorder can cause sleep disturbance and cause serious accidents. In addition, if the person works in a place with a voice warning system, he may not be able to react to it. Derived from the Latin word "tinniere" meaning bell, tinnitus is hearing a sound that is not in the environment.[1] Since the sound does not come from outside, it

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occurs inside the patient's head and the patient hears the sound involuntarily.[2] Although it is seen at a rate of 4.6% to 30% in the society, there are similar rates in all societies.[3]

Tinnitus causes significant emotional and cognitive problems in people. Although the percentage of incidence varies according to each age group, it shows symptoms such as depression, insomnia and irritability in adults.[4, 5] It was determined that the severity of depression increased and the quality of life deteriorated depending on the severity of tinnitus, and even in a study conducted by Crumber RW and Hassan GA, it was stated that 71% of patients with tinnitus were also depressed and some of these patients thought of suicide.[6] Although it has been reported that tinnitus may rarely cause suicide, it has been observed that those who committed suicide were older men and had high psychiatric comorbidity.[7]

Tinnitus may be due to factors such as acoustic trauma, head and neck injuries, temporamandibular joint inflammation, and Meniere's disease. The patient's occupation is associated with tinnitus. Tinnitus is more common in professions exposed to noise, especially musicians and soldiers. Musicians are in the highest risk group because they are constantly exposed to loud noise in the form of trauma, and soldiers are in the highest risk group.[8]

Tinnitus is divided into objective and subjective. Objective tinnitus, the sound heard by the patient may be heard by another person, different from the patient. Its incidence is about 1% among tinnitus patients and the sound can be heard by the physician with the help of a stethoscope. The cause of objective tinnitus may be cerebrovascular structural disorders, middle ear and eardrum structural deformations, brain surgeries or head traumas.[9]

In subjective tinnitus, only the patient hears the sound. The condition that causes tinnitus can occur anywhere from the external ear canal to the auditory center.[10]

Subjective tinnitus can be caused by many diseases, conditions or drugs such as acoustic trauma, sudden hearing loss, Meniere's disease, head trauma, multiple sclerosis, hyperthyroidism, hypothyroidism, diabetes, chemotherapy, antibiotics, depression, pregnancy, diuretics.[11]

EPIDEMIOLOGY OF TINNITUS

According to the American Tinnitus Association, an estimated 50 million people in the United States have chronic tinnitus that persists for more than six months.[12] It is severe enough to interfere with daily activities for 12 million people. These people are effectively isolated from society to varying degrees due to their tinnitus. Tinnitus can occur in children[13] and increases with age.[14, 15] Tinnitus is more common in males than females and is more likely to occur in smokers.[12]

THE RELATIONSHIP BETWEEN TINNITUS AND ATTENTION

Attention can also be defined as the orientation of perception to one or more stimuli.[16] Scientific knowledge about attention is based on neuropsychological and electroneurophysiological testing, neuroimaging studies, and animal experiments. Regarding intelligence, the frontal eye areas, posterior parietal cortex, and cingulate cortex areas have been associated. In a disorder that occurs in one of these parts or in the neural connections between each other, a syndrome called neglect syndrome occurs in which the patient ignores half of his body and acts accordingly.[11, 17] In a study by Tegg-Quinn et al., it was stated that the control of attention management and cognitive skills such as understanding, learning skills and reasoning ability under the name of intelligence were impaired in patients with tinnitus.[18]

THALAMUS

The thalamus is the region in the center of the brain that contains nerve fibers that extend in all directions to the cerebral cortex. The thalamus, which occupies a small place in the central nervous system, is of great importance in terms of anatomy and functionality, inversely proportional to its size. Except for the nerve impulses related to smell, all sensory nerve impulses first go to the thalamus and then to the cerebral cortex. It not only transmits nerve messages to the cortex, but also plays an important role in the processing of messages. The thalamus has a great role in being aware of the events occurring in the environment, being alert to these events, processing and regulating the functions related to attention and acting in response (Fig. 1).[19]

SUPPLEMENTARY MOTOR CORTEX (SMA)

Although its function is not known exactly, it is thought that it has an important effect between cognition and action in the acquisition of motor skills by making and applying the action plan, when to do which movement, when it is in front of the primary motor cortex.[20] Studies have shown that the complementary motor and premotor cocci interact strongly with areas in the precentral, supramarginal and superior frontal gyrus, rolandic operculum, thalamus, putamen, and cerebellum.[21] Studies indicate that the complementary motor cortex has an important role in cognitive areas such as actuation, time and spatial processing, numerical cognition, music and language processing, and working memory (Fig. 2).[22]

Studies on the connection between tinnitus and hearing loss take the first place in the literature search. In a study

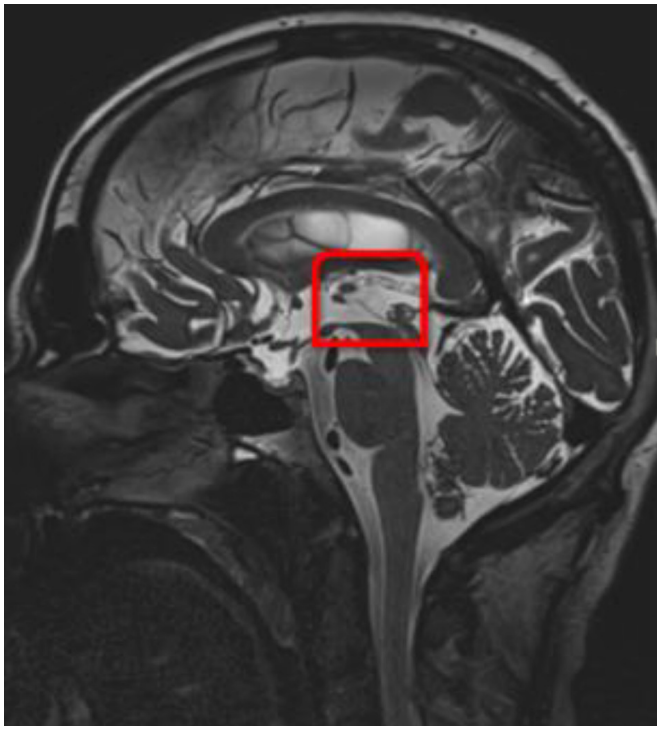

Figure 1. Brain MRI Thalamus in the Sagittal Plane.

by Xu et al., it was found that sensorineural hearing loss with tinnitus is related to dysfunctions inside and outside the classical auditory network in the brain, and that the left anterior insula, right precentral gyrus and superior frontal gyrus, and dorsal anterior cingulate cortex and middle frontal gyrus, superior parietal gyrus, and complementary They found that the connections between the motor area decreased. They conducted their studies on 32 individuals with tinnitus and 30 healthy individuals with audiological testing, fMRI scanning and neuropsychological tests.[23]

In a study by Vanneste and De Ridder in 2012, quantitative electroencephalography (qEEG) method showed that areas such as anterior cingulate cortex, auditory cortex (primary and secondary), dorsal lateral prefrontal cortex, insula, complementary motor cortex, orbitofrontal cortex (inferior frontal cortex) of tinnitus patients work together. They proposed that any secondary network of areas not related to the auditory pathway, such as the parahippocampus, posterior cingulate cortex, and precuneus, can explain the tinnitus mechanism.[24]

In a study by Anna et al., it was clearly stated that studies in this area were insufficient. In the same study, audiological test and anxiety questionnaire were applied to the patient and control groups, and Magnetic Resonance Imaging method was applied to the study group. or tinnitus distress measurements. The field of attention and perception management was not mentioned. This study was conducted with 28 left-handed tinnitus patients and 12 healthy individuals.[25]

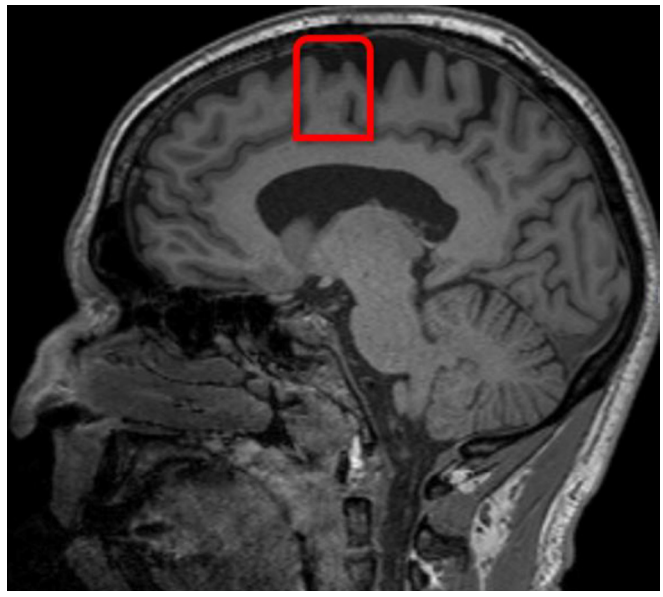

Figure 2. Brain MRI Supplementary Motor Cortex in the Sagittal Plane.

In a different study by Qien Chen et al., emphasizing that there is little research on the subject, tinnitus and hearing loss were studied with similar techniques.[26] The same study was conducted with 20 right-handed tinnitus patients and 22 healthy individuals.

In a different study conducted by Vanneste et al. in 2011, 10 patients with chronic tinnitus and 8 patients with new tinnitus disease examined the changes in their neural networks by using eeg and fMRI and phantom sound, respectively, by making more than one examination within a certain period of time.[27]

The resting state fMRI method was used between 31 patients with both tinnitus and hearing loss and 33 healthy individuals in Lee et al.'s study conducted in 2007, which is seen as a pilot study in tinnitus studies.[28]

Zhang et al. examined the thalamic connections of 31 patients with chronic tinnitus and 33 healthy individuals using the resting state fMRI method.[29]

It has been determined that similar numbers of patients and hearing loss have been studied in the researched studies.[28, 30-32]

The aim of this study is to analyze the pathway made by the thalamus with the complementary motor of individuals with tinnitus by using the DTI neuroimaging method and to try to reveal what kind of changes, if any, can be reflected in the daily life of the individual with tinnitus.

Methods

This study was discussed by Acıbadem Mehmet Ali Aydınlar University Medical Research Evaluation Commission (ATADEK) at the 2022/11 ATADEK meeting on 24 June 2022 and it was found to be medically ethical with the decision number 2022-11/50.

This thesis study was carried out with brain MRI data of patients with tinnitus complaints for two years or more and without hearing loss and healthy individuals. 47 cases with bilateral tinnitus and 42 healthy individuals were included in the study. The number of female participants in the patient group was 22, and the number of male participants was 25. In healthy individuals in the control group, the number of female participants was 28 and the number of male participants was 14. The mean age of the patient group was 38.78, the mean age of the female patient was 32.86, and the mean age of the male patient was 44. The mean age of the healthy individuals in the control group was 46.07, the mean age of the female healthy participant was 53, and the mean age of the male healthy participant was 43. The percentage of female patients in the patient group was 46.8%, and the percentage of female patients in the entire study was 24.72%. The percentage of male patients in the patient group was 53.2%, and the percentage of male patients in the entire study was 28.08%. The percentage of healthy female participants in the control group was 33.33%, and the percentage of healthy female participants in the entire study was 15.74%. The percentage of healthy male participants in the control group was 66.67%, and the percentage of healthy male participants in the whole study was 31.46%. The age distribution table of the patient and control groups is given in Table 1.

MR imaging procedures of patients in the patient and control groups were performed at the Radiology Department of Acıbadem Taksim Hospital with a 3T (Magnetom, Siemens, Erlangen, Germany) device with 64-channel brain coil. In addition to routine whole brain MRI, single shot diffusion weighted EPI sequence with b value of 1000 mm/s^2 was applied. Sequences were arranged parallel to the corpus colossus in the axial plane from craniocervical to vertex and diffusion tensor images were obtained. Display parameters for DTI; TR=10700 ms, TE=116 ms, Section Thickness= 2 mm, Number of Sections=70, FOV=250 mm. Fat suppression was performed using IR. Diffusion tensor images were obtained (Fig. 3).

Table 1. Age distribution of the patient and control groups

Age Range	Number of Patient Group	Number of Control Group
≤18	0	1
19-29	10	2
30-39	18	12
40-49	9	9
50-59	9	8
60-69	1	9
70≤	0	1

The resulting DTI images were processed in three steps using the DSI Studio (http://dsi-studio.labsolver.org) program. In the first step, image reconstruction was performed. Generalized q-sampling imaging (GQI) was used to perform this reconstruction. Second, corrections were made for distortion, motion artifacts, and b-matrix redirection. For network reconstruction, identified regions of the cerebrum were selected from the automated anatomical labeling (AAL) atlas. Edge identification was performed with the connection probability between each pair of nodes in the network. When the analysis was performed, diffusion indices and mean values were obtained according to the selected regions. The data were saved as an excel file (Table 2).

All connections between the selected regions were analyzed with the "DSI Studio" program. The data was saved as an excel file. The Excel file creates a database of visual information in the whole brain connectogram circular map.

Circular diagrams containing the connection and structure information of the connectograms were obtained by using the freely available "Circos" software (Fig. 4).

In this study, the data in the excel table obtained for two independent groups, the patient and the control, were tested

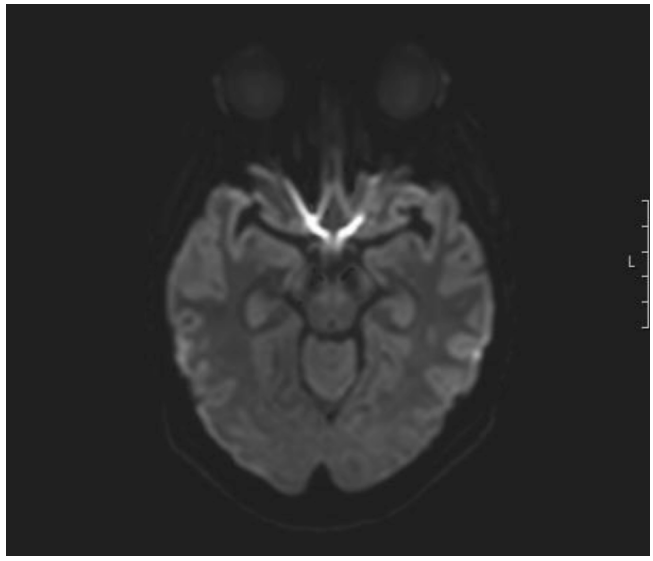

Figure 3. Axial Diffusion Image.

Table 2. Analysis of Thalamus Connection

	THALAMUS	Tinnitus Avg+SD/Med. (Min.- Maks.)	Control Avg+SD/Med. (Min.- Maks.)	P
1	Thalamus_L_Precentral_L	269884,07±301742,48/194401 (0-980256)	0,56±1,96/0,09 (0-13)	<0,001
2	Thalamus_L_Precentral_R	98936,62±159807,91/5541,5 (0-581482)	4125,32±27359,17/0,04 (0-181481)	<0,001
3	Thalamus_L_Frontal_Sup_L	253890,91±192257,72/265807 (0,29-961404)	93758,1±182104,73/0,74 (0-920635)	<0,001
4	Thalamus_L_Frontal_Sup_R	121192,23±190494,09/66,5 (0,11-829412)	13226,02±50955,12/0,25 (0-294737)	<0,001
5	Thalamus_L_Frontal_Sup_Orb_L	332643,19±281599,44/277150,5 (0,86-976667)	146380,52±181940,93/40962,5 (0,11-627778)	<0,001
6	Thalamus_L_Frontal_Mid_L	261690,86±282985,29/162037 (0,17-958824)	43741,29±116615,25/0,4 (0-551667)	<0,001
7	Thalamus_L_Frontal_Mid_R	48891,45±113649,2/0,37 (0-598485)	7790,14±36105,7/0,09 (0-174242)	<0,001
8	Thalamus_L_Frontal_Mid_Orb_L	194811,33±232091,76/136214 (0,22-863333)	52052,88±137489,79/0,42 (0-715873)	<0,001
9	Thalamus_L_Frontal_Inf_Oper_L	161363,36±299268,68/0,64 (0-971429)	2392,39±15868,99/0 (0-105263)	<0,001
10	Thalamus_L_Frontal_Inf_Oper_R	30817,55±74126,23/0,22 (0-265217)	0,45±1,94/0 (0-11)	<0,001
11	Thalamus_L_Frontal_Inf_Tri_L	238492,42±229227,62/166623 (0-824444)	11955,59±47828,29/0,13 (0-264912)	<0,001
12	Thalamus_L_Frontal_Inf_Orb_L	288099,21±292256,56/215438,5 (0,09-916667)	21814,11±61343,49/0,41 (0-271429)	<0,001
13	Thalamus_L_Rolandic_Oper_L	58702,58±191551,69/0,05 (0-742222)	0,03±0,15/0 (0-1)	<0,001
14	Thalamus_L_Supp_Motor_Area_L	156324,11±173381,7/127712 (0,22-835294)	45172,89±114090,69/0,59 (0-505882)	<0,001
15	Thalamus_L_Supp_Motor_Area_R	74775,01±114089,6/4477,5 (0-514583)	13124,4±62625,99/0,09 (0-377778)	<0,001
16	Thalamus_L_Olfactory_L	94243,5±191571,6/0,83 (0-827273)	2714,65±18006,86/0 (0-119444)	<0,001
17	Thalamus_L_Olfactory_R	34470,03±72101,46/0,29 (0-259259)	0,03±0,16/0 (0-1)	<0,001
18	Thalamus_L_Frontal_Sup_Medial_ R	90825,78±128782,41/8589 (0,07-371212)	17258,35±58604,09/0,18 (0-290278)	<0,001
19	Thalamus_L_Frontal_Med_Orb_L	181090,73±210543,18/142118 (0,18-954545)	60350,93±99940,54/0,71 (0-401587)	<0,001
20	Thalamus_L_Frontal_Med_Orb_R	128744,1±148736,72/112938,5 (0-741667)	21833,51±50987,32/0,34 (0-184058)	<0,001
21	Thalamus_L_Rectus_L	236280,7±240016,31/212086 (0,38-996491)	78297,65±136546,11/0,77 (0-560417)	<0,001
22	Thalamus_L_Rectus_R	155198,81±233590,78/25000 (0,19-962745)	33447,88±73838,69/0,41 (0-337255)	<0,001
23	Thalamus_L_Insula_L	123509,39±206321,23/0,95 (0-823077)	0,08±0,18/0 (0-1)	<0,001
24	Thalamus_L_Cingulum_Ant_L	164824,8±198408,42/129481,5 (0-823333)	20622,74±61676,71/0,23 (0-327778)	<0,001
25	Thalamus_L_Cingulum_Ant_R	827,61±5359/0,33 (0-34731)	0,08±0,21/0 (0-1)	<0,001
26	Thalamus_L_Cingulum_Mid_L	129624,41±162217,33/38235,5 (0,05-502381)	4478,26±27359,84/0,08 (0-181159)	<0,001
27	Thalamus_L_Cingulum_Mid_R	51102,56±118143,02/0,44 (0-466667)	0,15±0,61/0 (0-4)	<0,001
28	Thalamus_L_Hippocampus_L	172650,1±201218,95/118518,5 (0-853333)	26519,74±79237,1/0,11 (0-347619)	<0,001
29	Thalamus_L_Hippocampus_R	143400,58±165475,99/120798 (0-606061)	3220,12±21357,04/0 (0-141667)	<0,001
30	Thalamus_L_ParaHippocampal_L	219361,55±230214,76/137164,5 (0,14-764286)	10744,68±49608,77/0,21 (0-306667)	<0,001
31	Thalamus_L_ParaHippocampal_R	66381,39±107487,62/0,82 (0-369231)	0,43±1,84/0 (0-12)	<0,001
32	Thalamus_L_Amygdala_L	125521,69±211839,06/5196,5 (0-848485)	6073,42±28900,11/0 (0-163889)	<0,001
33	Thalamus_L_Amygdala_R	23930,12±72006,78/0 (0-358974)	0,01±0,04/0 (0-0,19)	<0,001
34	Thalamus_L_Calcarine_L	265882,08±221730,6/214108 (0,63-798148)	100373,28±156610,36/0,9 (0,09-491304)	<0,001
35	Thalamus_L_Cuneus_L	119479,56±190096,19/72612 (0,12-824074)	23338,77±76999,35/0,24 (0-446667)	<0,001
36	Thalamus_L_Lingual_L	244713,92±254781,71/154282,5 (0,2-994444)	84971,79±129094,88/0,98 (0-483333)	<0,001
37	Thalamus_L_Lingual_R	130608,89±163546,89/115714,5 (0,26-624444)	37027,56±103986,03/0,41 (0-577778)	<0,001
38	Thalamus_L_Occipital_Sup_L	128530,33±166803,77/63368,5 (0-715789)	11010,25±66580,42/0,16 (0-440476)	<0,001
39	Thalamus_L_Occipital_Mid_L	271249,88±290014,61/185714,5 (0,22-972222)	0,92±3,42/0,18 (0-22)	<0,001
40	Thalamus_L_Occipital_Mid_R	32256,58±72847,47/0,16 (0-289394)	0,48±1,94/0 (0-11)	<0,001
41	Thalamus_L_Occipital_Inf_L	23554,42±64767,8/0,33 (0-257407)	0,09±0,18/0 (0-1)	<0,001
42	Thalamus_L_Fusiform_L	152332,05±201532,46/47707 (0,09-642424)	18296,25±47588,85/0,28 (0-188333)	<0,001
43	Thalamus_L_Fusiform_R	36786,78±89379,24/0,51 (0-389474)	0,53±1,46/0,13 (0-8)	<0,001
44	Thalamus_L_Postcentral_L	280196,25±285426,34/192846 (0,04-886667)	0,49±1,31/0,17 (0-8)	<0,001
45	Thalamus_L_Postcentral_R	129911,67±215127,53/0,79 (0-755556)	0,56±2,31/0,05 (0-15)	<0,001
46	Thalamus_L_Parietal_Sup_L	278397,79±284829,61/209433,5 (0-913726)	2759,99±18306,07/0,06 (0-121429)	<0,001
47	Thalamus_L_Parietal_Sup_R	82666,58±143785,39/0,79 (0-566667)	2475,24±16415,56/0,02 (0-108889)	<0,001
48	Thalamus_L_Parietal_Inf_L	30400,91±85612,37/0,23 (0-414286)	0,04±0,14/0 (0-0,89)	<0,001
49	Thalamus_L_Angular_L	21365,76±61491,75/0 (0-253333)	0±0,02/0 (0-0,08)	<0,001
50	Thalamus_L_Precuneus_L	365161,65±350273,62/325490,5 (0,14-982456)	53231,2±99339,37/0,37 (0-402222)	<0,001
51	Thalamus_L_Precuneus_R	143708,83±208716,59/58660 (0-815686)	10762,52±39564,63/0,12 (0-186667)	<0,001
52	Thalamus_L_Paracentral_Lobule_ L	245798,7±281761,69/123170 (0-890196)	5144,67±22558,52/0,15 (0-111765)	<0,001
53	Thalamus_L_Paracentral_Lobule_ R	101579,49±198435,23/0,3 (0-909804)	0,18±0,63/0 (0-4)	<0,001
54	Thalamus_L_Caudate_L	206791,52±269234,93/121719,5 (0-979167)	36938,3±149873,13/0,22 (0-957143)	<0,001
55	Thalamus_L_Caudate_R	210063,21±234420,99/99797 (0-709091)	3106,23±20603,3/0 (0-136667)	<0,001
56	Thalamus_L_Putamen_L	319075,63±302509,34/221666,5 (0,17-990909)	50729,38±146844,48/0,35 (0-803704)	<0,001
57	Thalamus_L_Putamen_R	65981,16±132619,86/0,79 (0-566667)	0,3±1,2/0,08 (0-8)	<0,001
58	Thalamus_L_Pallidum_L	209657,52±267138,45/127354,5 (0-995833)	14551,86±76305,45/0,19 (0-485714)	<0,001
59	Thalamus_L_Pallidum_R	107138,73±187150,19/9,48 (0-911111)	0,34±0,94/0,09 (0-5)	<0,001

Table 2. CONT.

	THALAMUS	Tinnitus Avg+SD/Med. (Min.- Maks.)	Control Avg+SD/Med. (Min.- Maks.)	P
60	Thalamus_L_Thalamus_R	218340,42±279310,13/115714,5 (0-911111)	0,25±1,09/0 (0-7)	<0,001
61	Thalamus_L_Temporal_Sup_L	40504,3±91809,73/0,24 (0-380392)	0,16±0,6/0 (0-4)	<0,001
62	Thalamus_L_Temporal_Pole_Sup_ L	199977,7±203837,14/159626 (0,13-914583)	30841,11±64143,34/0,36 (0-219697)	<0,001
63	Thalamus_L_Temporal_Pole_Sup_ R	19640,01±52520,06/0,4 (0-206061)	3005,68±19933,12/0,07 (0-132222)	<0,001
64	Thalamus_L_Temporal_Mid_L	118572,57±181052,28/39999,5 (0-764444)	7255,78±33998,33/0,07 (0-182716)	<0,001
65	Thalamus_L_Temporal_Mid_R	14778,16±47858,89/0,23 (0-217949)	0,56±2,33/0 (0-14)	<0,001
66	Thalamus_L_Temporal_Pole_Mid_L	133211±155932,46/75680 (0-550794)	3704,44±24567,48/0,16 (0-162963)	<0,001
67	Thalamus_L_Temporal_Pole_Mid_R	47681,13±96146,71/0,42 (0-398246)	3106,65±20603,24/0,06 (0-136667)	<0,001
68	Thalamus_L_Temporal_Inf_L	225966,01±239136,13/140595 (0-962963)	12360,86±54643,36/0,19 (0-337333)	<0,001
69	Thalamus_L_Temporal_Inf_R	80632,48±123072,5/0,92 (0-593056)	3350,37±22216,39/0,1 (0-147368)	<0,001
70	Thalamus_L_Cerebelum_Crus1_L	123959,18±168367,65/72363 (0,09-713636)	22162,36±78446,22/0,23 (0-427083)	<0,001
71	Thalamus_L_Cerebelum_Crus1_R	60918,95±102734,9/0,55 (0-426984)	2509,98±16634,81/0,14 (0-110345)	<0,001
72	Thalamus_L_Cerebelum_Crus2_L	144168,89±203851,88/46767,5 (0-859649)	27979,94±94062,67/0,13 (0-542857)	<0,001
73	Thalamus_L_Cerebelum_Crus2_R	114231,79±172244,48/0,84 (0-642105)	24946,35±68969,46/0,22 (0-331944)	<0,001
74	Thalamus_L_Cerebelum_3_L	52144,86±139909,64/0 (0-744444)	0,1±0,6/0 (0-4)	<0,001
75	Thalamus_L_Cerebelum_4_5_L	193231,09±255889,9/123333 (0-971429)	20927,3±71190,92/0,21 (0-414815)	<0,001
76	Thalamus_L_Cerebelum_6_L	61901,16±122478,82/0,46 (0-568519)	0,65±3,45/0,05 (0-23)	<0,001
77	Thalamus_L_Cerebelum_6_R	32199,17±134164,95/0,43 (0-830952)	0,83±3,32/0,11 (0-20)	<0,001
78	Thalamus_L_Cerebelum_7b_L	56994,4±113631,42/0,68 (0-596491)	402,89±2647,37/0,08 (0-17564)	<0,001
79	Thalamus_L_Cerebelum_8_L	128875,02±215124,83/18,98 (0-885714)	13573,73±52095,74/0,12 (0-239394)	<0,001
80	Thalamus_L_Cerebelum_8_R	90019,49±146414,93/26,5 (0-715789)	13340,41±52738,52/0,1 (0-258333)	<0,001
81	Thalamus_L_Cerebelum_9_L	181025,92±270757,02/74198,5 (0-928205)	12662,61±59976,67/0 (0-335714)	<0,001
82	Thalamus_L_Cerebelum_9_R	5780,61±30815,53/0,37 (0-195556)	287,12±1902,34/0 (0-12619)	<0,001
83	Thalamus_L_Vermis_3	172021,96±264992,5/27515,5 (0-942857)	6818,74±31809,68/0,13 (0-166667)	<0,001
84	Thalamus_L_Vermis_4_5	118574,2±150998,09/13772,5 (0-496667)	35621,78±79548,81/0,23 (0-256667)	<0,001
85	Thalamus_L_Vermis_6	10147,76±41461,05/0,19 (0-231481)	0,27±1,66/0 (0-11)	<0,001
86	Thalamus_L_Vermis_7	6247,94±28490,03/0 (0-151852)	0±0,02/0 (0-0,14)	<0,001
87	Thalamus_L_Vermis_8	16199,45±93933,32/0 (0-608333)	0±0/0 (0-0)	<0,001
88	Thalamus_R_Precentral_L	51364,43±95674,46/0,45 (0-366667)	0,28±1,5/0,03 (0-10)	<0,001
89	Thalamus_R_Precentral_R	209324,48±257805,58/135937,5 (0-985185)	36245,25±74259,96/0,41 (0-266667)	<0,001
90	Thalamus_R_Frontal_Sup_L	65835,32±110877,46/0,74 (0-527778)	0,59±2,25/0,09 (0-14)	<0,001
91	Thalamus_R_Frontal_Sup_R	294517,94±274593,9/232300 (0,25-936667)	81051,52±130828,92/0,86 (0-514493)	<0,001
92	Thalamus_R_Frontal_Sup_Orb_L	30652,29±78256,39/0,42 (0-355556)	0,37±1,19/0,1 (0-7)	<0,001
93	Thalamus_R_Frontal_Sup_Orb_R	238447,42±277062,61/133333 (0,24-892982)	38367,7±106281,13/0,35 (0-557971)	<0,001
94	Thalamus_R_Frontal_Mid_L	39415,3±117658,6/0,32 (0-682222)	0,24±0,95/0 (0-5)	<0,001
95	Thalamus_R_Frontal_Mid_R	256363,8±268845,54/186458 (0,37-987037)	57833,66±115774,47/0,56 (0-468627)	<0,001
96	Thalamus_R_Frontal_Mid_Orb_R	192384,24±252601,94/85145,5 (0-836842)	45676,92±108972,09/0,33 (0-604167)	<0,001
97	Thalamus_R_Frontal_Inf_Oper_L	3876,81±25123,81/0 (0-162821)	0±0,01/0 (0-0,09)	<0,001
98	Thalamus_R_Frontal_Inf_Oper_R	148118,72±257841,07/46,5 (0-894737)	17016,69±50536,99/0,14 (0-233333)	<0,001
99	Thalamus_R_Frontal_Inf_Tri_L	29019,11±70508,05/0,22 (0-291228)	0,05±0,17/0 (0-1)	<0,001
100	Thalamus_R_Frontal_Inf_Tri_R	195052,95±217409,21/151717 (0,14-871667)	60201,89±110045,94/0,48 (0-364815)	<0,001
101	Thalamus_R_Frontal_Inf_Orb_L	9965,84±38368,23/0,1 (0-203448)	0,15±0,67/0 (0-4)	<0,001
102	Thalamus_R_Frontal_Inf_Orb_R	257150,07±283991,11/163158 (0-942857)	48883,2±114391,26/0,43 (0-591111)	<0,001
103	Thalamus_R_Rolandic_Oper_R	102420,75±193132,14/0,48 (0-770833)	0,36±1,23/0,02 (0-8)	<0,001
104	Thalamus_R_Supp_Motor_Area_L	284216,8±304438,75/140759 (0,18-903509)	36107,84±84631,23/0,42 (0-333333)	<0,001
105	Thalamus_R_Supp_Motor_Area_R	249082,52±244144,72/166569 (0,09-898235)	54400,86±115606,15/0,55 (0-540476)	<0,001
106	Thalamus_R_Olfactory_L	19931,06±50586,4/0 (0-190909)	0±0/0 (0-0)	<0,001
107	Thalamus_R_Olfactory_R	32415,2±79873,69/0 (0-375758)	0±0/0 (0-0)	<0,001
108	Thalamus_R_Frontal_Sup_Medial_L	276539,36±272492,36/199444,5 (0,14-953623)	80185,06±139606,15/0,74 (0-538095)	<0,001
109	Thalamus_R_Frontal_Sup_Medial_R	228511,04±245032,7/159444,5 (0,17-843333)	38813,31±92416,74/0,47 (0-407407)	<0,001
110	Thalamus_R_Frontal_Med_Orb_R	242832,73±275068,53/162318,5 (0-901852)	27487,75±63767,12/0,25 (0-284314)	<0,001
111	Thalamus_R_Rectus_R	136723,82±227637,46/84 (0-833333)	65,62±433,38/0,12 (0-2875)	<0,001
112	Thalamus_R_Insula_R	107066,16±158997,86/12,5 (0-689583)	4024,92±26696,22/0 (0-177083)	<0,001
113	Thalamus_R_Cingulum_Ant_L	96134,66±176804,6/0,77 (0-822807)	0,14±0,22/0,02 (0-0,73)	<0,001
114	Thalamus_R_Cingulum_Ant_R	43704,43±115763,36/0,33 (0-660417)	0,04±0,16/0 (0-1)	<0,001
115	Thalamus_R_Cingulum_Mid_L	102712,05±155699,08/68,5 (0-713726)	0,2±0,76/0 (0-5)	<0,001
116	Thalamus_R_Cingulum_Mid_R	113348,73±164971,57/577,5 (0-814815)	0,06±0,17/0 (0-1)	<0,001
117	Thalamus_R_Hippocampus_L	74642,74±119795,69/0,75 (0-397436)	0,17±0,9/0 (0-6)	<0,001
118	Thalamus_R_Hippocampus_R	197143,03±254740/78565 (0-937037)	14618,59±59885,3/0 (0-366667)	<0,001

Table 2. CONT.

	THALAMUS	Tinnitus Avg+SD/Med. (Min.- Maks.)	Control Avg+SD/Med. (Min.- Maks.)	P
119	Thalamus_R_ParaHippocampal_L	82301,02±114371,22/0,83 (0-319444)	0,45±2,25/0 (0-15)	<0,001
120	Thalamus_R_ParaHippocampal_R	225265,55±235092,94/169419 (0-785185)	3282,92±21775,74/0 (0-144444)	<0,001
121	Thalamus_R_Amygdala_R	55394,59±106076,48/0,43 (0-435897)	0±0,01/0 (0-0,09)	<0,001
122	Thalamus_R_Calcarine_L	68157,95±124580,14/0,81 (0-656863)	10805,82±37901,37/0,27 (0-175926)	<0,001
123	Thalamus_R_Calcarine_R	127842,59±187686,3/1837,5 (0-733333)	14702,53±47453,41/0,19 (0-179487)	<0,001
124	Thalamus_R_Cuneus_R	72055,49±114946,54/0,53 (0-390196)	0,13±0,33/0 (0-2)	<0,001
125	Thalamus_R_Lingual_L	148675,45±198084,24/37502,5 (0-829167)	9847,19±37523,32/0,23 (0-182051)	<0,001
126	Thalamus_R_Lingual_R	272037,14±312956,93/136481,5 (0,19-980952)	40483,99±82089,97/0,47 (0-323077)	<0,001
127	Thalamus_R_Occipital_Sup_L	28402,96±97695,57/0,11 (0-466667)	0,04±0,16/0 (0-1)	<0,001
128	Thalamus_R_Occipital_Sup_R	45872±83053,81/0,61 (0-340741)	0,06±0,13/0 (0-0,58)	<0,001
129	Thalamus_R_Occipital_Mid_L	28198,94±81254,34/0,5 (0-351282)	0,05±0,16/0 (0-1)	<0,001
130	Thalamus_R_Occipital_Mid_R	108858,35±181741,17/29,5 (0-805882)	2417,15±16032,7/0,02 (0-106349)	<0,001
131	Thalamus_R_Fusiform_L	11348,75±51639,71/0,39 (0-262745)	0,28±1,2/0,04 (0-8)	<0,001
132	Thalamus_R_Fusiform_R	176233,28±219785,13/121566 (0,08-809524)	2855,86±18941,03/0,16 (0-125641)	<0,001
133	Thalamus_R_Postcentral_L	90015,11±121682,26/18,37 (0-497101)	0,27±1,2/0,04 (0-8)	<0,001
134	Thalamus_R_Postcentral_R	247883,32±274585,96/143933 (0-831373)	39051,14±117793,73/0,32 (0-658824)	<0,001
135	Thalamus_R_Parietal_Sup_L	80532,74±143221,7/0,77 (0-478947)	0,15±0,62/0 (0-4)	<0,001
136	Thalamus_R_Parietal_Sup_R	251873,41±253457,63/198684 (0-947059)	6780,5±33057,8/0,11 (0-196667)	<0,001
137	Thalamus_R_Angular_R	38476,64±90329,63/0,09 (0-327451)	3305,82±21928,16/0 (0-145455)	<0,001
138	Thalamus_R_Precuneus_L	132205,19±203744,7/21,5 (0-888889)	0,46±1,34/0,22 (0-9)	<0,001
139	Thalamus_R_Precuneus_R	278912,89±301108,15/120657,5 (0-938889)	5481,48±25556,94/0,1 (0-133333)	<0,001
140	Thalamus_R_Paracentral_Lobule_ L	104707,26±187206,16/0,83 (0-766667)	0,42±2,1/0,07 (0-14)	<0,001
141	Thalamus_R_Paracentral_Lobule_ R	207631,68±233692,7/148447,5 (0-805882)	0,12±0,19/0,07 (0-1)	<0,001
142	Thalamus_R_Caudate_L	80973,32±143584,27/0,61 (0-598148)	0,16±0,75/0 (0-5)	<0,001
143	Thalamus_R_Caudate_R	228211,32±276679,07/144629,5 (0-903333)	3093,76±20519,46/0,14 (0-136111)	<0,001
144	Thalamus_R_Putamen_L	56794,06±119387,15/0,67 (0-570833)	0,45±2,27/0,02 (0-15)	<0,001
145	Thalamus_R_Putamen_R	125829,21±205253,14/9411 (0-846667)	0,26±0,64/0,05 (0-4)	<0,001
146	Thalamus_R_Pallidum_L	55266,23±105231,59/0,36 (0-388889)	0,13±0,75/0 (0-5)	<0,001
147	Thalamus_R_Pallidum_R	130187,09±212312,21/0,53 (0-837037)	14583,38±81671,84/0 (0-533333)	<0,001
148	Thalamus_R_Thalamus_L	218340,42±279310,13/115714,5 (0-911111)	0,25±1,09/0 (0-7)	<0,001
149	Thalamus_R_Temporal_Sup_R	95924,62±195439,81/0,75 (0-975556)	10008,71±37512,09/0,03 (0-158974)	<0,001
150	Thalamus_R_Temporal_Pole_Sup_ R	84737,34±168540,21/0,72 (0-733333)	16499,98±58241,33/0,12 (0-314583)	<0,001
151	Thalamus_R_Temporal_Mid_L	14609,09±40618,97/0 (0-144928)	0,05±0,3/0 (0-2)	<0,001
152	Thalamus_R_Temporal_Mid_R	93683,72±140058,07/0,87 (0-458333)	0,44±1,7/0,05 (0-11)	<0,001
153	Thalamus_R_Temporal_Pole_Mid_R	151171,55±236493,45/18125 (0-940909)	6976,49±32490,23/0,08 (0-168056)	<0,001
154	Thalamus_R_Temporal_Inf_L	16778,78±63280,87/0,33 (0-355556)	0,07±0,3/0 (0-2)	<0,001
155	Thalamus_R_Temporal_Inf_R	212318,67±253199,83/130909,5 (0-972549)	2488,16±16328,68/0,13 (0-108333)	<0,001
156	Thalamus_R_Cerebelum_Crus1_L	71035,1±143751,8/0,72 (0-582051)	2550,7±16918,07/0,03 (0-112222)	<0,001
157	Thalamus_R_Cerebelum_Crus1_R	133018,32±174606,35/6074 (0-611594)	3327,69±22067,02/0,13 (0-146377)	<0,001
158	Thalamus_R_Cerebelum_Crus2_L	92524,39±158942,05/0,93 (0-596154)	4995,62±33128,82/0,08 (0-219753)	<0,001
159	Thalamus_R_Cerebelum_Crus2_R	195446,43±276805,8/62934,5 (0-976191)	16691,62±60985,4/0,16 (0-293056)	<0,001
160	Thalamus_R_Cerebelum_3_L	15899,57±45162,48/0 (0-196667)	0±0,01/0 (0-0,06)	<0,001
161	Thalamus_R_Cerebelum_3_R	24195,23±72404,38/0,19 (0-355556)	0,16±0,9/0 (0-6)	<0,001
162	Thalamus_R_Cerebelum_4_5_L	149896,72±175413,06/125494,5 (0-623333)	2489,65±16511,29/0,08 (0-109524)	<0,001
163	Thalamus_R_Cerebelum_4_5_R	11748,1±44082,52/0,36 (0-236364)	0,16±0,48/0 (0-3)	<0,001
164	Thalamus_R_Cerebelum_6_L	25304,56±69233,47/0,28 (0-279167)	0,05±0,16/0 (0-1)	<0,001
165	Thalamus_R_Cerebelum_6_R	68725,07±136661,46/0,65 (0-643478)	0,23±0,74/0,01 (0-4)	<0,001
166	Thalamus_R_Cerebelum_7b_L	14503,5±46112,7/0,27 (0-194667)	0,24±1,06/0 (0-7)	<0,001
167	Thalamus_R_Cerebelum_7b_R	49647,27±102365,71/0,62 (0-382609)	0,69±3,32/0,04 (0-22)	<0,001
168	Thalamus_R_Cerebelum_8_L	33928,54±71143,78/0,46 (0-258025)	0,16±0,75/0 (0-5)	<0,001
169	Thalamus_R_Cerebelum_8_R	200108,91±223283,52/131176,5 (0-721429)	5064,63±33589,29/0,11 (0-222807)	<0,001
170	Thalamus_R_Cerebelum_9_L	22679,59±60987,95/0,38 (0-208889)	0,04±0,08/0 (0-0,37)	<0,001
171	Thalamus_R_Cerebelum_9_R	74842,98±107594,79/18,97 (0-366667)	0,06±0,17/0 (0-1)	<0,001
172	Thalamus_R_Vermis_3	251073,86±268948,09/119285,5 (0-755556)	3463,33±22972,28/0 (0-152381)	<0,001
173	Thalamus_R_Vermis_4_5	132992,51±179951,83/43832,5 (0-677778)	7846,56±38321,43/0,11 (0-228571)	<0,001
174	Thalamus_R_Vermis_6	28372,2±82443,4/0,28 (0-410606)	0,05±0,3/0 (0-2)	<0,001
175	Thalamus_R_Vermis_7	3130,37±20270,91/0 (0-131373)	0±0/0 (0-0)	<0,001
176	Thalamus_R_Vermis_8	37923,83±125723,85/0 (0-553846)	0±0/0 (0-0)	<0,001
177	Thalamus_R_Vermis_9	6217,69±28146,48/0 (0-133333)	0±0,02/0 (0-0,16)	<0,001
178	Thalamus_R_Vermis_10	14923,3±67871,83/0 (0-380556)	0,01±0,04/0 (0-0,27)	<0,001

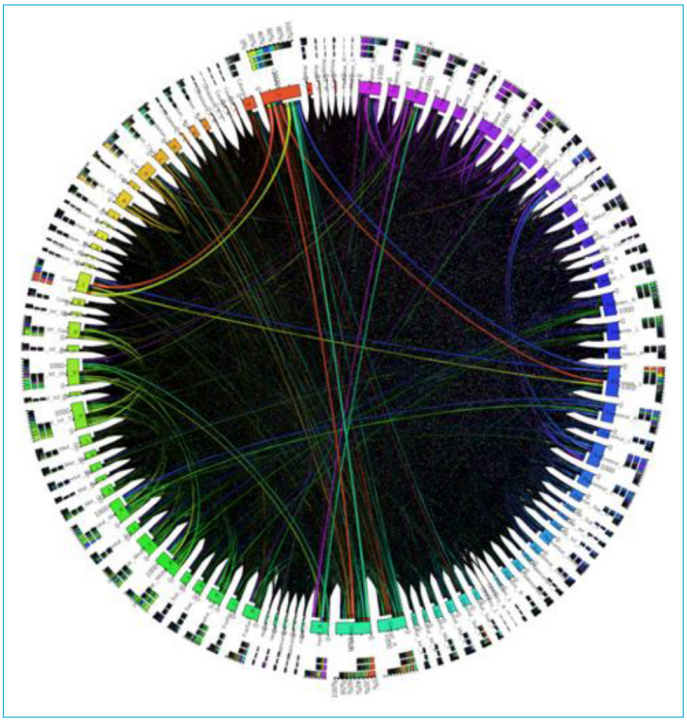

Figure 4. Circular Connectogram Diagram.

with the Shapiro Wilk test for the conformity of continuous variables to the normal distribution. Descriptive statistics were used to describe continuous variables (mean (Avg.), standard deviation (SD), minimum (Min.), median (Med.), maximum (Max.)).

The comparison of two independent and non-normally distributed variables was made using the Mann-Whitney U test.

Statistical significance level was determined as 0.001. Comparative analyzes were performed using SPSS v24 Program.

The raw data obtained in the study were analyzed with the heat map method secondly. Pearson correlation numbers were calculated by averaging the values of all patients on the same pathways. The matrix showing the correlation coefficients between all networks is also calculated as excel tables. According to these tables, color maps were obtained for both the patient group and the control group.

Results

The data obtained by analyzing the images with the DSI Studio program were calculated statistically, and the table related to the thalamus below was obtained according to the value of $p<0.001$.

In order to view the data from a larger structural perspective, the average of the values of all participants on the same pathways in the tinnitus group and control group was calculated using the graphical visualization technique "heat map". Pearson correlation numbers were calculated. Thus, it is thought that areas close to dark red are positively correlated, while light colored areas are negatively correlated (Fig. 5).

The connectivity relationship of the control group is given in Figure 6. Dark red indicates a strong positive relationship, while dark blue indicates a strong negative relationship.

An increase in the networks between the thalamus and the supplementary motor cortex (supplementary motor area) was detected in the tinnitus group. In addition, it is seen that the pathways of the thalamus together with the hippocampus, upper and middle occipital area and frontal area increase, the pathways with the hippocampus and cerebellum decrease, and the pathways leading to the cuneus and insula decrease. It has been determined that the connection of the vermis region with the cerebellum in patients with tinnitus is reduced. ($p<0.001$).

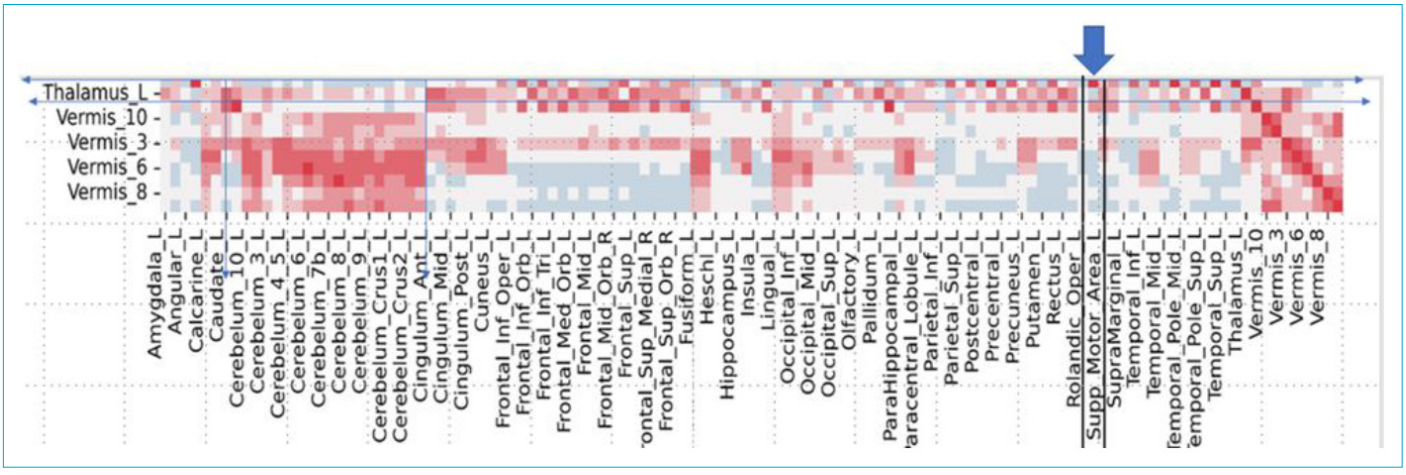

Figure 5. The connectivity relationship of the tinnitus group is shown in the diagram.

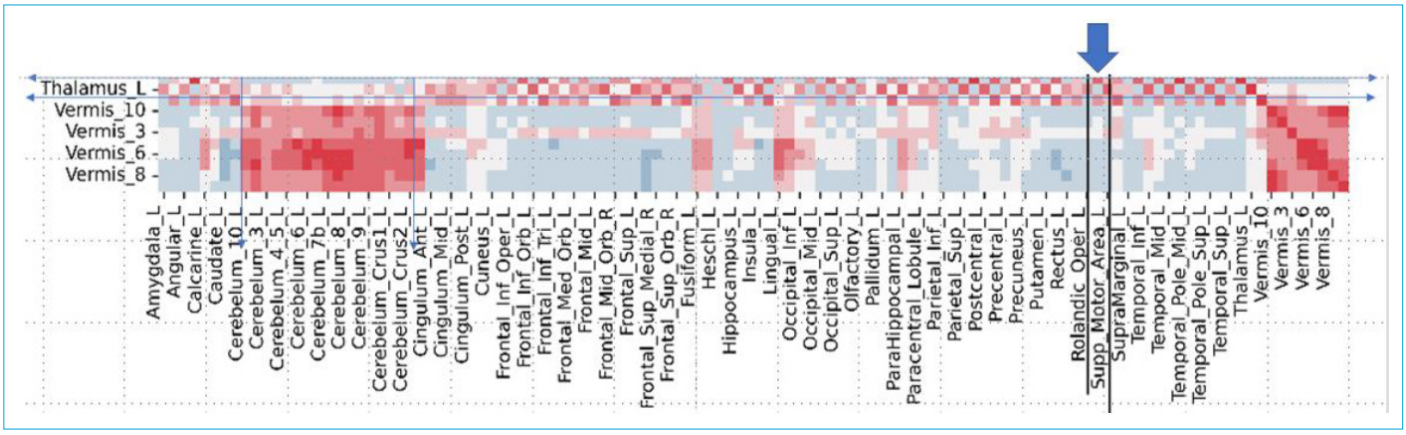

Figure 6. The connectivity relationship of the tinnitus group is shown in the diagram.

Discussion

DTI-MR, which was first proposed by Peter Basser to show micro-structural changes in the brain in 1994, was used in the following years to investigate clinical conditions such as schizophrenia, autism, traumatic brain injury, multiple sclerosis, and old age.[33] Conditions such as tinnitus and sensorineural hearing loss, where conventional imaging methods are insufficient, have also been the subject of research in DTI-MRI and fMRI in recent years.

These studies have focused heavily on changes in auditory pathways and have obtained many different findings. All these studies are aimed at clarifying tinnitus, and there are fewer studies investigating brain network changes in tinnitus.[34, 35]

Hallam et al. stated that individuals with tinnitus show significant cognitive problems compared to normal individuals.[36] In other publications on the effect of tinnitus on cognitive functions, they also stated that memory functions are affected and that it has a negative effect on the provision and execution of attention.[18, 37]

The thalamus transmits all sensory nerve impulses, first to the thalamus and then to the cerebral cortex, except for nerve impulses related to smell. The thalamus is responsible for not only transmitting nerve messages to the cortex, but also for the processing of messages, being aware of the events around the individual, being alert to these events, processing and regulation of attention-related functions and acting in response.[19] It is stated that the complementary motor area has an important effect between cognition and action in the acquisition of motor skills by making and applying the action plan, when to do which movement, when it is in front of the primary motor cortex.[20]

Conclusion

In chronic bilateral tinnitus cases, the patient hears an unreal sound and only the sound that the patient hears is very disturbing to the individual. Tinnitus increases with age and is more common in men than women. Patients with tinnitus stated that they heard tinnitus more in the left ear than in the right ear.[38]

If the individual with tinnitus does particularly dangerous work while working at work, tinnitus; Concentration disorder can cause sleep disturbance and cause serious accidents. In addition, if the person works in a place with a voice warning system, he may not be able to react to it. In this study, thalamus and complementary motor area connections of individuals with tinnitus were tried to be examined. From the data obtained, it is seen that the connections of talamasun differ in different areas.

Important functions of the complementary motor area and the thalamus; These are cognitive actions in which attention plays an important role, such as noticing the stimulus coming from the environment, being alert to the stimulus, planning and implementing the reaction action.[19, 20] With the deterioration of the connectivity of the two structures, it can have a significant negative impact on the lives of individuals with tinnitus.

Disclosures

Ethics Committee Approval: This research was produced from the data obtained from the thesis study numbered 787226 "Examination of the effect of chronic tinnitus (tinnitus) on brain connections". This study was discussed by Acıbadem Mehmet Ali Aydınlar University Medical Research Evaluation Commission (ATADEK) at the 2022/11 ATADEK meeting on 24 June 2022 and it was found to be medically ethical with the decision number 2022-11/50.

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