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Morphometry of some elements of limbic system in normal population: a quantitative MRI study

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Abstract

MRI is an important research tool which enables to investigate the brains of neuropsychiatric patients in vivo. In our study we tried to measure the volumes of some limbic system structures in the normal population to be utilized for further MRI morphometric studies in neuropsychiatry. We measured the volumes of hippocampus and corpus amygdaloideum (amygdaloid body), and the widths (thickness) of fornix and corpus mammillare (mammillary body) in 42 healthy volunteers without any neuropsychiatric pathology. The 1.5 T MRI was taken at oblique coronal plane using a section thickness of 3 mm without any gap. The volumes of hippocampus and corpus amygdaloideum were normalized according to intracranial area. We also investigated right-left volume differences for hippocampus and corpus amygdaloideum and set a formula as % difference rate for fornix and corpus mammillare width. We found the right hippocampus and corpus amygdaloideum larger than the left. No sex effect were evaluated. In addition, the larger hippocampus did not mean larger fornix. As a conclusion, the MRI morphometric data for normal population and the relations of this data with certain parameters such as side, sex, age must be collected to assess the pathological values in MRI morphometry.

Key words: limbic system, morphometry, MRI, hippocampus, amygdaloid body, fornix, mammillary body, volume, width

Introduction

Limbic system comprises components of the brain which are important for memory, emotions and cognitive functions. Hippocampus and corpus amygdaloideum (amygdaloid body) are important components of this system [1]. Fornix is the unique efferent of hippocampal formation. The corpus mammillare (mammillary body) is an important component of the hypothalamus where fornix relays there the information coming from hippocampus.

MRI (Magnetic Resonance Imaging) is an important research tool where the brains of neuropsychiatric patients can be investigated in vivo. There are many studies in the literature where anatomical structures in the brain are measured quantitatively in terms of volume, area, width and length. Hippocampus is a very popular structure regarding MRI morphometry. The cranial MRI morphometry comprises studies in which hippocampal volume has been measured in several neuropsychiatric disorders. Hippocampal volume varied considerably in various neuropsychiatric diseases such as Alzheimer [2], schizophrenia [3], major depression [4-5], temporal lobe epilepsy [6], vascular dementia [7], geriatric depression [8], alcoholism [9], post-traumatic stress disorder [10-11], traumatic brain injury [12], fragile – X syndrome [13], hydrocephalus with normal pressure [14], Turner Syndrome [15], Down Syndrome [16], Parkinson's disease [17], herpes simplex encephalitis [18], Cushing's Syndrome [19], dementia with Lewy bodies [20]. Further, changes in morphology of corpus amygdaloideum have been reported in diseases such as autism [21], schizophrenia [3], major depression [4], Alzheimer's disease [22], temporal lobe epilepsy [23] and obsessive–compulsive disorder [24]. There are few studies concerning the fornix and corpus mammillare. Morphological changes of the fornix have been observed in temporal lobe epilepsy [25] and recently in schizophrenia [26]. Additionally, changes in the size of corpus mammillare have been shown in alcoholism [27] and temporal lobe epilepsy [28].

In this study we aimed to measure the volumes of some limbic system structures i.e. hippocampus, corpus amygdaloideum, fornix and corpus mammillare in the normal population to be utilized for further MRI morphometric studies in neuropsychiatry.

Material and Methods

This study was conducted on 42 healthy volunteers (23 males, 19 females) with a mean age of 31.09 ± 12.06. All the subjects were right-handed except a male subject. The subjects of the study did not have any neurological, psychiatric disorders and were not under any drugs, chemical substances (i.e. oral contraceptives for female subjects, cortisone etc.) affecting the morphology of the brain. None was using alcohol.

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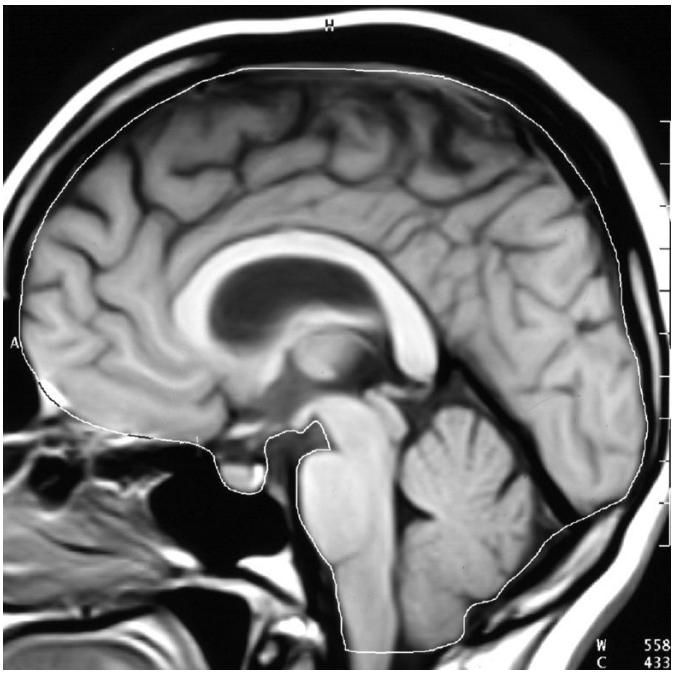

Figure 1 Intracranial measurement of mid-sagittal area of a subject.

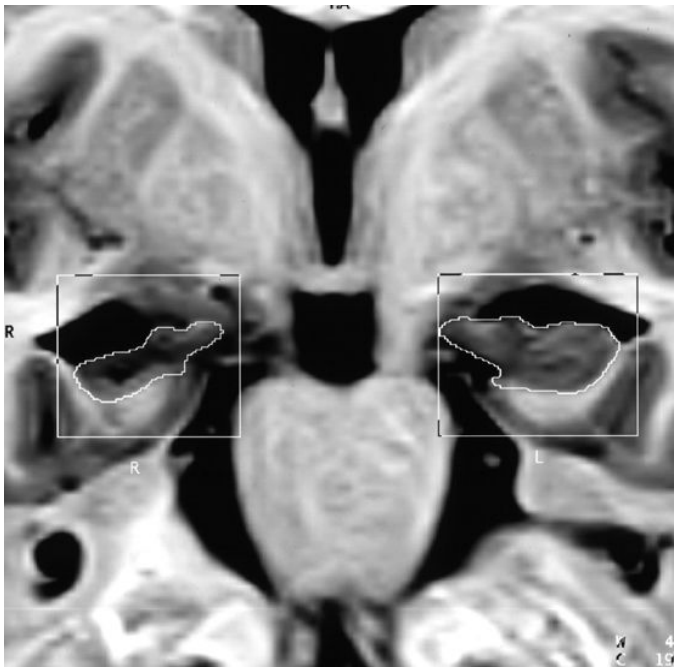

Figure 2 Hippocampal area measurement on a section where the hippocampus is seen.

MRI PROTOCOL

In our study hippocampus and corpus amygdaloideum volumes, width of fornix and mammillary bodies were measured on 1.5 T MRI unit (Magnetom Vision Plus, Siemens, Erlangen, Germany).

The measurement of intracranial area was performed at the midsagittal plane using sagittal T1 weighted spin echo (SE) sequence. The images of hippocampus and corpus amygdaloideum were acquired at oblique coronal plane using a section thickness of 3 mm without any gap and using T1 turbo inversion recovery (IR) sequence. Therefore the images of fornix and mammillary bodies on both sides were acquired on the coronal plane at turbo IR sequence with high resolution using a section thickness of 3 mm without any gap.

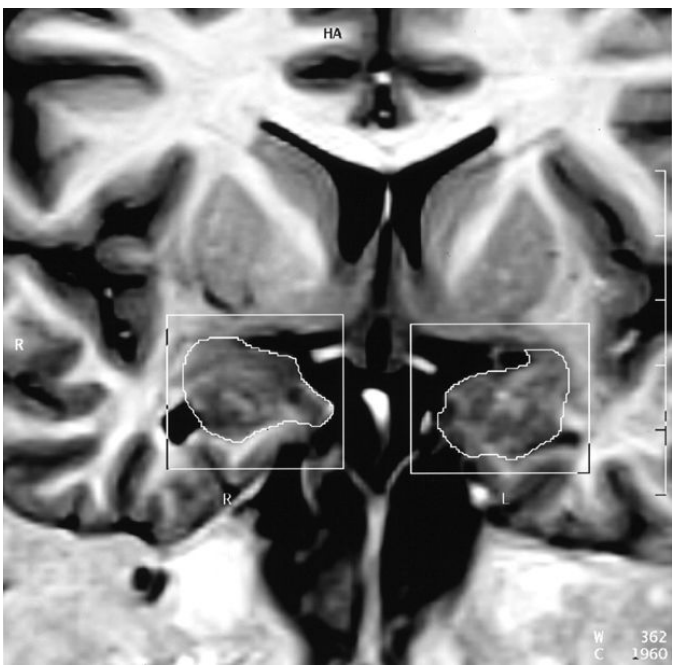

Figure 3 Corpus amygdaloideum area measurement on a section where the corpus amygdaloideum is seen.

MORPHOMETRIC ASSESSMENTS

The brain size can affect the volumes of hippocampus and corpus amygdaloideum. Assessing the images by the raw data without being normalized according to brain size one can get wrong results especially when bilateral atrophy exists [29-31]. Considering these factors, we normalized the hippocampus and corpus amygdaloideum volumes. Hippocampus and corpus amygdaloideum volumes were normalized using Gullap's [32] formula (Formula 1).

We used Cavalieri's principle while performing volumetric measurements [33]. After sending all the image data to a work-station hippocampus and corpus amygdaloideum were drawn manually by a cursor in each section seen afterwards the area measurement was calculated automatically (Figs. 2, 3). The sum of the areas, multiplied by the section thickness (3 mm) [33]. The raw hippocampus and corpus amygdaloideum volumes were acquired and were normalized according to the formula mentioned above using MAS (Fig. 1).

$$NV = \frac{(MMAG)\ X\ (HCAV)}{(MAS)}$$

NV	normalized volume
MMAG	mean mid-sagittal area of the group
HCAV	hippocampus or corpus amygdaloideum volume
MAS	mid-sagittal area of the subject

Formula 1 Formula for the normalization of the volumes of hippocampus and corpus amygdaloideum.

The fornix widths were measured at the section where the crus fornicis of the right and left were gather to form the corpus fornicis (Fig. 4). Corpus mammillare width was measured at the section where hippocampal digitations were seen at the pes hippocampi (Fig. 5). Because of the overlapping of fornix and corpus mammillare sizes between the normal subjects and pathological subjects we calculated (Formula 2) the fornix or corpus mammillare % difference rates in order to be used in future studies of neuropsychiarty [28].

The boundaries for the measurement of hippocampus [34] were alveus and uncal recess caudally, crus fornicis dorsally, plexus choroideus superiorly, subiculum and parahippocampal gyrus inferiorly, temporal horn laterally, and cisterna ambiens (perimesencephalic cistern) medially (Fig. 6).

The boundaries for the measurement of corpus amygdaloideum [2] were alveus and uncal recess caudally, optic tract dorsally, a horizontal line drawn from entorhinal sulcus superiorly, temporal horn and white matter of lobus temporalis inferolaterally, and gyrus ambiens medially.

STATISTICS

The results of our study were assessed by SPSS 7.0 statistic programme. The results obtained from the population were analized using t-test, Mann-Whitney test and Pearson's correlations. For all the comparisons "p" values less than 0.05 were considered as significant.

This study was approved by the local ethics committee of our university.

$$\%DR = \frac{(LS) - (SS)}{(LS)} \times 100$$

%DR	% difference rate
LS	larger side
SS	smaller side

Formula 2 Formula for the fornix or corpus mamillare % difference rates.

Results

The mean number of hippocampal sections evaluated on the right side was 13.02±1.024 (10-15), on the left was 13.14±1.049 (11-15). For corpus amygdaloideum the mean number on the right was 4.62±0.491 (4-5) and on the left side it was 4.64±0.577 (4-6).

The demographic data of the study group are shown in Table 1.

The results of the quantitative measurements are given below.

1. Hippocampus and corpus amygdaloideum volumes and fornix and corpus mammillare width:

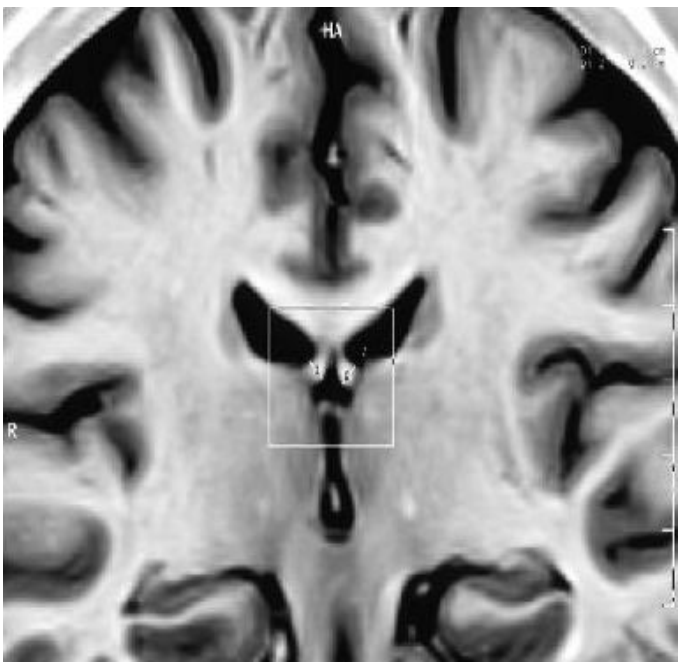

Figure 4 Fornix width measurement.

The mean of midsagittal intracranial area was 145.16±10.06 mm² (126.26-178.59). The mean volumes of hippocampus and corpus amygdaloideum are shown in Table 2. The mean widths of fornix and corpus mammillare width are shown in Table 3.

2. Normalized right–left volume differences of hippocampus and amygdala and % difference rates of fornix and corpus mammillare:

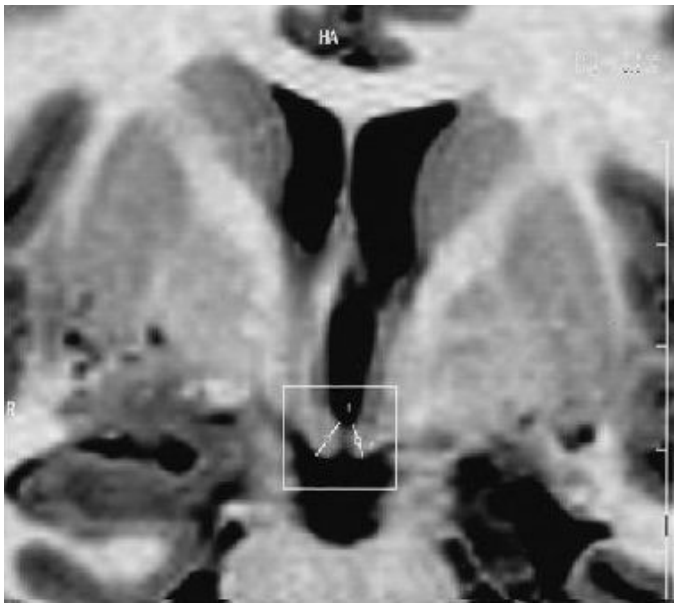

Figure 5 Corpus mammillare width measurement.

The mean of the normalized right–left difference for hippocampus volume was 150.47±121.83 mm³ (4.78-434.96). The mean of the normalized right–left difference for corpus amygdaloideum was found as 156.52±141.83 mm³ (5.14–682.53).

In the female subjects (n=19) the mean of the normalized right–left difference for hippocampus volume was 167.11±138.53 mm³ (4.78-418.80) while it was 136.73±107.34 mm³ (12.70-434.96) for the male subjects (n= 23). There was no significant difference between both groups (p>0.05).

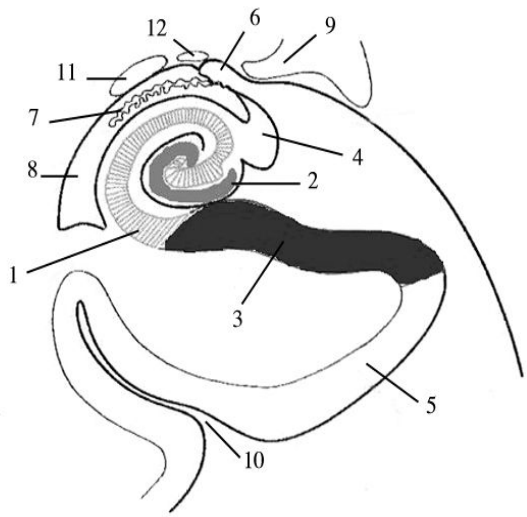

Figure 6 The illustration shows a histological section at the level of the body of the formatio hippocampi.1: hippocampus, 2: gyrus dentatus, 3: subiculum, 4: fimbria, 5: gyrus parahippocampalis, 6: fissura choroidea, 7: plexus choroideus, 8: cornu inferior ventruculi lateralis, 9: corpus geniculatum laterale, 10: sulcus collateralis, 11: cauda nuclei caudati, 12: stria terminalis.

In the female subjects (n=19) the mean of the normalized right–left difference for corpus amygdaloideum volume was 156.10±161.94 mm^3 (5.14–682.53). For the male subjects (n=23) it was 156.85±126.62 mm^3 (15.63-487.15). There was no significant difference between both groups (p>0.05).

Table 1 Demographic data in the study group including age, height (cm), weight (kg) and number of years of education. Min: minimum value, Max: maximum value, SD: standard deviation).

Study Group	Age (years)	Height (cm)	Weight (kg)	Education (years)
Mean	31.09	168	65.5	11.97
Min-Max	(13-62)	(150-189)	(40-90)	(0-17)
SD	12.06	9.57	14.80	4.21

The mean of the fornix % difference rate was 3.92±3.70 (0-14.81). The mean of the corpus mammillare % difference rate was 2.76±2.12 (0-9.43).

The mean of fornix % difference rate of the female cases (n=19) was 3.35 (0-14.81) while the male cases (n=23) had the mean of fornix % difference rate as 4.38 (0-14.29). There was no difference between female and male cases in terms of fornix % difference rate (p>0.05).

Table 2 The means, range and standard deviations (SD) of normalized hippocampus and corpus amygdaloideum volumes. RHV: right hippocampus volume, LHV: left hippocampus volume, RCAV: right corpus amygdaloideum volume, LCAV: left corpus amygdaloideum volume.

Parameters	RHV (mm^3)	LHV (mm^3)	RCAV (mm^3)	LCAV (mm^3)
Mean	3803.54	3698.29	2048.38	1983.91
Range	(3092.91-4573.74)	(3088.13-4504.47)	(1628.33-2805.22)	(1404.65-2645.85)
SD	402.86	381.26	260.92	241.23

The mean of corpus mammillare % difference rate of the female subjects (n=19) was 2.48 % (0–5.66) while the male subjects (n=23) had the mean of corpus mammillare % difference rate as, 2.99 % (0–9.43). There was no difference between female and male cases in terms of corpus mammillare % difference rate (p>0.05).

3. The relation of intracranial area with the sizes of anatomical structures measured:

In our study group, there was no correlation between intracranial area and all the sizes of the anatomical structures measured (p>0.05).

Table 3 The means, range and standard deviations (SD) of fornix and corpus mammillare width. RFW: right fornix width, LFW: left fornix width, RCMW: right corpus mamillare width, LCMW: left corpus mammillare width.

Parameters	RFW (mm)	LFW (mm)	RCMW (mm)	LCMW (mm)
Mean	3.10	3.13	4.84	4.83
Range	(1.9-4.9)	(2.0-4.8)	(3.8-5.7)	(3.8-5.9)
SD	0.05	0.05	0.04	0.04

4. Right-left side difference in the sizes of anatomical structures measured:

There was no right-left side difference for fornix and corpus mammillare width (p>0.05). Right hippocampus and corpus amygdaloideum were larger than the left side (p<0.05).

In the female subjects there was a right-left difference for hippocampus in favor of right side being larger (p<0.05). Rigth corpus amygdaloideum of the female subjects was slightly but not statistically significantly larger than the left (p>0.05). There was no right–left difference for the fornix width and corpus mammillare width of the female subjects (p>0.05).

In the male subjects there was no right–left difference for the sizes of hippocampus, corpus amygdaloideum, fornix and corpus mammillare (p>0.05).

5. The effect of sex on the sizes of anatomical structures measured:

There was no difference between the male and female subjects for the sizes of anatomical structures except for the intracranial area where male subjects have larger (p<0.05) intracranial area (Tables 4, 5).

Table 4 The comparison of the hippocampus and corpus amygdaloideum volumes between male and female subjects. RHV: right hippocampus volume, LHV: left hippocampus volume, RCAV: right corpus amygdaloideum volume, LCAV: left corpus amygdaloideum volume.

Sex	RHV (mm^3)	LHV (mm^3)	RCAV (mm^3)	LCAV (mm^3)
Male	3802.25±397.06 (3130.68-4573.74)	3738.30±375.44 (3099.47-4449.75)	2039.72±320.10 (1628.33-2805.22)	2001.47±262.14 (1404.65-2645.85)
Female	3805.11±420.68 (3092.91-4485.20)	3649.86±392.82 (3088.13-4504.47)	2058.87±172.10 (1749.83-2299.65)	1962.65±218.37 (1566.87-2254.89)
p	>0.05	>0.05	>0.05	>0.05

6. The correlation between age and the size of anatomical structures:

There was no correlation between all the quantitative parameteres and age (p>0.05).

7. The correlations between the sizes of anatomical structures:

There was no relation between the volumes of hippocampus and corpus amygdaloideum on both sides (p>0.05). There was no correlation between right hippocampus volume and width of fornix and corpus mammillare on both sides, fornix and corpus mammillare % difference rates either (p>0.05). There was a positive correlation between right and left corpus amygdaloideum volumes (p<0.001, r=0.678), and also there was a positive correlation between right and left fornix width (p<0.05, r=0.954).

Table 5 The comparison of the fornix and corpus mammillare width between male and female subjects. RFW: right fornix width, LFW: left fornix width, RCMW: right corpus mammillare width, LCMW: left corpus mammillare width.

Sex	RFW (mm)	LFW (mm)	RCMW (mm)	LCMW (mm)
Male	3.11±0.06 (1.9-4.9)	3.10±0.05 (2.0-4.8)	4.94±0.04 (4.1-5.7)	4.90±0.04 (4.1-5.9)
Female	3.11±0.05 (2.3-4.1)	3.16±0.04 (2.5-4.1)	4.72±0.03 (3.8-5.3)	4.74±0.03 (3.8-5.3)
p	>0.05	>0.05	>0.05	>0.05

8. Values for further studies concerning neuropsychiatric disorders:

2 Standard Deviations below the mean of hippocampus volumes was 2997.82 mm^3 for the right and 2935.77 mm^3 for the left. It was 1526.54 mm^3 for the right corpus amygdaloideum volume and it was 1501.45 mm^3 for the left corpus amygdaloideum volume.

The results obtained from the present study show that the right fornix width below 3 mm and the left fornix width below 3.03 mm can be considered as “pathological”. The given values are 2 Standard Deviatons below the mean of the forementioned structures. 2 Standard Deviations below the mean of right corpus mammillare was 4.76 mm and for the left corpus mammillare the same value was 4.77 mm. 2 Standart Deviations above the mean of the study group for fornix % difference rate was 11.32. It was above 7 for corpus mammillare % difference rate.

Discussion

In studies where hippocampal volumes were measured on MRI, in the normal population, hippocampus volume on the right was between 1501.4 – 6010 mm^3 and on the left was 1880 – 5880 mm^3 [35-50]. The probable reason of such a wide range can be the different criteria used for hippocampal boundaries in different MRI research units. Additionally, the different software used can be considered as an other reason [41]. In the normal population, normal values for corpus amygdaloideum volume relatively has a less wider range. In the literature right corpus amygdaloideum volumes were reported between 1080 – 3910 mm^3 and left were between 1080 – 3840 mm^3 [35, 37, 45, 47, 51]. The right and left hippocampus volumes found in our study were 3803.54 mm^3 - 3698.29 mm^3, respectively, and the right and left corpus amygdaloideum volumes were 2048.38 mm^3 - 1983.91 mm^3 respectively. Our findings are parallel to the data presented in the literature (Table 2).

There are few studies where fornix and corpus mammillare widths have been measured on MRI. In 10 healthy subjects Ng et al. [28] found the mean of fornix % difference rate as 3.1 %, and the mean of corpus mammillare % difference rate as 1.6 %. We found the mean of fornix % difference rate as 3.92 % which was in concordance with the finding of Ng et.al. However the mean of the corpus mammillare % difference rate (2.76 %) was 1.5 times more than the value of Ng. et al [28]. As our study comprises a larger group than the study Ng et. al., it can be suggested that our findings may be more reliable.

RIGHT-LEFT DIFFERENCES IN THE SIZES OF ANATOMICAL STRUCTURES MEASURED

In the literature numerous studies demonstrated that right hippocampus was larger than left [35, 42, 45-46, 52-55]. In some studies the right hippocampus was larger but it was not statistically significant [2, 51, 56-58]. Therefore, an asymmetry of hippocampus with right side being larger was proposed as a "pyshiological asymmetry" [2, 51]. However, in a considerable amount of studies it was reported that there was no right-left difference for hippocampus volume [9, 33, 44, 48, 59-65]. There is no consensus whether there is a right–left difference for hippocampus volume. Our findings demonstrate a pyshiological asymmetry of hippocampus where right is larger than the left. Inconsistency persists on the right-left difference for corpus amygdaloideum volume. Some investigators found that the right corpus amygdaloideum is larger than the left [24-25]. However, there are also studies reporting symmetric corpus amygdaloideum in the normal population [31, 51, 53, 59, 65]. But we found the right corpus amygdaloideum larger than the left in our study. Bilir et al. [66] found fornix and corpus mammillare volumes larger on the right side in 17 healthy volunteers. But we could not find right-left diffrence in fornix and corpus mammillare sizes using width measurements.

THE EFFECT OF SEX ON THE SIZES OF ANATOMICAL STRUCTURES MEASURED

The effect of sex on these anatomical structures is a conflicting matter in the literature. There are researchers reporting no sex difference on hippocampus and corpus amygdaloideum volumes [44, 60, 63, 67]. However, there are also studies where hippocampus and corpus amygdaloideum volumes were found larger in male [24, 31]. In one study hippocampus volume was reported as being slightly larger in women [57]. In another study in which fornix area was measured it was seen that sex did not have any effect on fornix size [26]. In another study the diameter of corpus mammillare was reported as being larger in men [47]. In the present study we did not find any sex effect on the sizes of hippocampus, corpus amygdaloideum, fornix and corpus mammillare.

THE RELATION OF THE SIZES OF ANATOMICAL STRUCTURES WITH AGE

Due to the heterogen age groups of the present study, it was not possible to conclude an effect of age on the limbic structures measured. We could not find any age effect on the sizes of these anatomical structures either. But it has already shown that hippocampus and corpus amygdaloideum volumes decrease by aging [42, 65]. But there is a conflict about the effect of age on hippocampus volume as in another study Sullivan et al. [68] found that hippocampus volume did not decrease by increasing age.

THE INTER-RELATION OF ANATOMICAL STRUCTURES

Our study confirms the findings of Zahajszky et al. [69] where no relation between hippocampus and fornix size.

MRI volumetry is extremely important in neuropsychiatry research. Additionally, hippocampus volumetry has been used as a complementary diagnostic tool prior to epileptic surgery [58]. Regarding epilepsy surgery each epilepsy unit has to get the normative values of hippocampal volumes for their unit. Therefore, we acquired it for the epilepsy unit at our university in this study. For epilepsy or any related disorder one has to know the normal values for anatomical structures to asses the pathological values. As a conclusion, the MRI morphometric data for normal population and the relations of this data with certain parameters such as side, sex, age must be collected to assess the pathological values in MRI morphometry.

Finally, MRI morphometry in neuropsychiatry is full of concflicting results mostly depending on the MRI methodology and the criteria used for the boundaries. Therefore it will be good if a worldwide consensus on the boundaries of these structures when performing volumetric measurements.

Conclusions

The results of the present study can be summarized as:

1. As many researchers use the "2 Standard Deviations below the mean of the control group" for a given disorder we introduced these values in our study.

2. Right hippocampus and corpus amygdaloideum are larger than the left hippocampus and corpus amygdaloideum in the normal population.

3. There is no right–left difference for the sizes of fornix and corpus mammillare.

4. Sex has no effect on the sizes of hippocampus, corpus amygdaloideum, fornix and corpus mammillare.

5. The larger hippocampus does not mean larger fornix.

References

[1] Wen HT, Rhoton AL Jr, de Oliveira E, Cardoso AC, Tedeschi H, Baccanelli M, Marino R Jr. Microsurgical anatomy of the temporal lobe: part 1: mesial temporal lobe anatomy and its vascular relationships as applied to amygdalohippocampectomy. Neurosurgery. 1999 (45) 549-591.

[2] Lehericy S, Baulac M, Chiras J, Pierot L, Martin N, Pillon B, Deweer B, Dubois B, Marsault C. Amygdalohippocampal MR volume measurements in the early stages of Alzheimer disease. AJNR Am. J. Neuroradiol. 1994 (15) 927-937.

[3] Gur RE, Turetsky BI, Cowell PE, Finkelman C, Maany V, Grossman RI, Arnold SE, Bilker WB, Gur RC. Temporolimbic volume reductions in schizophrenia. Arch. Gen. Psychiatry. 2000 (57) 769-775.

[4] Mervaala E, Fohr J, Kononen M, Valkonen-Korhonen M, Vainio P, Partanen K, Partanen J, Tiihonen J, Viinamaki H, Karjalainen AK, Lehtonen J. Quantitative MRI of the hippocampus and corpus amygdaloideum in severe depression. Psychol. Med. 2000 (30) 117-125.

[5] Bremner JD, Narayan M, Anderson ER, Staib LH, Miller HL, Charney DS. Hippocampal volume reduction in major depression. Am. J. Psychiatry. 2000 (157) 115-118.

[6] Cendes F, Andermann F, Gloor P, Lopes-Cendes I, Andermann E, Melanson D, Jones-Gotman M, Robitaille Y, Evans A, Peters T. Atrophy of mesial structures in patients with temporal lobe epilepsy: cause or consequence of repeated seizures? Ann. Neurol. 1993 (34) 795-801.

[7] Fein G, Di Sclafani V, Tanabe J, Cardenas V, Weiner MW, Jagust WJ, Reed BR, Norman D, Schuff N, Kusdra L, Greenfield T, Chui H. Hippocampal and cortical atrophy predict dementia in subcortical ischemic vascular disease. Neurology. 2000 (55)1626-1635.

[8] Steffens DC, Byrum CE, McQuoid DR, Greenberg DL, Payne ME, Blitchington TF, MacFall JR, Krishnan KR. Hippocampal volume in geriatric depression. Biol. Psychiatry. 2000 (48) 301-309.

[9] Laakso MP, Vaurio O, Savolainen L, Repo E, Soininen H, Aronen HJ, Tiihonen J. A volumetric MRI study of the hippocampus in type 1 and 2 alcoholism. Behav. Brain. Res. 2000 (109) 177-186.

[10] Stein MB, Koverola C, Hanna C, Torchia MG, McClarty B. Hippocampal volume in women victimized by childhood sexual abuse. Psychol. Med. 1997 (27) 951-959.

[11] Bremner JD, Randall P, Scott TM, Bronen RA, Seibyl JP, Southwick SM, Delaney RC, McCarthy G, Charney DS, Innis RB. MRI-based measurement of hippocampal volume in patients with combat-related posttraumatic stress disorder. Am. J. Psychiatry. 1995 (152) 973-981.

[12] Bigler ED, Blatter DD, Anderson CV, Johnson SC, Gale SD, Hopkins RO, Burnett B. Hippocampal volume in normal aging and traumatic brain injury. AJNR Am. J. Neuroradiol. 1997 (18) 11-23.

[13] Reiss AL, Lee J, Freund L. Neuroanatomy of fragile X syndrome: the temporal lobe. Neurology. 1994 (44) 1317-1324.

[14] Golomb J, de Leon MJ, George AE, Kluger A, Convit A, Rusinek H, de Santi S, Litt A, Foo SH, Ferris SH. Hippocampal atrophy correlates with severe cognitive impairment in elderly patients with suspected normal pressure hydrocephalus. J. Neurol. Neurosurg. Psychiatry. 1994 (57) 590-593.

[15] Murphy DG, DeCarli C, Daly E, Haxby JV, Allen G, White BJ, McIntosh AR, Powell CM, Horwitz B, Rapoport SI, et al. X-chromosome effects on female brain: a magnetic resonance imaging study of Turner's syndrome. Lancet. 1993 (342) 1197-1200.

[16] Pearlson GD, Breiter SN, Aylward EH, Warren AC, Grygorcewicz M, Frangou S, Barta PE, Pulsifer MB. MRI brain changes in subjects with Down syndrome with and without dementia. Dev. Med. Child. Neurol. 1998 (40) 326-334.

[17] Laakso MP, Partanen K, Riekkinen P, Lehtovirta M, Helkala EL, Hallikainen M, Hanninen T, Vainio P, Soininen H. Hippocampal volumes in Alzheimer's disease, Parkinson's disease, with and without dementia, and in vascular dementia: An MRI study. Neurology. 1996 (46) 678-681.

[18] Caparros-Lefebvre D, Girard-Buttaz I, Reboul S, Lebert F, Cabaret M, Verier A, Steinling M, Pruvo JP, Petit H. Cognitive and psychiatric impairment in herpes simplex virus encephalitis suggest involvement of the corpus amygdaloideum-frontal pathways. J. Neurol. 1996 (243) 248-256.

[19] Starkman MN, Giordani B, Gebarski SS, Berent S, Schork MA, Schteingart DE. Decrease in cortisol reverses human hippocampal atrophy following treatment of Cushing's disease. Biol. Psychiatry. 1999 (46) 1595-1602.

[20] Hashimoto M, Kitagaki H, Imamura T, Hirono N, Shimomura T, Kazui H, Tanimukai S, Hanihara T, Mori E. Medial temporal and whole-brain atrophy in dementia with Lewy bodies: a volumetric MRI study. Neurology. 1998 (51) 357-362.

[21] Aylward EH, Minshew NJ, Goldstein G, Honeycutt NA, Augustine AM, Yates KO, Barta PE, Pearlson GD. MRI volumes of corpus amygdaloideum and hippocampus in non-mentally retarded autistic adolescents and adults. Neurology. 1999 (53) 2145-2150.

[22] Maunoury C, Michot JL, Caillet H, Parlato V, Leroy-Willig A, Jehenson P, Syrota A, Boller F. Specificity of temporal corpus amygdaloideum atrophy in Alzheimer's disease: quantitative assessment with magnetic resonance imaging.. Dementia. 1996 (7) 10-14.

[23] Salmenpera T, Kalviainen R, Partanen K, Pitkanen A. Hippocampal and amygdaloid damage in partial epilepsy: a cross-sectional MRI study of 241 patients. Epilepsy Res. 2001 (46) 69-82.

[24] Szeszko PR, Robinson D, Alvir JM, Bilder RM, Lencz T, Ashtari M, Wu H, Bogerts B. Orbital frontal and corpus amygdaloideum volume reductions in obsessive-compulsive disorder. Arch. Gen. Psychiatry. 1999 (56) 913-919.

[25] Kuzniecky R, Bilir E, Gilliam F, Faught E, Martin R, Hugg J. Quantitative MRI in temporal lobe epilepsy: evidence for fornix atrophy. Neurology. 1999 (53) 496-501.

[26] Davies DC, Wardell AM, Woolsey R, James AC. Enlargement of the fornix in early-onset schizophrenia: a quantitative MRI study. Neurosci. Lett. 2001 (301) 163-166.

[27] Sullivan EV, Lane B, Deshmukh A, Rosenbloom MJ, Desmond JE, Lim KO, Pfefferbaum A. In vivo corpus mammillare volume deficits in amnesic and nonamnesic alcoholics. Alcohol Clin. Exp. Res. 1999 (23) 1629-1636.

[28] Ng SE, Lau TN, Hui FK, Chua GE, Lee WL, Chee MW, Chee TS, Boey HK. MRI of the fornix and mamillary body in temporal lobe epilepsy. Neuroradiology. 1997 (39) 551-555.

[29] Cendes F, Andermann F, Gloor P, Evans A, Jones-Gotman M, Watson C, Melanson D, Olivier A, Peters T, Lopes-Cendes I, et al. MRI volumetric measurement of corpus amygdaloideum and hippocampus in temporal lobe epilepsy. Neurology. 1993 (43) 719-725.

[30] Free SL, Li LM, Fish DR, Shorvon SD, Stevens JM. Bilateral hippocampal volume loss in patients with a history of encephalitis or meningitis. Epilepsia. 1996 (37) 400-405.

[31] Free SL, Bergin PS, Fish DR, Cook MJ, Shorvon SD, Stevens JM. Methods for normalization of hippocampal volumes measured with MR. AJNR Am. J. Neuroradiol. 1995 (16) 637-643.

[32] Gullap S. Temporal lob epilepsisinde hipokampusun volumetrik MR incelemesi. Specialization thesis. Department of Neurology, Gazi University Medical School, Ankara, 1999, 25.

[33] Cook MJ, Fish DR, Shorvon SD, Straughan K, Stevens JM. Hippocampal volumetric and morphometric studies in frontal and temporal lobe epilepsy. Brain. 1992 (115) 1001-1015.

[34] Watson C, Andermann F, Gloor P, Jones-Gotman M, Peters T, Evans A, Olivier A, Melanson D, Leroux G. Anatomic basis of amygdaloid and hippocampal volume measurement by magnetic resonance imaging. Neurology. 1992 (42) 1743-1750.

[35] Niemann K, Hammers A, Coenen VA, Thron A, Klosterkotter J. Evidence of a smaller left hippocampus and left temporal horn in both patients with first episode schizophrenia and normal control subjects. Psychiatry Res. 2000 (99) 93-110.

[36] DeCarli C, Hatta J, Fazilat S, Fazilat S, Gaillard WD, Theodore WH. Extratemporal atrophy in patients with complex partial seizures of left temporal origin. Ann. Neurol. 1998 (43) 41-45.

[37] Watson C, Cendes F, Fuerst D, Dubeau F, Williamson B, Evans A, Andermann F. Specificity of volumetric magnetic resonance imaging in detecting hippocampal sclerosis. Arch. Neurol. 1997 (54) 67-73.

[38] Kuzniecky RI, Bilir E, Gilliam F, Faught E, Palmer C, Morawetz R, Jackson G. Multimodality MRI in mesial temporal sclerosis: relative sensitivity and specificity. Neurology. 1997 (49) 774-778.

[39] Kalviainen R, Salmenpera T, Partanen K, Vainio P, Riekkinen P, Pitkanen A. Recurrent seizures may cause hippocampal damage in temporal lobe epilepsy. Neurology. (50)1998 1377-1382.

[40] Marsh L, Morrell MJ, Shear PK, Sullivan EV, Freeman H, Marie A, Lim KO, Pfefferbaum A. Cortical and hippocampal volume deficits in temporal lobe epilepsy. Epilepsia. 1997 (38) 576-587.

[41] Jack CR Jr, Theodore WH, Cook M, McCarthy G. MRI-based hippocampal volumetrics: data acquisition, normal ranges, and optimal protocol. Magn Reson Imaging. 1995 (13) 1057-1064.

[42] Tisserand DJ, Visser PJ, van Boxtel MP, Jolles J. The relation between global and limbic brain volumes on MRI and cognitive performance in healthy individuals across the age range. Neurobiol. Aging. 2000 (21) 569-576.

[43] Fernandez G, Effenberger O, Vinz B, Steinlein O, Elger CE, Dohring W, Heinze HJ. Hippocampal malformation as a cause of familial febrile convulsions and subsequent hippocampal sclerosis. Neurology. 1998 (50) 909-917.

[44] Woermann FG, Barker GJ, Birnie KD, Meencke HJ, Duncan JS. Regional changes in hippocampal T2 relaxation and volume: a quantitative magnetic resonance imaging study of hippocampal sclerosis. J. Neurol. Neurosurg. Psychiatry. (65) 656-664.

[45] Kuzniecky R, Bilir E, Gilliam F, Faught E, Martin R, Hugg J. Quantitative MRI in temporal lobe epilepsy: evidence for fornix atrophy. Neurology. 1999 (53) 496-501.

[46] Quigg M, Bertram EH, Jackson T. Longitudinal distribution of hippocampal atrophy in mesial temporal lobe epilepsy. Epilepsy Res. 1997 (27) 101-110.

[47] Bernasconi A, Cendes F, Lee J, Reutens DC, Gotman J. EEG background delta activity in temporal lobe epilepsy: correlation with volumetric and spectroscopic imaging. Epilepsia. 1999 (40) 1580-1586.

[48] Briellmann RS, Jackson GD, Kalnins R, Berkovic SF. Hemicranial volume deficits in patients with temporal lobe epilepsy with and without hippocampal sclerosis. Epilepsia. 1998 (39) 1174-1181.

[49] Achten E, Deblaere K, De Wagter C, Van Damme F, Boon P, De Reuck J, Kunnen M. Intra- and interobserver variability of MRI-based volume measurements of the hippocampus and corpus amygdaloideum using the manual ray-tracing method. Neuroradiology. 1998 (40) 558-566.

[50] Deicken RF, Pegues M, Amend D. Reduced hippocampal N-acetylaspartate without volume loss in schizophrenia. Schizophr. Res. 1999 (37) 217-223.

[51] Kalviainen R, Salmenpera T, Partanen K, Vainio P, Riekkinen P Sr, Pitkanen A. MRI volumetry and T2 relaxometry of the corpus amygdaloideum in newly diagnosed and chronic temporal lobe epilepsy. Epilepsy Res. 1997 (28) 39-50.

[52] Giedd JN, Vaituzis AC, Hamburger SD, Lange N, Rajapakse JC, Kaysen D, Vauss YC, Rapoport JL. Quantitative MRI of the temporal lobe, corpus amygdaloideum, and hippocampus in normal human development: ages 4-18 years. J. Comp. Neurol. 1996 (366) 223-230.

[53] Pruessner JC, Li LM, Serles W, Pruessner M, Collins DL, Kabani N, Lupien S, Evans AC. Volumetry of hippocampus and corpus amygdaloideum with high-resolution MRI and three-dimensional analysis software: minimizing the discrepancies between laboratories. Cereb. Cortex. 2000 (10) 433-442.

[54] Pfluger T, Weil S, Weis S, Vollmar C, Heiss D, Egger J, Scheck R, Hahn K. Normative volumetric data of the developing hippocampus in children based on magnetic resonance imaging. Epilepsia. 1999 (40) 414-423.

[55] Matsumoto H, Simmons A, Williams S, Pipe R, Murray R, Frangou S. Structural magnetic imaging of the hippocampus in early onset schizophrenia. Biol. Psychiatry. 2001 (49) 824-831.

[56] Lehericy S, Semah F, Hasboun D, Dormont D, Clemenceau S, Granat O, Marsault C, Baulac M. Temporal lobe epilepsy with varying severity: MRI study of 222 patients. Neuroradiology. 1997 (39) 788-796.

[57] Cheon JE, Chang KH, Kim HD, Han MH, Hong SH, Seong SO, Kim IO, Lee SG, Hwang YS, Kim HJ. MR of hippocampal sclerosis: comparison of qualitative and quantitative assessments. AJNR Am. J. Neuroradiol. 1998 (19) 465-468.

[58] Murro AM, Park YD, King DW, Gallagher BB, Smith JR, Yaghmai F, Toro V, Figueroa RE, Loring DW, Littleton W. Seizure localization in temporal lobe epilepsy: a comparison of scalp-sphenoidal EEG and volumetric MRI. Neurology. 1993 (43) 2531-2533.

[59] Callen DJ, Black SE, Gao F, Caldwell CB, Szalai JP. Beyond the hippocampus: MRI volumetry confirms widespread limbic atrophy in AD. Neurology. 2001 (57) 1669-1674.

[60] Lencz T, McCarthy G, Bronen RA, Scott TM, Inserni JA, Sass KJ, Novelly RA, Kim JH, Spencer DD. Quantitative magnetic resonance imaging in temporal lobe epilepsy: relationship to neuropathology and neuropsychological function. Ann. Neurol. 1992 (31) 629-637.

[61] Spencer SS, McCarthy G, Spencer DD. Diagnosis of medial temporal lobe seizure onset: relative specificity and sensitivity of quantitative MRI. Neurology. 1993 (43) 2117-2124.

[62] Cendes F, Leproux F, Melanson D, Ethier R, Evans A, Peters T, Andermann F. MRI of corpus amygdaloideum and hippocampus in temporal lobe epilepsy. J. Comput. Assist. Tomogr. 1993 (17) 206-210.

[63] Lawson JA, Nguyen W, Bleasel AF, Pereira JK, Vogrin S, Cook MJ, Bye AM. ILAE-defined epilepsy syndromes in children: correlation with quantitative MRI. Epilepsia. 1998 (39) 1345-1349.

[64] Bhatia S, Bookheimer SY, Gaillard WD, Theodore WH. Measurement of whole temporal lobe and hippocampus for MR volumetry: normative data. Neurology. 1993 (43) 2006-2010.

[65] Mu Q, Xie J, Wen Z, Weng Y, Shuyun Z. A quantitative MR study of the hippocampal formation, the corpus amygdaloideum, and the temporal horn of the lateral ventricle in healthy subjects 40 to 90 years of age. AJNR Am. J. Neuroradiol. 1999 (20) 207-211.

[66] Bilir E, Craven W, Hugg J, Gilliam F, Martin R, Faught E, Kuzniecky R. Volumetric MRI of the limbic system: anatomic determinants. Neuroradiology. 1998 (40) 138-144.

[67] Gur RC, Gunning-Dixon F, Bilker WB, Gur RE. Sex differences in temporo-limbic and frontal brain volumes of healthy adults. Cereb. Cortex. 2002 (12) 998-1003.

[68] Sullivan EV, Marsh L, Mathalon DH, Lim KO, Pfefferbaum A. Age-related decline in MRI volumes of temporal lobe gray matter but not hippocampus. Neurobiol. Aging. 1995 (16) 591-606.

[69] Zahajszky J, Dickey CC, McCarley RW, Fischer IA, Nestor P, Kikinis R, Shenton ME. A quantitative MR measure of the fornix in schizophrenia. Schizophr. Res. 2001 (47) 87-97.

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