International Journal of Sciences: Basic and Applied Research (IJSBAR)

ISSN 2307-4531
(Print & Online)

http://gssrr.org/index.php?journal=JournalOfBasicAndApplied

Is there any Difference in Corpus Callosum Heights between Healthy Adults and Diabetic patients? A Retrospective MR Study

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Abstract

As its integrity is essential for cognitive performances, it is surprising that there are no adequate studies in terms of the corpus callosum changes in diabetic patients. Consequently, the aim of this paper is to show how corpus callosum craniocaudal dimensions are changed by diabetes mellitus.

The study was designed as a retrospective investigation. The study group included 50 patients who had suffered from diabetes mellitus for at least 10 years and were admitted for brain magnetic resonance imaging between the years 2011 and 2014 suffering from headaches. From cranial MR images the craniocaudal length of the corpus callosum was measured from the lowest parts of the genu, corpus and splenium on the midline of the corpus callosum on T2-weighted MR images.

According to the analysis, disease status has a high effect on the corpus, genu and splenium heights of the corpus callosum ($t(99) = 5.66 - 4.99 - 6.06$ $p<0.05$). Before the age of 71, all the parts of the corpus callosum heights are relatively low in diabetes mellitus-diseased subjects when compared to non-diseased ones. Before 71, age has no effect on corpus callosum heights. After 71, both age and diabetes mellitus have an effect on the heights of the corpus part of the corpus callosum.

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Before the age of 71, corpus callosum height reduction may contribute to a cognitive decline in patients with diabetes mellitus. After 71, both age and diabetes mellitus have an effect on the heights of the corpus part of the corpus callosum. So after this age, cognitive decline may be even more pronounced.

As its integrity is essential for cognitive performances it is surprising that there are no adequate studies in terms of the corpus callosum changes in diabetic patients. According to the analysis in our study, disease status has a high effect on the corpus, genu and splenium heights of the corpus callosum. This study needs to be followed with a new study that investigates cognitive performance changes with corpus callosum height reduction in patients with diabetes mellitus.

Keywords: corpus callosum; craniocaudal dimensions ; diabetes mellitus.

1. Introduction

As its integrity is essential for cognitive performances, it is surprising that there are no adequate studies in terms of the corpus callosum changes in diabetic patients. It is not known exactly whether diabetes mellitus has any effect on corpus callosum heights. Consequently, this paper shows how corpus callosum craniocaudal dimensions are changed by diabetes mellitus.

2. Material and Methods

The study was designed as a retrospective investigation. In our study, individuals were subdivided into four groups according to age (under 50, 51–60, 61–70 and over 70), two groups according to gender (58 males and 41 females) and two groups depending on whether they were diseased or not. The study group included 50 patients who had suffered from diabetes mellitus for at least 10 years and were admitted for brain magnetic resonance imaging between the years 2011 and 2014 suffering from headaches. In the study, a control group was formed with 49 individuals who were admitted for brain magnetic resonance imaging (MRI) suffering only from a headache and without any additional disease. No patient satisfied the criteria for dementia. All had normal laboratory test results for vitamin B_{12} levels and thyroid hormone levels. A GE 1.5 Tesla MR scanner (General Electric Magnetom Essenza Syngo MR) in Bilecik State Hospital Radiology Department was used. T1-weighted sagittal and axial images were obtained with the use of a spin echo pulse sequence. Axial proton-weighted and T2-weighted images were also obtained with spin echo pulse sequences. The slice thickness was 3 mm for sagittal images and 5 mm for axial images. From cranial MR images the craniocaudal length of the corpus callosum was measured from the lowest parts of the genu, corpus and splenium on the midline of the corpus callosum on T2-weighted MR images.

3. Results

In statistical analysis [Table 1]:

Approximately 15% of the subjects examined were 50 years and under, about 32% were in the age range 51–60, 23% were in the 61–70 age range and 29% were aged 71 years and above. About 59% of the respondents were

male subjects and 41% were females.

Table 1: Descriptive statistics

Age groups	**N**	**%**
50 and under	15	15.2
51–60	32	32.3
61–70	23	23.2
71 and above	29	29.3
Total	99	100.0
Diseased	**N**	**%**
no	50	50.5
yes	49	49.5
Total	99	100.0
Gender	**N**	**%**
male	58	58.6
female	41	41.4
Total	99	100.0

1. The correlation between disease status and corpus callosum height

In the study an independent t-test was used for the purpose of determining whether there was an effect of disease status on the measurement of corpus callosum height. The results obtained are summarized in the table below [Table 2].

Table 2: Disease status and measurements

	Disease status	n	Mean	Std. Deviation	t	P
Genu	yes	49	49.3469	26.31821	4.99718	0.00
	no	50	77.9000	30.34647		
Corpus	yes	49	27.4694	11.16748	5.66607	0.00
	no	50	44.3400	17.66769		
Splenium	yes	49	61.3673	34.44966	6.06937	0.00
	no	50	98.2200	25.36935		

According to the analysis, disease status has a high effect on the corpus, genu and splenium heights of the corpus callosum ($t_{(99)}$ =5.66 – 4.99 – 6.06 p<0.05). Corpus, genu and splenium heights were relatively low in diseased subjects when compared to non-diseased subjects. In contrast, corpus, genu and splenium measurements were very high in non-diseased persons compared to diseased individuals.

2. The effect of gender on genu, corpus and splenium heights in corpus callosum analysis

For the purpose of determining whether there was an effect of gender on the genu, corpus and splenium heights of the corpus callosum, an independent t-test was used. The results are summarized in the following table [Table 3].

Table 3: The effect of gender on genu, corpus and splenium heights

	gender	n	Mean	Std. Deviation	T	P
Genu	male	58	68.4483	31.11956	1.76552	.08062
	female	41	57.1463	31.73292		
Corpus	male	58	38.3793	16.51244	1.67861	.09645
	female	41	32.6098	17.30878		
Splenium	male	58	89.2759	33.02195	3.26670	.00150
	female	41	66.8293	34.58822		

The analysis determined whether the gender of the subjects had an effecton the heights of the genu, corpus and splenium parts of the corpus callosum ($t_{(99)}$ =1.679 – 1.765 p>0.05). There was no effect of gender on the genu and corpus heights of the corpus callosum. But splenium measurements were found to be different according to gender ($t_{(99)}$ =3.266 p<0.05). The splenium measurements were lower in female individuals than in males.

3. Does gender have an effect on the genu, corpus and splenium heights of the corpus callosum in diseased individuals?

To determine whether gender and disease status have an effect on the heights of the genu, corpus and splenium of the corpus callosum, two-way analysis of variance (MANOVA) was used. The results are summarized in the following table [Table 4].

According to the results, in diseased individuals gender had no effect on the genu and corpus heights of the corpus callosum (F=0.53 – 1.53, p>0.05). The genu and corpus heights of female and male diseased individuals were quite similar. But the gender of diseased individuals had an effect on the splenium heights of the corpus callosum (F=2.53, p<0.05).

Bonferroni pairwise comparisons revealed that the average height of the splenium of the corpus callosum in

female diseased subjects was lower than that in male subjects ($p < 0.05$).

Table 4: The effect of gender on genu, corpus and splenium heights in diseased individuals

Heights	Gender	Disease status	Mean	Std. Deviation	n	F	P
Genu	male	no	81.5833	27.18337	36	0.53	0.47
		yes	46.9545	24.84519	22		
		Total	68.4483	31.11956	58		
	female	no	68.4286	36.70823	14		
		yes	51.2963	27.77356	27		
		Total	57.1463	31.73292	41		
Corpus	male	no	45.1944	16.32845	36	1.53	0.68
		yes	27.2273	9.26299	22		
		Total	38.3793	16.51244	58		
	female	no	42.1429	21.24892	14		
		yes	27.6667	12.68251	27		
		Total	32.6098	17.30878	41		
Splenium	male	no	100.5833	29.27444	36	2.53	0.05
		yes	70.7727	30.88062	22		
		Total	89.2759	33.02195	58		
	female	no	92.1429	7.96007	14		
		yes	53.7037	35.84563	27		
		Total	66.8293	34.58822	41		

4. **Does age have an effect on the genu, corpus and splenium heights of the corpus callosum?**

To determine whether age has an effect on the heights of the genu, corpus and splenium of the corpus callosum, one-way analysis of variance (ANOVA) was used. The results are summarized in the following table [Table 5].

Genu and splenium measurements seemed to be quite indistinguishable by age groups ($F = 1.78 – 1.495$, $p > 0.05$). Corpus measurements were found to vary by age groups ($F = 4.200$, $p > 0.05$). To investigate the cause of the difference, post hoc analysis (Sidak test) was performed and the corpus measured values were found to be lower in the 71 and above group than in the other age groups ($p < 0.05$).

When we evaluate the results,

Disease status had a high effect on the corpus, genu and splenium heights of the corpus callosum ($t_{(99)} = 5.66 – 4.99 – 6.06$, $p < 0.05$). Corpus, genu and splenium heights were lower in diseased subjects than in non-diseased subjects.

Table 5: The effect of age on genu, corpus and splenium heights

	Age groups	n	mean	Std deviation	F	P
Genu	50 and under	15	62.400	33.449	1.781	0.156
	51–60	32	72.000	33.819		
	61–70	23	65.913	31.704		
	71 and above	29	53.690	26.770		
	Total	99	63.768	31.711		
Corpus	50 and under	15	34.733	14.844	4.200	0.008
	51–60	32	43.063	16.932		
	61–70	23	37.783	15.395		
	71 and above	29	29.483	16.713		
	Total	99	35.990	17.001		
Splenium	50 and under	15	72.333	41.491	1.495	0.221
	51–60	32	90.344	32.375		
	61–70	23	73.174	41.787		
	71 and above	29	77.897	27.772		
	Total	99	79.980	35.299		

It was determined whether the gender of the subjects had an effect on the heights of the genu, corpus and splenium parts of the corpus callosum ($t_{(99)} = 1.679 – 1,765$, $p > 0.05$). There was no effect of gender on the genu and corpus heights of the corpus callosum. But splenium measurements were found to be different according to gender ($t_{(99)} = 3.266$, $p < 0.05$). The splenium measurements were lower in female individuals than in males.

The gender of diseased individuals had an effect on the splenium heights of the corpus callosum ($F = 2.53$, $p < 0.05$). The average height of the splenium of the corpus callosum in female diseased subjects was lower than that in male subjects ($p < 0.05$).

Genu and splenium measurements seemed to be quite indistinguishable by age groups ($F = 1.78 – 1.495$, $p > 0.05$). Corpus measured values were found to be lower in the 71 and above group than in the other age groups($p < 0.05$).

We see that before the age of 71, the heights of all the parts of the corpus callosum (genu, corpus and splenium) are lower in diabetes mellitus diseased subjects than in non-diseased ones. Before 71, age has no effect on corpus callosum heights. We know that the corpus callosum is an important part of the brain for cognitive functions. So as a result, before the age of 71, corpus callosum height reduction may contribute to cognitive decline in patients with diabetes mellitus. After 71, both age and diabetes mellitus have an effect on the heights

of the corpus part of the corpus callosum. So after this age, cognitive decline may be even more pronounced. In healthy adults, splenium heights are lower in women than in men, and therefore cognitive dysfunction may be more prominent in women than in men due to the addition of disease-related corpus callosum height reduction.

4. Discussion

The principal interhemispheric commissure is the corpus callosum (CC). The mature CC contains myelinated (70%) and unmyelinated fibers (30%), glial cells (astrocytes and oligodendrocytes) and neurons. The human CC has been divided into five anatomical regions, which include, from front to back, the genu, the rostrum, the body and trunk – often subdivided into anterior, middle and posterior body – the isthmus and the splenium. There are no clear borders between regions. The different callosal regions have different fiber compositions. Large-diameter fibres have been described in the posterior part of the splenium and in the body, where interhemispheric sensory fibers cross the commissure and exchange information at high speed, whereas small fibers mainly connecting association cortical areas are found in the rostrum, genu and anterior body [1,2]. The anterior half of the human CC (genu, rostrum and body) contains fibers interconnecting frontal association cortical areas. The isthmus mostly contains primary motor, somatosensory and auditory fibers. In the splenium, primary visual and association temporo-occipital and parietal commissural fibers are mixed, forming a single segment with the hippocampal commissure through which parahippocampal fibers cross [3].

Its known functions include: interhemispheric exchange of information, integration of inputs reaching one or both hemispheres, facilitation of some cortical activities and inhibition of cortical functions [4,5]. It has recently been shown that the size of the human CC positively correlates with intelligence and that its integrity is essential for cognitive performances; thus CC resection and microstructural or developmental alterations are often associated with cognitive decline [6].

Corpus callosum volume changes are a curiosity in non-operated individuals, because infarcts of the corpus callosum are not common and are attributed to a rich blood supply from three main arterial systems: the anterior communicating artery, the pericallosal artery and the posterior pericallosal artery [7]. The pericallosal branch of the anterior cerebral artery is most often the main vascular supply to the body. The subcallosal and medial callosal arteries, branches of the anterior communicating artery, provide the main supply for the anterior portion of the corpus callosum. The posterior pericallosal artery, a branch of the posterior cerebral artery, supplies the splenium.

In what circumstances are corpus callosum dimensions affected? Chrysikopoulos et al. suggest that ısolated infarcts of the anterior and posterior cerebral arteries are uncommon, accounting for 12% of all infarcts, and when present are found in conjunction with generalized atherosclerotic disease [7]. Chrysikopoulos et al. found that the splenium of the corpus callosum was affected more often than were the body and genu. All of the patients in David L. Kasow et al.'s series had long histories of hypertension and three of the five patients had insulin-dependent diabetes mellitus, predisposing them to generalized atherosclerosis. In David L. Kasow et al.'s series, all of the lesions involved the genu, body or both, whereas none involved the splenium. The difference in the location of the infarcts in their study, as compared with that reported by Chrysikopoulos et al.,

may be due to the difference in the patient population; i.e. patients with diabetes and hypertension develop generalized atherosclerosis, which in turn increases the incidence of anterior circulation infarction.

These studies have suggested that patients with diabetes and hypertension develop generalized atherosclerosis resulting in changes in size of the corpus callosum. Diabetes mellitus is a complex metabolic disease that can have devastating effects on multiple organs in the body. Diabetes is the leading cause of end-stage renal disease and is also a common cause of vision loss, neuropathy and cardiovascular disease. A less addressed and not as well recognized complication of diabetes is cognitive dysfunction. Cognitive deficits in persons with diabetes mainly affect the areas of psychomotor efficiency, attention, learning and memory, mental flexibility and speed, and executive function [8,9]. Patients with type 1 and type 2 diabetes mellitus have been found to have cognitive deficits that can be attributed to their disease. The exact pathophysiology of cognitive dysfunction in diabetes is not completely understood but it is likely that hyperglycaemia, vascular disease, hypoglycaemia and insulin resistance play significant roles.

However, the determinants of the accelerated cognitive decline in DM are less clear. The most studied hypothesis proposes that the primary cause of the association may be linked to diabetic vascular disease and inadequate cerebral circulation, with subsequent silent ischaemic damage induced by diabetes. Hyperglycaemia and hyperinsulinaemia may lead to widespread brain microangiopathy by inducing hyperphosphorylation and amyloid oligomerization [10].

5. Conclusion

As its integrity is essential for cognitive performances it is surprising that there are no adequate studies in terms of the corpus callosum changes in diabetic patients. According to the analysis in our study, disease status has a high effect on the corpus, genu and splenium heights of the corpus callosum. This study needs to be followed with a new study that investigates cognitive performance changes with corpus callosum height reduction in patients with diabetes mellitus.

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