

Relationship between Structural Brain Measurements and Motor Function in Patients with Stroke

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Abstract: Stroke is the main cause of death and disabilities around the world. It primarily affects the upper extremity function which leads to dependency and decrease the quality of life. The extent to which pathological insult in the brain is related to its functional outcome is not yet defined well. The primary purpose of this study was to investigate whether the structural MRI of cortical thickness correlated with the extent of upper extremity disability. Thirteen subjects with a mean age of 71.15 \pm 4.27 having acute stroke were enrolled. FreeSurfer software was used to calculate the cortical thickness in both ipsilesional and contralesional hemispheres obtained by the structural MRI, upper extremity function was assessed with fugl meyer assessment, general disability was assessed using modified rankin scale and activities of daily living was evaluated using barthel index scores. Study findings demonstrated a significant correlation between ipsilesional cortical thickness and fugl meyer assessment (r=0.7597; p=0.0035), modified rankin scale (r= -0.7325; p= 0.0005) and barthel index (r= 0.7808; p= 0.0023). This study showed a significant correlation between cortical thickness and the upper extremity motor function.

Keywords: Upper Limb, Stroke Rehabilitation, Structural MRI, Cortical Thickness

1. Introduction

Stroke is the main cause of death and disabilities around the world. It will lead to persistent loss of functional disabilities which will in turn lead to dependency and affect the quality of life [1]. Ischemic stroke accounts for 80% of the pathology leading to a decrease in the cerebral blood flow due to obstruction of arterial blood vessels supplying the brain [2]. The Incidence of first-time stroke in Saudi Arabia is 29.8/100,000/year [3]. As reported by World Health Organization (WHO), about 15,000,000 individual experience the effects of stroke every year, however, about 5,000,000 from these die and another 5,000,000 are disabled [3].

Stroke patients are present with motor weakness, sensory disturbance, or cognitive disorders. More than 85% of 566 000 post-stroke patient suffer from hemiparesis, resulting in impairment of the Upper Extremity (UE) immediately after stroke. About 55% to 75% of the survivors continue to have UE functional impairment [4].

According to a Dutch prospective epidemiological study

(TESS survey), it showed that regaining independence in activities of daily life (ADL) by 58% of the patients who survive a first stroke, moreover 82% of the stroke patients will walk independently again with or without utilization of an assistive device.

Functional improvement develops during the first 2 months. However, the significant improvement is limited to 4 to 5 months after stroke [5]. The delayed recovery of the UE motor function and ADL improvement occur in the earlier 6 to 12 months after stroke and may continue gradually up to one year. Functional improvement of the weak UE is associated with motor recovery in both brain hemispheres [1]. For maximum recovery and high improvement, optimum rehabilitation is strongly recommended throughout this period, even after discharge to home [1, 6].

The process of recovery following an injury, the brain undergoes a significant reorganization of its functions, resulting in functional recovery lasting over a period of weeks to months following the initial injury [7]. This postlesional reorganization occurs mostly in the premotor cortex, dorsolateral prefrontal cortex and the supplementary motor area which has been assumed to play the most important role in recovery following any type of brain injury [8]. Treatment approaches which can facilitate this reorganization process by enhancing the cortical plasticity might have a very important role in improving the functional outcome following neuronal injury [8-11].

Hence, there is a need for finding out the exact relation between the structural and functional changes of the brain with motor function. Thus, the aim of the study was to find the correlation between the structural and functional brain measurements using MRI with the motor functions of the UE using the Fugl Meyer Assessment-Upper Extremity (FMA-UE). Here the general disability was assessed using modified rankin scale (mRS) and activities of daily living (ADL) was evaluated using barthel index (BI) scores.

FMA-UE is one of the most widely used quantitative measures of motor impairment, it is an index to evaluate the sensory and motor weaknesses in post-stroke patient [12]. The Modified Rankin Scale (MRS) is used to classify grade of independence with reference to functional level before stroke [13]. The Barthel Index (BI) assessing dependence or disability in ADL of stroke patients was developed especially for young stroke patients (< 65 years), but now it has a wider application in the older patients [14, 15].

Neuroimaging technique Structural Magnetic Resonance Imaging (structural MRI) was used to get more details about cerebral gray matter density. Literature has shown that functional neuroimaging techniques are the best way to assess on how the patient recovers after stroke and to follow up the recovery process. However, there has not been much literature or research showing a definite mechanism of how the UE motor function impairment happens, and what leads to their recovery [16].

2. Methods

2.1. Participants

Thirteen consecutive patients who came to the stroke outpatient clinic of King Abdulaziz Hospital (KAUH) and have fulfilled the following criteria were recruited.

2.2. Inclusion Criteria

(i) First-time acute ischemic stroke patients within one month of stroke onset; (ii) FMA-UE \geq 20 points.

2.3. Exclusion Criteria

(i) Contraindication to MRI like (e.g., metal implants, pacemaker, claustrophobia); (ii) Associated neurological or psychiatric diseases; (iii) Cognitive impairment, that may interfere with the assessment procedure; or (iv) Have a previous history of neurodegenerative disorder, seizures, or

head trauma; (v) Pregnancy. (vi) Bilateral stroke.

2.4. Study Design

Correlative design comparing the different outcome measures were used. The study was approved by the institutional ethics committee of faculty of applied medical scienes. Patients who came to the stroke outpatient clinic of KAUH were recruited to our study after getting informed consent from each subject. Study subjects were assessed with the outcome measures, which are mentioned following and was referred to the radiology department to do the MRI which was a routine protocol, data for the structural MRI was obtained from this procedure.

2.5. Magnetic Resonance Imaging (MRI) Acquisition

T1-weighted А high-resolution scan (TR/TE)7425/3.64ms, FOV=256×256mm, 160 sagittal slices, flip angle 6°, voxel size=1mm) was performed on each enrolled participant. In this method, we calculated the cortical thickness by measuring the average distance from the white matter (WM) surface to the nearest point on the pial surface, and from the same point on the pial surface return again to the nearest point on the white matter surface. Free-Surfer software was used to calculate this distance with standard settings including normalization of intensity, registration, stripping of the skull, WM segmentation, WM boundary tessellation, tessellated surface smoothing and correction of the automatic topology in native space. The boundary between WM and the pial from the tessellated surface was found by using the deformable surface algorithm, considered as the initial points for measurement of thickness. The limit of the thickness value in the FreeSurfer software is 5 millimeters [17].

2.6. Fugl-Meyer Assessment-Upper Extremity (FMA-UE)

The FMA-UE is a valid and reliable scale used to evaluate upper extremity and motor and sensory function (2). The FMA-UE consists of 66 points divided into 4 categories: the (i) Shoulder, elbow and forearm, (contains 18 items with maximum score of 36 points), (ii) the wrist (5 items with maximum score of 10 points), (iii) the hand (7 items with maximum score of 14 points), and (iv) coordination (3 items with maximum score of 6 points) [12, 18]. The scoring is based on a 3-point ordinal scale (0= no function, 1= partial function, 2= complete function) [12].

2.7. Modified Rankin Scale (mRS)

The mRS is an ordinal scale that measures disability in stroke patients and comprises of 6 grades, where grade 0 indicates "no symptoms", 5 for "severe disability", and 6 for "death" [13].

3. Results

3.1. Statistical Analysis

Data was analyzed using graph pad prism version 6. Normality was tested with the D'Agostino and Pearson normality test, Shapiro and Wilk normality test and the KS normality test. Parametric analysis tools were used for the normally distributed data, and nonparametric analysis tools were used for non-normally distributed data.

3.2. Participants

The Demographic data for the participants are provided in (Table 1). Thirteen participants meeting our criteria were recruited, including eight males and five females with mean age of 71.15 ± 4.279 .

Pt (n)	Age	Sex	Side of lesion	Cortical thickness			DI	DG
				Ipsilesional	Contralesional	FMA-UE	ы	mks
1	65	М	R	1.34	2.14	33	65	3
2	72	М	R	1.25	2.06	26	55	4
3	74	М	L	1.46	2.23	32	60	3
4	78	М	R	1.57	2.13	34	65	3
5	68	F	R	1.40	1.98	32	55	3
6	76	М	L	1.14	1.83	27	50	4
7	68	F	R	1.04	1.96	31	55	3
8	67	F	R	1.67	2.23	29	60	3
9	71	М	R	1.54	2.18	33	65	3
10	77	М	L	1.89	2.41	36	65	2
11	70	F	R	2.02	2.56	40	80	2
12	66	М	L	1.90	2.58	42	80	2
13	73	F	R	1.46	2.14	34	75	2
$Mean \pm SD$	71.15±4.27	8M\5F	9R\4L	1.52±0.29	2.19±0.22	33±4.54	63.85±9.60	2.84±0.68
Median	71			1.467	2.147	33	65	3
Range	(65-78)			(1.04-2.02)	(1.83-2.58)	(26-42)	(50-80)	(2-4)
95% CI	(68.57-73.74)			(1.34-1.6)	(2.05-2.32)	(30.25-35.75)	(58.04-69.65)	(2.43-3.26)

Table 1. Demographic characteristic and the baseline scores of FMA-UE, BI and mRS.

Abbreviation: FMA-UE, Fugl-Meyer assessment-Upper Extremity; BI, Barthel Index; mRS, modified Rankin Scale.

3.3. Correlation of Cortical Thickness to FMA-UE

The spearman correlation was used to see the relationship between the cortical thickness and the FMA-UE. The rvalue showed a positive significant correlation between the ipsilesional cortical thickness $[1.52\pm0.29; 95\%$ CI (1.34-1.67)] and the FMA-UE $[33\pm4.54; 95\%$ CI (30.25-35.75)]where [(r=0.7597; p=0.0035) 95% CI (0.34-0.92)] (Figure 1).

3.4. Correlation of Cortical Thickness to BI

Positive significant correlation was also reported between the ipsilesional cortical thickness [1.52 ± 0.29 ; 95% CI (1.34-1.67)] with the BI [63.85 ± 9.60 ; 95% CI (58.04-69.65)] where [(r= 0.7808; p= 0.0023) 95% CI (0.38-0.93)] (Figure 1)

3.5. Correlation of Cortical Thickness to mRS

The scores were significantly correlated between ipsilesional cortical thickness $[1.52\pm0.29; 95\%$ CI (1.34-1.67)] with the mRS $[2.84\pm0.68; 95\%$ CI (2.43-3.26)] where (r= -0.7325; p= 0.0005) 95% CI (-0.91 - (-0.28)] (Figure 1).

3.6. Comparison of Cortical Thickness Ipsilesional Vs Contralesional

An unpaired t-test was used to compare between the ipsilesional cortical thickness $[1.52\pm0.29;$ CI (1.39-1.67)] and contralesional cortical thickness $[2.19\pm0.22;$ 95% CI (2.05-2.32)], and it demonstrates that there is a significant difference between the thickness of both sides (p< 0.0001) with difference of means $[0.67\pm0.11;$ 95% CI (0.46-0.88)] (Figure 2)

Correlation of Ipsilesional cortical thickness and FMA



Correlation of Ipsilesional cortical thickness and BI



Correlation of Ipsilesional cortical thickness and mRS



Figure 1. Correlation of ipsilesional cortical thickness with FMA, BI and mRS.



Figure 2. Comparison between ipsilesional cortical thickness and contralesional cortical thickness.

4. Discussion

The intended study was done to find the correlation between cortical thickness and upper extremity function in patients with stroke, the results suggest a positive significant correlation between the ipsilesional cortical thickness and the functional scales measured by FMA-UE, mRS and BI.

In a Similar previous study, they have examined the brain structural changes by taking structural MRI and used the neurological deficiency scale, FMA scale and modified Barthel index to evaluate the neurological function deficits, motor function and self-care abilities of eleven ischemic stroke patients and fifteen healthy participants. In order to determine whether gray matter density (GMD) changes in ischemic stroke patients, and how it is related to the clinical variables. They have found that the GMD is lower in ischemic stroke patients and higher in the healthy participants, and It was reported that the correlation between GMD and FMA scores is negative (r=-0.609 p= 0.047) [2].

Another similar study have investigated the relation between GMD and the motor function of the hemiparetic arm of eighty-five chronic stroke patients using voxel-based morphometry, motor activity log (MAL) and Wolf motor function test (WMFT). Further, decreased GMD of the contralesional and to a lesser extent in the ipsilesional motor areas, associates with lower functional levels according to WMFT, and the decrease in both contralesional and ipsilesional cortices associates with lower scores of MAL [19].

Finally, the study of Paul et al., 2016 have examined upper extremity motor function by WMFT to assess functional ability through the use of timed and functional task of 17 patients with chronic ischemic stroke and 11 healthy participants, to determine anatomical changes of the cortex related to upper extremity motor function in chronic stroke patients. They found that the hand area has thinner gray matter in the ipisilesional hemisphere. They also proposed that there is a correlation between cortical thickness and upper extremity function, and was reported that ipsilesional cortical thickness of chronic stroke patient was not significant (R^2 change=0.005, p=0.088) [20].

This study revealed that when the cortical thickness is less the function could be deprived, and this can be used in further studies to prove whether the function improves when the cortical thickness increases or not after a follow-up for 3 months.

Several limitations should be noted: As the research in this area is very limited we were not able to get enough literature back up for formulating a good design for the intended study. Due to the technical limitations we had to compromise to limit the sample size to 13. The patients were not followed up, which could have predicted rehabilitation outcome of the subjects.

5. Conclusion

This study demonstrates a relationship between the cortical

thickness and the upper extremity function. Future studies are recommended using cortical thickness as a biomarker for the prediction of prognosis of upper extremity functions after stroke.

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