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Biochemical and structural magnetic resonance imaging in chronic stroke and the relationship with upper extremity motor function

Mohamed Mahmoud Mostafa¹, Eman Mahmoud Awad¹, Ahmed Mohamed Hazzou¹, Mohamed Khaled Ahmed Elewa¹, Tougan Taha Abdel Aziz¹ and Dalia Maher Samy^{2*}

Abstract

Background: Recovery of upper extremity (UE) motor function after stroke is variable from one to another due to heterogeneity of stroke pathology. Structural and biochemical magnetic resonance imaging of the primary motor cortex (M1) have been used to document reorganization of neural activity after stroke.

Objective: To assess cortical biochemical and structural causes of delayed recovery of UE motor function impairment in chronic subcortical ischemic stroke patients.

Methodology: A cross-sectional study with fifty patients were enrolled: thirty patients with chronic (> 6 months) subcortical ischemic stroke suffering from persistent UE motor function impairment (not improved group) and twenty patients with chronic subcortical ischemic stroke and improved UE motor function (improved group). We recruited a group of (16) age-matched healthy subjects. Single voxel proton magnetic resonance spectroscopy (1H-MRS) was performed to measure *N*-acetylaspartate (NAA) and glutamate+glutamine (Glx) ratios relative to creatine (Cr) in the precentral gyrus which represent M1 of hand area in both ipsilesional and contralesional hemispheres. Brain magnetic resonance imaging (MRI) to measure precentral gyral thickness is representing the M1 of hand area. UE motor function assessment is using the Fugl Meyer Assessment (FMA-UE) Scale.

Results: The current study found that ipsilesional cortical thickness was significantly lower than contralesional cortical thickness among all stroke patients. Our study found that ipsilesional NAA/Cr ratio was lower than contralesional NAA/Cr among stroke patients. UE and hand motor function by FMA-UE showed highly statistically significant correlation with ipsilesional cortical thickness and ipsilesional NAA/Cr ratio, more powerful with NAA/Cr ratio.

Conclusion: We concluded that persistent motor impairment in individuals with chronic subcortical stroke may be at least in part related to ipsilesional structural and biochemical changes in motor areas remote from infarction in form of decreased cortical thickness and NAA/Cr ratio which had the strongest relationship with that impairment.

Keywords: Stroke, Biochemical and structural, MRI, Upper extremity motor function

* Correspondence: dalia84maher@yahoo.com

²El Sahel Teaching Hospital, Cairo 11697, Egypt

Full list of author information is available at the end of the article

Introduction

Motor impairment of one side of the body is a major cause of disability in activities of daily living. Recovery from strokes varies from one patient to another due to the heterogeneity of the stroke pathology and rehabilitation strategies. While most stroke patients recover spontaneously, many are left with permanent neurological impairments [1].

Understanding the brain pathologies associated with upper extremity (UE) impairment after stroke, the underlying mechanisms of injury, and the processes associated with recovery is important for achieving good recovery and successful rehabilitation. Advancements in neuroimaging technology have made this possible. Structural and biochemical brain imaging of primary motor cortices has been used to document the reorganization of neural activity after stroke. Ipsilesional and contralesional primary motor cortices, as well as the dorsal premotor cortex, have been identified as areas that can undergo substantial post-stroke neuroplasticity [2].

Single voxel proton magnetic resonance spectroscopy (1H-MRS) is a non-invasive tool to measure the levels of certain metabolites. In acute stroke, the presence of a measurable lactate peak demonstrates a shift from aerobic to anaerobic metabolism in the brain. Previous studies have shown that this is a temporary effect, and levels return to an almost undetectable state within 3 weeks [3].

Biochemical changes have also been observed chronically within ipsilesional normal-appearing grey matter and have been associated with morphological changes in stroke patients [4].

N-Acetylaspartate (NAA) is a metabolite found exclusively in neurons and their processes. It is considered a putative marker of their integrity with specific roles in the central nervous system, including myelin synthesis, neuronal energetics, neuronal osmoregulation, and axonal–glial signaling [5].

In individuals with chronic stroke, lower NAA and higher myo-inositol (an astrocyte marker) concentrations have been reported within ipsilesional and contralesional primary motor cortices [6].

A positive correlation has been drawn between NAA, glutamate (Glu: the principle excitatory neurotransmitter in the human central nervous system), and UE function in a chronic stroke population [7].

Structural changes in regional cortical thickness have also been observed in individuals in the subacute phase (3 months of recovery) after subcortical ischemic stroke and have been linked to functional activation changes in individuals with chronic stroke [8, 9].

The purpose of this study is to assess cortical, biochemical, and structural causes of delayed recovery of UE motor function impairment in patients with chronic, subcortical ischemic stroke.

Subjects and methods

A cross-sectional study with fifty patients were enrolled: thirty patients with chronic (> 6 months) subcortical ischemic stroke suffering from persistent upper extremity motor function impairment (not improved group) and twenty patients with chronic subcortical ischemic stroke and improved upper extremity motor function (improved group).

All patients were recruited from El Sahel Teaching Hospital outpatient clinics.

Inclusion criteria

1. Eligible right handed patients aged between 50 and 70 years old.
2. Single clinically diagnosed chronic (> 6 months) subcortical ischemic stroke presented with UE motor impairment at the acute stage.
3. Radiologically apparent healthy precentral gyrus grey matter.

Exclusion criteria

1. Patients with disturbed consciousness level.
2. Patients with aphasia, cognitive impairment, UE apraxia, sensory deficit, or ataxia.
3. Patients with history of previous stroke.
4. Patients who had any contraindication for MRI or 1H-MRS.
5. Patients who underwent neuro-rehabilitation through transcranial magnetic brain stimulation or transcranial direct current brain stimulation.
6. Patients with uncontrolled diabetes mellitus.
7. Patients with chronic renal or hepatic failure.

We recruited right-handed age-matched (16) healthy subject group to be references for our results regarding Egyptian people.

Methods

All participants subjected to:

1. Full medical history and neurological examination.
2. Routine lab and imaging.
3. (1H-MRS) to measure NAA and Glx concentration as ratios of their peak heights to Cr peak height as a stable internal reference (NAA/Cr and Glx/Cr) in ipsilesional and contralesional precentral gyrus which represent the M1 of hand area (landmark of precentral gyrus), determined anatomically by the area that faces and forms the “middle knee” of the central sulcus, located just at the cross point between the precentral sulcus and the central sulcus, which is topographically located at the level of the distal end

of the superior frontal sulcus and is therefore also visible on the cortical surface [10] (Fig. 1).

- MRI brain to (a) quantify cortical thickness of the precentral gyrus representing the M1 of hand area in both ipsilesional and contralesional hemispheres through Picture Archiving and Communication System (PACS), presented in millimeters (mm) and (b) assess white matter disease by fazekas scale which divides the white matter in periventricular (PVWM) and deep white matter (DWM) through fluid attenuated recovery (FLAIR) film with the higher score means more severity.
- UE motor function assessment using the Fugl Meyer Assessment (FMA-UE) Scale [11].
- Modified rankin scale (mRS) to assess disability degree in stroke patients ranging from 0 to 5 with higher score indicating more disability [12].

Procedures

- MRI scans were completed on Ingenia 1.5 Tesla Philips, and a high-resolution axial T1-weighted (TR/TE 256/2

ms, flip angle 80°), axial flair (TR/TE 11000/140 ms, flip angle 90°), sagittal T1 (TR/TE 166/2 ms, flip angle 80°), and coronal T2 scan (TR/TE 6600/110 ms, flip angle 90°) were performed on each enrolled participant. In addition, single voxel 1H-MRS (TR/TE = 2000/31, 2000/144 ms) was performed to measure metabolite ratios. A single 15-mm × 15 mm × 15 mm voxel was centered over the M1 of hand area in both ipsilesional and contralesional hemispheres. Localization of hand representation for each individual and corresponding voxel placement was determined using known anatomical coordinates described above.

- Assessment of affected UE motor function by FMA-UE with score ranges from 0 to 66 from which 14 points represent hand motor function with higher scores indicating better motor function.

In our study, the improved group had score from 64 to 66 for UE motor function and 14 for hand, the not improved group with score < 64 for UE and < 14 for the hand.

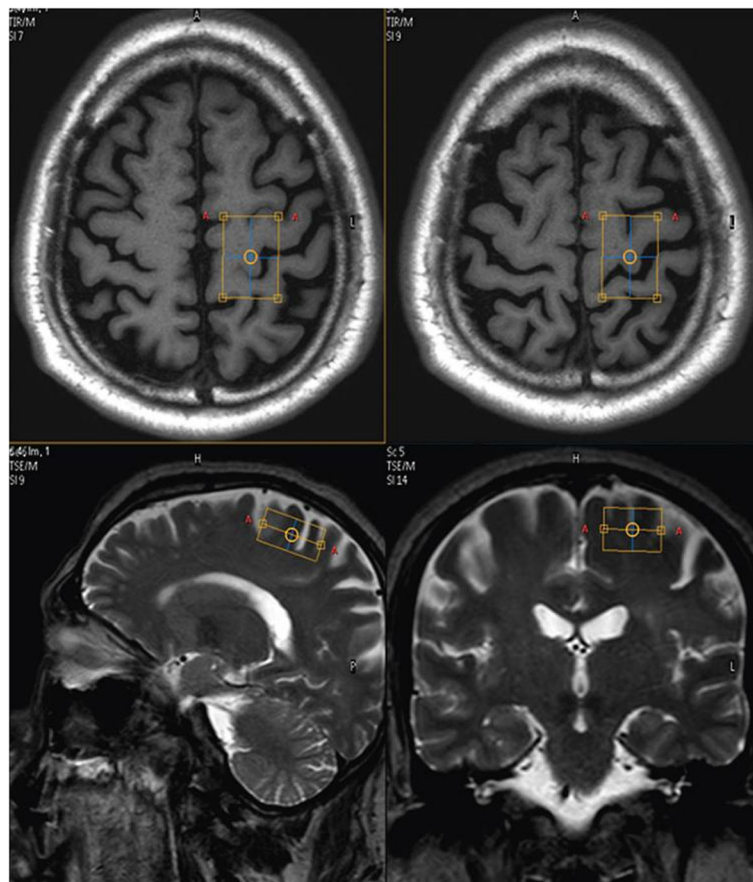


Fig. 1 Precentral gyrus, which represents the M1 of hand area (landmark of precentral gyrus), determined anatomically by the area that faces and forms the “middle knee” of the central sulcus, located just at the cross point between the precentral sulcus and the central sulcus, which is topographically located at the level of the distal end of the superior frontal sulcus and is therefore also visible on the cortical surface

Statistical analysis

The collected data was revised, coded, tabulated, and introduced to a PC using Statistical package for Social Science (SPSS 20). Data was presented, and suitable analysis was done according to the type of data obtained for each parameter.

- i. Descriptive statistics
 1. Mean, standard deviation (\pm SD), and range for parametric numerical data, while median and interquartile range (IQR) for non-parametric numerical data.
 2. Frequency and percentage of non-numerical data.
- ii. Analytical statistics:
 1. Paired *t* test
 2. Student *T*
 3. Chi-square test
 4. Correlation analysis (using Pearson's and Spearman's method)
 5. Regression coefficient for determination of the strongest predictor for FMA- UE.

**P* value: level of significance

-*P* > 0.05: non-significant (NS).

-*P* < 0.05: significant (S).

-*P* < 0.01: highly significant (HS).

Results

Descriptive data

Our study groups included 24 males (48%) and 26 females (52%). The age of the patients ranged from 50 to 70 years with a mean age of 59.04 ± 6.104 .

All patients were assessed with brain MRI. Twenty six cases (52%) had left subcortical infarction and 24 cases (48%) had right subcortical infarction. Among them, 15 cases (30%) had presented with capsular infarction, 11 cases (22%) had presented with pontine infarction, 5 cases (10%) had presented with thalamic infarctions, two cases (4%) had a basal ganglia infarction, and 17 cases (34%) had other subcortical area infarctions.

Comparisons

Comparing the demographic data and risk factors between the two study groups, neither age, gender nor risk factors had statistically significant difference between both groups.

Both groups also were matched as regard the radiological data, but significant difference was found in faze-kas (PVWM) score regarding score zero among the two groups.

As regards to the improved group, there was no statistically significant difference between ipsilesional and contralesional (cortical thickness, NAA/Cr ratio, and Glx/Cr ratio), while in not improved group, there was a highly statistically significant difference between ipsilesional and contralesional (cortical thickness, NAA/Cr ratio, and Glx/Cr ratio) with *P* = (0.002, < 0.001, and < 0.001), respectively.

As regards to all stroke patients, there was a statistically significant difference between ipsilesional and contralesional cortical thickness, and a highly statistically significant difference between ipsilesional and contralesional (NAA/Cr ratio and Glx/Cr ratio) with *P* = (0.011, 0.001, and 0.009), respectively. All details are in Table 1.

As regards ipsilesional cortical thickness, there was a highly statistically significant difference *P* = 0.007 between the not improved and the improved groups with mean 2.48 mm in the not improved group vs 2.87 mm in the improved group. As regards to NAA/Cr ratio, there was a highly statistically significant difference *P* = 0.001 between the not improved and the improved groups with mean 1.54 in the not improved group vs 1.83 in the improved group, but GLX/Cr ratio had no statistically significant difference between the two groups. All details are in Table 2.

There was no statistically significant difference between both groups neither in contralesional cortical thickness, NAA/Cr ratio, nor GLX /Cr ratio although the mean of the not improved group higher than that of the improved group as regards to NAA/Cr ratio and GLX/Cr ratio.

Table 1 Comparison between ipsilesional and contralesional cortical thickness and metabolite ratios in the improved, not improved, and all stroke groups

	Improved <i>N</i> = 20		Contralesional		Paired <i>t</i> test	
	Mean	SD	Mean	SD	<i>P</i> value	sig.
Cortical thickness	2.87	0.45	2.89	0.48	0.854	NS
NAA/Cr ratio	1.83	0.28	1.86	0.37	0.750	NS
GLX/Cr ratio	0.25	0.15	0.25	0.16	0.980	NS
Not improved, <i>N</i> = 30						
Cortical thickness	2.48	0.50	2.77	0.46	0.002	HS
NAA/Cr ratio	1.54	0.29	1.86	0.24	0.000	HS
GLX/Cr ratio	0.21	0.17	0.34	0.20	0.000	HS
All stroke group, <i>N</i> = 50						
Cortical thickness	2.63	0.50	2.81	0.47	0.011	S
NAA/Cr ratio	1.65	0.31	1.86	0.30	0.001	HS
GLX/Cr ratio	0.23	0.16	0.31	0.19	0.009	HS

Paired *t* test, *S* significant, *HS* highly significant, *NS* non-significant, NAA/Cr N-acetylaspartate/creatine ratio, GLX/Cr glutamate/creatine ratio

Table 2 Comparison in ipsilesional (cortical thickness and metabolite ratios) between the two study groups

	Not improved		Improved		t test	
	Mean	SD	Mean	SD	p value	sig.
Ipsilesional cortical thickness	2.48	0.49	2.87	0.44	0.007	HS
Ipsilesional NAA/ Cr ratio (height)	1.54	0.29	1.83	0.28	0.001	HS
Ipsilesional GLX/Cr ratio (height)	0.21	0.17	0.25	0.15	0.346	NS

t test, HS highly significant, NS non-significant, NAA/Cr N-acetylaspartate/creatine ratio, GLX/Cr glutamate/creatine ratio

Correlations

As regards to ipsilesional cortical thickness, there was highly significant positive correlation with FMA-UE and FMA of the hand with $P = 0.002$ and 0.006 , respectively and highly significant negative correlation with mRS with $P = 0.001$; also, ipsilesional NAA/Cr ratio had a highly significant positive correlation with FMA-UE and FMA of the hand with $P = 0.006$ and 0.008 , respectively and highly significant negative correlation with mRS with $P = 0.001$, but contralesional cortical thickness, contralesional NAA/Cr ratio, and both ipsilesional and contralesional GLX/Cr ratios had no any correlations with mRS, FMA-UE, and FMA of the hand. All details are in Table 3.

As regards to regression coefficient test for FMA -UE there was highly statistically significance with ipsilesional cortical thickness and ipsilesional NAA/Cr ratio, more powerful with NAA/Cr ratio which means that every one point change in NAA/Cr ratio associated with 27.58 points increase in FMA score. Also regarding regression coefficient test for FMA of the hand there was highly statistically significance with ipsilesional cortical thickness and significant correlation with ipsilesional NAA/Cr ratio, more powerful with NAA/Cr ratio which means that every one point change in NAA/Cr ratio associated with 5.76 points increase in FMA score. Table 4 shows details.

As regards to time from onset, there was highly significant positive correlation with ipsilesional NAA/Cr ratio with $P = 0.003$, and no any correlation with ipsilesional, contralesional cortical thickness, contralesional NAA/Cr

ratio, ipsilesional, contralesional GLX/Cr ratio, mRS, FMA-UE, and FMA of the hand.

As regards to fazekas score (PVWM and DWM), there was no significant correlation with mRS.

Data of healthy subjects

We recruited 16 healthy subjects to be references for our results regarding Egyptian people with age range from 50–66 years and mean of age was 57.25 ± 4.99 SD years, mean of right cortical thickness was 2.96 ± 0.31 SD mm, and that of left cortical thickness was 2.96 ± 0.4 SD mm. As regards to NAA/Cr ratio, the mean of right hemisphere was 2.01 ± 0.34 SD while that of left hemisphere was 1.89 ± 0.32 SD. As regards to GLX/Cr ratio, the mean of right hemisphere was 0.3 ± 0.19 SD while that of the left hemisphere was 0.31 ± 0.16 SD with no significant differences between the two hemispheres in healthy subjects for any of the variables.

Discussion

In the current study, we assessed the NAA/Cr and Glx/Cr ratios in the M1 of the hand area in individuals in the chronic stage of stroke recovery. These metabolites were selected for two reasons: first, changes in both of these metabolites have been reported in individuals with chronic stroke and were also associated with UE impairment. Second, an observed decrease in cortical thickness is most likely explained by neuronal death, which can be assessed using NAA as a marker of neuronal integrity [4, 6, 13].

As regards UE motor function, we found a high significant correlation between the ipsilesional NAA/Cr

Table 3 Correlation of cortical thickness and metabolites ratios with mRS, FMA-UE, and FMA of the hand

Whole sample, N = 50		Ipsilesional cortical thickness	Contralesional cortical thickness	Ipsilesional NAA/Cr ratio (height)	Contralesional NAA/Cr ratio (height)	Ipsilesional GLX/Cr ratio (height)	Contralesional GLX/Cr ratio (height)
FMA-UE > 6 months	Rs	0.429	0.096	0.383	0.026	0.148	- 0.154
	p value	0.002	0.507	0.006	0.856	0.306	0.285
FM hand > 6 months	Rs	0.384	0.074	0.369	0.060	0.134	- 0.154
	p value	0.006	0.609	0.008	0.677	0.354	0.284
mRS	Rs	- 0.468	- 0.022	- 0.456	-0.106	- 0.217	0.180
	p value	0.001	0.878	0.001	0.465	0.130	0.212

NAA/Cr N-acetylaspartate/creatine ratio, GLX/Cr glutamate/creatine ratio, FMA-UE Fugl Meyer Assessment-upper extremity, FMA Fugl Meyer Assessment, mRS Modified Rankin Scale

Table 4 Regression coefficient test for FMA-UE and FMA of the hand

FMA-UE > 6 months	Regression coefficient	95% CI	p value	sig.
Ipsilesional cortical thickness	19.20	6.84–31.55	0.003	HS
Ipsilesional NAA/Cr ratio	27.58	7.59–47.57	0.008	HS
FMA hand > 6 months				
Ipsilesional cortical thickness	5.10	2.19–8.01	0.001	HS
Ipsilesional NAA/Cr ratio	5.76	1.05–10.47	0.018	S

S significant, HS highly significant, NAA/Cr N-acetylaspartate/creatinine ratio, GLX/Cr glutamate/creatinine ratio, FMA-UE Fugl Meyer Assessment-upper extremity, FMA Fugl Meyer Assessment

ratio and both the FMA-UE score and FMA score of the hand. This is in agreement with Jones et al. and Craciunas et al. [3, 7].

Regarding the contralesional NAA/Cr ratio, our results showed no correlation with either the FMA-UE score or FMA score of the hand. These results are contrary to the findings of Goldzik et al. [14], who found a positive correlation between a contralesional prefrontal NAA/Cr ratio and recovery after stroke. However, the researchers did not relate the area where the metabolite ratios were measured to a specific clinical deficit in the patients studied.

While the ipsilesional Glx/Cr ratio showed a highly significant reduction in comparison with the contralesional Glx/Cr ratio in the stroke patients, we observed no association between this decrease and UE motor function, which is consistent with Jones et al.'s study [3] but contrary to Cirstea et al.'s study [6]. The latter found that the Glx concentration in motor areas was correlated with arm motor impairment in individuals with chronic stroke; this disagreement may be due to the small sample size used by the previous study compared to the sample size in the current study.

Other studies support the hypothesis that a decrease in ipsilesional Glx levels is associated with UE motor performance based on reported changes in intracortical excitability after a stroke, as well as a correlation found between the Glx concentration in the motor cortex and global motor cortical excitability (assessed by transcranial magnetic stimulation), which predict motor recovery after stroke [15–18]. However, further investigations are needed to resolve this issue.

In our study, we found a high significant correlation between ipsilesional cortical thickness and the FMA-UE score and FMA score of the hand. This finding is in agreement with Jones et al. [3] and Gauthier et al. [19], who noted that decreases in grey matter density in non-infarcted motor regions in individuals with chronic stroke correlates with the WMFT of UE motor function.

With regard to the regression coefficient test for the FMA-UE, it was highly statistically significant with both

ipsilesional cortical thickness and the ipsilesional NAA/Cr ratio, but it was more powerful with the latter; every 1-point change in the NAA/Cr ratio was associated with a 27.58-point increase in the FMA-UE score.

In addition, the regression coefficient test for the FMA of the hand showed high statistical significance with both ipsilesional cortical thickness and the ipsilesional NAA/Cr ratio, but it was more powerful with NAA/Cr ratio, as every 1-point change in this ratio was associated with an increase of 5.76 points in the FMA score of the hand. This finding is in agreement with Jones et al. [3], who concluded that the NAA concentration, a marker for neuronal integrity, in spared ipsilesional motor cortical areas that may contribute to UE motor function in individuals in the chronic stage post-stroke. So, while stroke impairs both the structure and biochemistry in the ipsilesional hemisphere, our data suggest that ipsilesional cortical NAA in the motor hand area has the strongest relationship with motor function of the UE and the hand, which may have an impact on future pharmacotherapies and rehabilitation methods in treating stroke.

Our study posits a highly significant reduction in the ipsilesional NAA/Cr ratio compared to the contralesional NAA/Cr ratio among stroke patients and in the group that showed no improvement. However, no significant difference was found among the group that showed improvement or in the hemispheres of healthy subjects.

We also observed a decrease in the ipsilesional and contralesional NAA/Cr ratios in all stroke patients (with mean values of 1.65 and 1.86, respectively) in comparison with healthy subjects (with mean values of 2.01 in the right hemisphere and 1.89 in the left hemisphere) for healthy subjects. Our results are consistent with previous findings in stroke studies [3, 6, 7].

Because these biochemical changes were observed in brain regions remote from the infarct, it is possible that diaschisis could explain these results. Diaschisis is a common dysfunction after stroke caused by the impairment of function in intact brain regions connected to, but distant from the area of infarct [20].

The current study also revealed decrease in ipsilesional Glx/Cr ratio among stroke patients in comparison with healthy subjects with a mean of 0.23 versus 0.30 and 0.31 in the right and left healthy hemispheres, respectively.

Our study found highly significant reduction in ipsilesional Glx/Cr ratio than the contralesional side among stroke patients and also among not improved group, but no significant difference between ipsilesional Glx/Cr ratio and contralesional Glx/Cr ratio among improved group or among both hemispheres in healthy subjects, which is consistent with Jones et al. [3].

A possible mechanism that may explain our findings of Glx and NAA concentration is neuronal death. Neuronal death following ischemic stroke is often attributed to improper homeostatic balance of Glu, as Glu cannot be taken up by either neurons or astrocytes, and levels of Glu rapidly rise in the extracellular space results in a cascade of cellular events such as intracellular calcium increase and mitochondrial dysfunction that ultimately leads to cellular death [21, 22] which in turn explains the metabolite ratios decrease in our study.

The current study also found that ipsilesional cortical thickness was significantly lower than contralesional cortical thickness among all stroke patients, and this significant difference was high among not improved group, but no significant difference among improved group or our healthy subjects group which is in agreement with Jones et al. [3] and Zhang et al. [23] who demonstrated that although the exact mechanisms for structural impairment of the ipsilesional M1 in subcortical stroke remain unclear, it is possible that retrograde degeneration may account for this finding.

For example, retrograde trans-synaptic degeneration in the retinal nerve fiber layer has been observed in patients with occipital lobe infarction [24].

Our results are also consistent with Duering et al. [25] who found that the integrity of the corticospinal tract potentially associated with the extent of focal cortical thinning in patients with incident subcortical infarcts.

Our study also observed that the mean of ipsilesional cortical thickness among not improved group was the lowest in comparison with improved group and right and left hemispheres of normal healthy group (2.48 mm, 2.87 mm, 2.96, and 2.97 mm), respectively, which consistent with Zhang et al. [23] who found that M1 cortical thinning is present even in stroke patients with improved global motor function, suggesting that motor recovery in these patients may be mainly associated with functional reorganization.

The limited use of the paretic limb in the not improved group may also explain our results about the thinning of the ipsilesional cortical thickness.

The current study revealed no statistically significant differences between improved and not improved groups as regards

to age, sex, risk factors, and radiological data except for fazekas scale (PVWM) which had statistically significant difference between the two study groups, After sub grouping by post hoc test, this difference was related to PVWM score 0 only as 4 of our improved patients had score 0, and no patients of the not improved group had this score, with no differences regarding other PVWM scores between the two groups.

As regards to time from onset, there was highly significant positive correlation with ipsilesional NAA/Cr ratio, and this is consistent with several reports which documented NAA concentration recovery in gray matter after stroke, suggesting that some degree of reversible neuronal injury accompanies ischemia [26].

In the current study, no correlation found between time from onset and contralesional NAA/Cr ratio which is inconsistent with Cristea et al. [6] who found positive correlation between the two items; as in that study, the range of duration post-stroke was wide (11–106 months) versus (7–18 months) in our study.

Time from onset also had no correlation with ipsilesional cortical thickness which in agreement with Brodtmann et al. [8] who found no change in ipsilesional cortical thickness overtime post-stroke.

In our study, no correlation noticed between time after stroke with mRS, FMA-UE score, and FMA score of the hand, and that is because recovery after stroke depends upon other multiple factors such as baseline function and disability, early mobilization, and if patients underwent physiotherapy or not.

Neither contralesional cortical thickness nor ipsilesional and contralesional GLX/Cr ratio had any correlation with time from onset that is may attributed to our narrow range regarding time after stroke.

As regards to fazekas scale, there was no any correlations with disability after stroke which disagree with Huo et al. [27] and Held et al. [28]; as in the current study, only 10% of patients had the higher fazekas score regarding PVWM and 0% regarding DWM which in agreement with Zerna et al. [29] who concluded that higher fazekas scale scores correlated with post-stroke outcome.

Conclusion

Our study concluded that persistent motor impairment in individuals with chronic subcortical stroke may be at least in part related to ipsilesional structural and biochemical changes in motor areas remote from infarction in form of decreased cortical thickness and NAA/Cr ratio which had the strongest relationship with that impairment.

Recommendations

1. Availability of software to measure absolute concentrations of brain metabolites.

2. Use of higher resolution MRI devices (more than 1.5 T) in future studies for more detailed structural and biochemical data.
3. Start study from acute phase and follow-up in the chronic phase.
4. Larger studies determine how rehabilitation methods may be related to metabolites or cortical thickness in chronic stroke.

Abbreviations

1H-MRS: Proton magnetic resonance spectroscopy; Cho: Choline; CNS: Central nervous system; Cr: Creatine; CSF: Cerebrospinal fluid; DWM: Deepwhite matter; FLAIR: Fluid-Attenuated Inversion Recovery; FMA: Fugl Meyer Assessment; FMA-UE: Fugl Meyer Assessment-upper extremity; fMRI: Functional magnetic resonance imaging; GLU: Glutamate; Glx: Glutamate and glutamine; IQR: Interquartile range; Lip: Lipids; M1: Primary motor cortex; ml: Myo-inositol; Mm: Millimeters; MRA: Magnetic resonance angiography; mRS: Modified Rankin Scale; NAA: N-Acetylaspartate; PWWM: Periventricular white matter; SD: Standard deviation; TE: Echo time; tNAA: Total n-acetylaspartate; TR: Repetition time; UE: Upper extremity

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Ethics approval and consent to participate

An approval of the study was obtained from Ain Shams University academic and ethical committee.

All participants signed an informed consent for participation in the study.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

Author details

¹Faculty of Medicine, Ain Shams University, Cairo, Egypt. ²El Sahel Teaching Hospital, Cairo 11697, Egypt.

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