Consciousness Emanates from the Neuronal Network of Coordination, A Fact Endorsed by Preserved Consciousness in Focal Ischemic Infarctions

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Abstract

Background: Consciousness has remained a difficult problem for the scientists to explore its relationship to the brain activity. This is the first paper that presents the significance of focal areas of the cerebral cortex for consciousness.
Objectives: To determine if consciousness is produced by the activity of the whole brain or one of its focal areas.
Methods: We have performed a prospective cross-sectional study in eighty patients of acute ischemic stroke. The neurovascular territory of the middle cerebral artery (MCA) was sectioned into four similar areas. The association of any of these focal areas to consciousness was observed after their dysfunction with ischemic strokes.
Results: Of the eighty patients, 57.5 % were males and 42.5 % were females. Mean age was 63 years ± 7 SD. The right-handed patients were 90 % (72) of the whole sample. Focal areas of the right MCA were generally less prone to consciousness disorder. Average statistics of the focal infarctions of the right MCA showed no tendency for consciousness disorder on the Glasgow coma scale (GCS) [Mean GCS of all focal areas; 14.5, SD; 0.71, 95 % CI; 14.27 to 14.72, P= 0.0000004]. Altered consciousness with focal infarctions of the territory of left MCA was also less likely [Mean GCS of all focal areas; 14.2, SD; 1.01, 95 % CI; 13.88 to 14.51, P= 0.0004].
Conclusion: Consciousness is not determined by the activity of a focal area of the cerebral cortex. Perhaps, we get our consciousness from the activity of "Neuronal Network of Coordination".

Key Words: Consciousness, Ischemic Stroke, Neurons, Brain, Middle Cerebral Artery, Hemisphere, Basal Ganglia, Corpus Callosum.

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Introduction

It has been difficult for the scientists to explore and understand the basic nature of consciousness for years (McGinn, 1989). We might be able to explain the psychic feelings of consciousness but its evolution from the intricate activity of the brain cells has remained arduous to interpret (Graziano, Kastner, 2011). Consciousness means an awareness of self and a feeling of being able to make decisions by a free will (Morin, 2006). Initially, cortical activity was recorded from the scalp of trained animals with metal electrodes in the form of surface deflections and hence the brain functions and conscious mind were believed to have electrical nature (Köhler et al; 1952; 1957).

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However, the invasive intracranial experiments of tantalum wire implantation, subpial slicing and insertion of mica plates into the cortices in cats did not disrupt their conscious behaviour that were trained to act in response to a stimulus and as a result the electrical nature of conscious mind could not be proved (Sperry et al; 1955; 1955). The research on trained animals has limited implications for us because the effects on consciousness are deduced only from their normal or impaired motor response. It is also not appropriate to explore the problem of consciousness by involving humans in the invasive experiments. However, the patients presenting to the hospital with natural pathological conditions of the brain will be appropriate for the study of consciousness (Edlow et al; 2014). We can apply clinical scales to these patients to appraise their conscious level and thus determine the significance of the diseased area of the brain for consciousness (McNarry, Goldhill, 2004). The simple fact whether consciousness is determined by the function of the whole brain or one of its focal areas is yet to be established in the literature. Usually, the impaired conscious level is observed in the clinical practice when there is a gross insult to the brain function. Such conditions include; generalized seizures, subarachnoid haemorrhage, lobar haemorrhage, subdural hematoma, cerebral oedema, systemic shock, hypoglycaemia, and the cerebral tumors (Bassin, Cooke, 2014). All these disorders produce a global brain dysfunction and do not help to determine if one of the focal areas of the brain will be more important than others for consciousness. If altered conscious level is not produced by dysfunction of focal areas of the brain then consciousness will be very likely related to the function of the whole brain.

There is a paucity of research on the significance of dysfunction of focal areas of the brain for consciousness. A review of the data for the disorder of consciousness shows information on the clinical conditions that cause generalized dysfunction of the brain i.e. altered consciousness in patients with head injury (Levin et al, 1988). The single pathological event that causes dysfunction of focal areas of the brain is the ischemic stroke. It causes necrosis and dysfunction of a specific area while the rest of the brain remains functional. The pathological event can be observed to determine the significance of dysfunction of focal areas of the brain for consciousness. In this paper, we will present the effects of focal ischemic infarctions on consciousness for the middle two-thirds of each hemisphere that dwell in the neurovascular territory of the middle cerebral artery (Gibo et al, 1981). The middle cerebral artery feeds cognitive areas of the brain that have significant influence on our conscious behaviour and include: the parietal lobe, temporal lobe and the frontal lobe (Toga et al, 2006). They possess special groups of neurons that perform critical analysis of the sensory information, develop its meaning, and perform conscious reasoning to show appropriate motor response to the stimulus (Baars et al, 2003).

Patients and Methods

Between 01-03-2019, and 26-07-2020, we examined all patients of acute ischemic stroke of the territory of the middle cerebral artery in the emergency department of District Head Quarter (DHQ) Teaching Hospital, Kohat, Pakistan. The location of the ischemic core was confirmed on computed tomography (CT) scan of the brain. All patients who presented to the emergency department with focal neurologic deficit were first evaluated by history and examination for acute cerebrovascular event, followed by computed tomography scan of the brain to confirm the ischemic infarction. The criteria applied for the selection of patients were as follows,

Determinants of Patients' Selection for the Study

- All patients of focal ischemic infarctions of the middle cerebral artery.
- Patients having well-defined margins of ischemic core on the CT brain. The CT scan outlines the ischemic core by 12 to 24 hours after the onset of symptoms with adequate precision.
- Patients who presented between 12 to 40 hours after the symptoms' onset for the management of stroke. If patients would arrive before the twelfth hour of symptoms, the study did not restrain them from early imaging and getting the appropriate treatment.
- No further evolution in the symptoms of stroke after the twelfth hour. This enabled us to appraise a stable relationship of the neurologic deficit to the ischemic core.
- The specification of age for the study was 40 to 70 years.

Patients' Exclusion Due to Concurrent Risk Factors for Consciousness Disorder

- Patients with localized oedema around the ischemic core and exerting a pressure effect on the surrounding areas.
- Seizures from the onset of ischemic stroke at the time of presentation.
- Haemorrhagic transformation of the ischemic core.
- Presence of systemic disorders that could affect the conscious level i.e. hypotension, liver failure, renal failure, pneumonia, hypoxia, hypoglycaemia and electrolyte imbalance.
- Occlusion of the main stem of the middle cerebral artery i.e. the M1 segment, that causes infarction of the whole territory of the middle cerebral artery (Hacke et al, 1996).

- *Exclusion of Cerebral Cortices with Less Physiologic Role for Consciousness*

The anterior frontal lobe is a pure motor area and executes the motor response determined by the premotor area (Roland, 1984). Similarly, the posterior occipital lobe only makes detection of an image and complete analysis is then performed by the visual association area (Pandya, Yeterian, 1985). Therefore, the anterior frontal lobe and the posterior occipital lobe were both declined from the present study, as they were less involved in the direct process of conscious meaning, reasoning and planning of a motor response.

Configuration of Neurovascular Territory of the Middle Cerebral Artery Into Four Triangular Areas

We divided the neurovascular territory of the middle cerebral artery (MCA) in each hemisphere into four separate areas and observed if consciousness was affected by acute ischemic stroke of these areas. Two areas of the middle cerebral artery i.e. MCA1 and MCA2 were formed at the level of the internal capsule on the axial sections of the CT brain as shown in figure 1. Another analogous pair of areas was formed at the level of the corona radiata and labelled as MCA3 and MCA4 respectively, as shown in figure 2.

We enrolled eighty patients in our study, 40 patients for each hemisphere and ten patients in each of the four areas. We examined more than two hundred patients of acute ischemic stroke to complete the data of all areas. The patients were kept equal between the two hemispheres and all areas to give equal representation and avoid bias on the basis of numbers of patients.

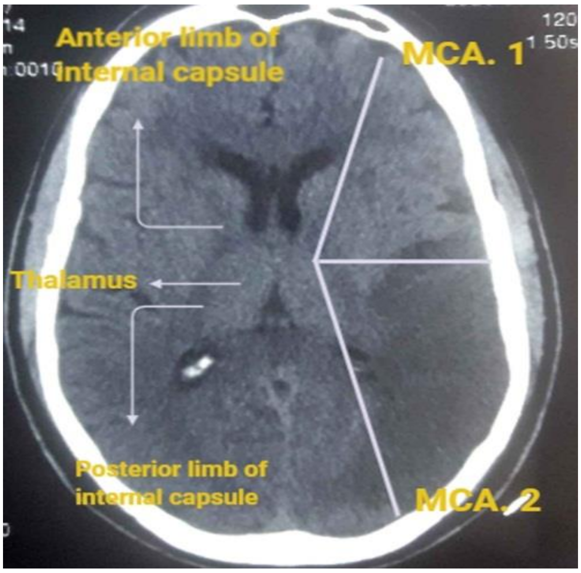


Figure 1. Two areas of the territory of the middle cerebral artery, MCA1 and MCA2, were configured at the level of the internal capsule. The purpose was to analyze the significance of different areas of the middle cerebral artery separately for consciousness during focal infarctions.

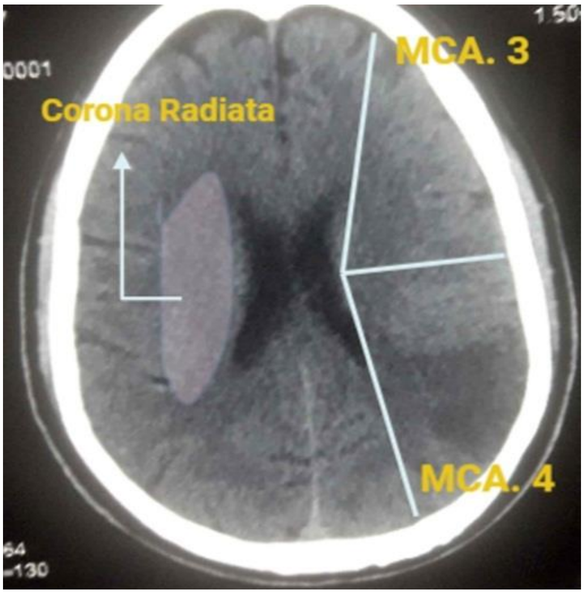


Figure 2. Two areas of the neurovascular territory of the middle cerebral artery, MCA 3 and MCA 4, configured at the level of the corona radiata.

Glasgow Coma Scale (GCS)

Glasgow coma scale is a clinimetric scale used for evaluation of conscious level of patients (Kung et al, 2011). We used the sum of individual scores of the three components of the Glasgow coma scale (GCS) to grade conscious level of patients. The GCS was scored at twelve to forty hours after the onset of focal neurologic deficit. The combination of three motor-responses i.e. eyes' opening to pain only, localization of noxious stimulus by appropriate motor response and confused speech, provided a definite evidence of altered conscious level in our patients. Therefore, a score of eleven was considered as the upper limit of altered conscious level on the Glasgow coma scale. The mean and standard deviation was determined for the Glasgow coma scale of each area. The scores of individual components of the Glasgow coma scale are given in table 1 as under.

Table 1. Glasgow Coma Scale

Numerical scoring of the three motor-responses of the Glasgow coma scale. Scores of 3 to 7 are attained by patients in coma. Accumulative scores of 8 to 11 represent altered conscious level and scores of 12 to 15 represent normal conscious level. Glasgow coma score of 11 i.e. Eyes response: 2, Motor response: 5, Verbal response: 4, is the upper limit of altered conscious level on the Glasgow coma scale.

EYES OPENING	MOTOR RESPONSE	VERBAL RESPONSE
4. Spontaneous	**6. obeys commands**	**5. Well oriented speech**
3. To sound	**5. Localizes pain stimulus**	**4. Confused**
2. To pain	**4. Withdrawal**	**3. Inappropriate words**
1. No response	**3. Abnormal flexion (decorticate)**	**2. Incomprehensible words**
	2. Abnormal extension (Decerebrate)	**1. No response**
	1. No response	

- *False Positive Reduction of Glasgow Coma Score*

Aphasia produced false positive reduction of five verbal points in the GCS despite that the patients would have adequate motor and eyes' responses. Aphasia was a clinical limitation to the Glasgow coma score in our study and such patients were excluded.

Z Score

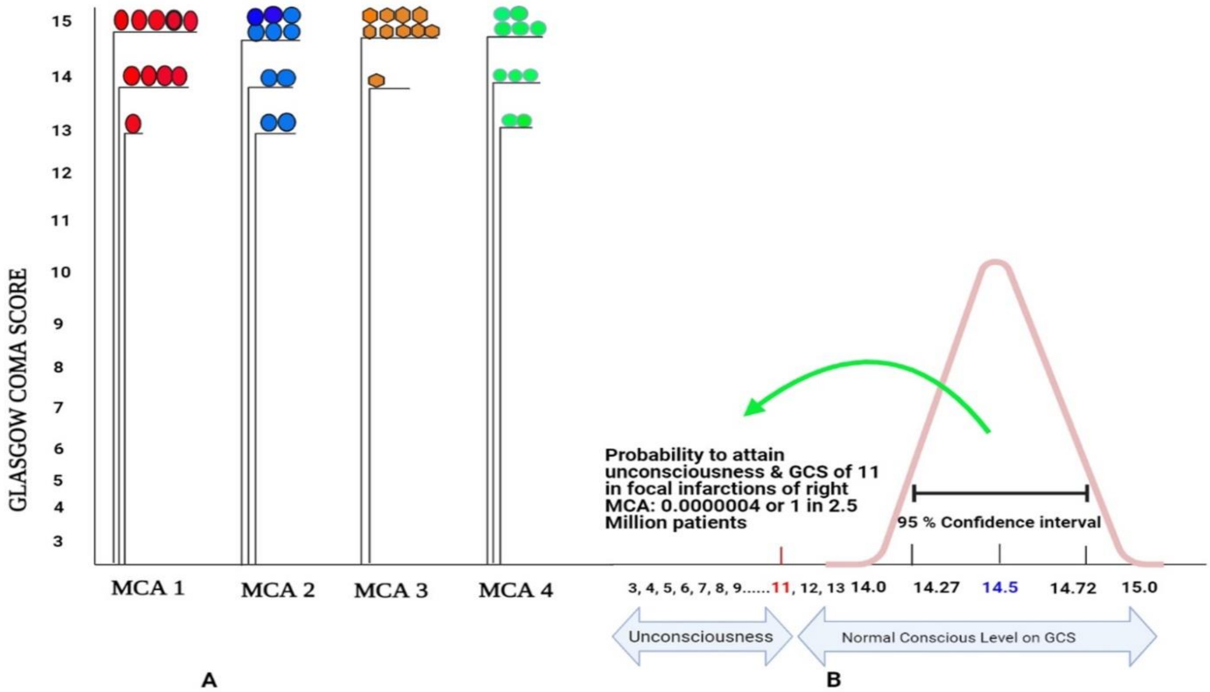
We calculated Z score to determine the probability of altered conscious level in the ischemic infarctions of each area against a score of eleven on the Glasgow coma scale. The Z score was calculated as follows,

$$\text{Eq.1} \quad \boldsymbol{Z} = \frac{x-\mu}{\sigma}$$

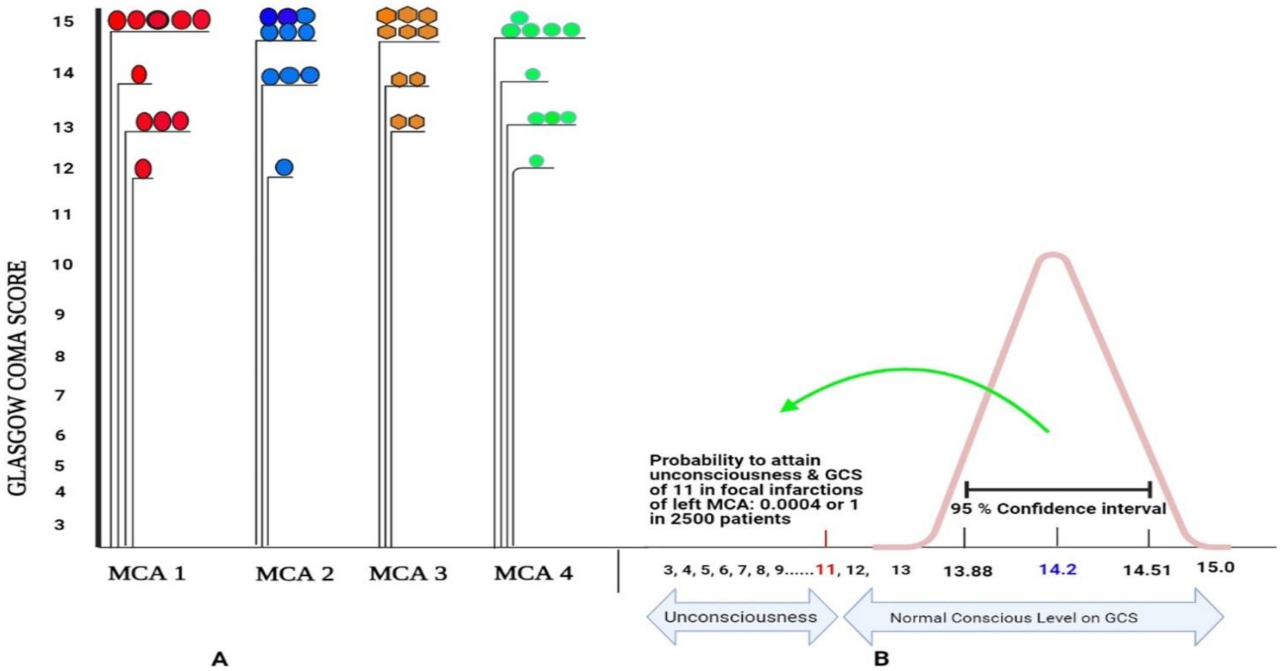
Where,
Z= Z score, X=11, **μ**= Mean of GCS of each area, and σ = standard deviation of GCS.
The exact value of the probability of altered conscious level in ischemic infarctions of each area was then calculated from the Z score with Microsoft Excel.

Results

Of the eighty patients, 57.5 % were males and 42.5 % were females. Mean age was 63 years ± 7 SD. The right-handed patients were 90 % (72) of the whole sample. Focal areas of the right middle cerebral artery were less prone to altered conscious level after ischemic infarctions [(MCA1: Mean GCS; 14.4, SD; 0.69, 95 % CI; 13.96 to 14.83, P= 4×10-7), (MCA2: Mean GCS; 14.4, SD; 0.84, 95 % CI; 13.87 to 14.92, P= 2.6×10-5), (MCA3: Mean GCS; 14.9, SD; 0.31, 95 % CI; 14.7 to 15, P= 3×10-36), (MCA4: Mean GCS; 14.3, SD; 0.82, 95 % CI; 13.79 to 14.81 P= 3×10-5)]. Accumulative result of all forty patients of the right MCA had no tendency for consciousness disorder [Mean GCS of all focal areas; 14.5, SD; 0.71, 95 % CI; 14.27 to 14.72, P= 0.0000004]. The results of the right hemisphere are given in table 2. The probability of altered conscious level from focal infarctions of the left middle cerebral artery was also less than 0.05 [(MCA1: Mean GCS; 14.0, SD; 1.1, 95 % CI; 13.28 to 14.71, P= 0.003), (MCA2: Mean GCS; 14.4, SD; 0.96, 95 % CI; 13.8 to 14.99, P= 0.0002), (MCA3: Mean GCS; 14.4, SD; 0.84, 95 % CI; 13.87 to 14.92, P= 0.00003), (MCA4: Mean GCS; 14.0, SD; 1.15, 95 % CI; 13.29 to 14.71, P= 0.004)]. Combined statistics of all forty patients, showed significance of normal conscious level in focal infarctions of the left MCA [Mean GCS of all focal areas; 14.2, SD; 1.01, 95 % CI; 13.88 to 14.51, P= 0.0004]. The results of the left hemisphere are given in table 3. The accumulative results of the two vessels' focal infarcts are illustrated in Graphs 1 and 2, respectively.



Graph 1. (A) Glasgow coma scores of ten patients, having focal infarctions, for each of the four areas of the right middle cerebral artery (MCA). (B) The mean Glasgow coma score (GCS) of all patients of the right middle cerebral artery follows a normal distribution curve. Based on standard error of mean, the 95 % confidence interval of the mean ranged from 14.27 to 14.72. The actual data of Glasgow coma scores of individual patients formed a left-skewed distribution curve around the mean of 14.5. Hence, the probability of GCS of 11 or less in focal infarctions of right MCA was 1 in 2.5 million patients.



Graph 2. (A) Values of Glasgow coma scores of individual patients of each of the four areas of the left middle cerebral artery (MCA). (B) The mean of Glasgow coma scores (GCS) of all forty patients of the left middle cerebral artery follows a normal distribution curve. Based on the standard error of mean (SEM), the 95 % confidence interval ranged from 13.88 to14.51. Actual values of the Glasgow coma scores of individual patients form a left-skewed distribution curve around the mean of 14.2. Therefore, the probability for altered conscious level in focal infarctions of left MCA at random was 1 in 2500 patients.

Table 2. The Mean, standard deviation, Z score and probability of unconsciousness on the basis of Glasgow coma score for focal infarctions in four different areas of the right middle cerebral artery (MCA).

The Glasgow coma scores of individual patients in each of the four areas were relatively similar and showed statistical significance for normal consciousness during focal infarctions of right MCA.

Serial No.	Right Hemisphere's GCS SCORE			
	MCA.1	MCA. 2	MCA. 3	MCA. 4
1.	15	14	15	14
2.	14	14	15	15
3.	14	15	15	14
4.	15	15	15	14
5.	15	15	15	15
6.	14	15	15	15
7.	13	13	15	13
8.	15	15	15	13
9.	14	13	14	15
10.	15	15	15	15
Mean GCS of each Area.	14.4	14.4	14.9	14.3
SD of each Area.	0.69	0.84	0.31	0.82
Z Score	-4.92	-3.4	-12.5	-4.02
P Value for unconsciousness	4×10^{-7}	2.6×10^{-5}	3×10^{-36}	3×10^{-5}

Table 3. The Mean, standard deviation, Z score and probability of unconsciousness on Glasgow coma score in focal infarctions of the four areas of left middle cerebral artery.

Individual patients had no proclivity for altered conscious level. Three patients, one each from the MCA.1, MCA.2 and MCA.4, attained Glasgow coma scores of 12, close to the cut off limit 11of the altered conscious level. The probability of altered conscious level with focal infarctions of left middle cerebral artery was < 0.05. 22

Serial No.	Left Hemisphere's GCS SCORE			
	MCA.1	MCA. 2	MCA. 3	MCA.4
1	15	15	14	15
2	15	15	15	13
3	15	15	15	15
4	13	14	13	14
5	14	15	15	15
6	15	15	14	15
7	12	12	15	13
8	15	15	15	15
9	13	14	13	13
10	13	14	15	12
Mean GCS of each area	14.0	14.4	14.4	14.0
SD of each area	1.1	0.96	0.84	1.15
Z score	-2.7	-3.5	-4	-2.6
P value for unconsciousness	0.003	0.0002	0.00003	0.004

Discussion

Ischemic stroke is an acute cerebrovascular event and caused by occlusion of a feeding vessel to the brain with consequent necrosis and dysfunction of a focal area (Ciccone et al, 2013). It is a frequent pathological event of the brain and can be used to evaluate the significance of focal areas of the brain for consciousness. We have an easy and appropriate clinimetric tool of the Glasgow coma scale that's commonly used to evaluate the conscious response of patients following an insult to the central nervous system. The Glasgow coma scale evaluates three main motor responses of a patient i.e. the verbal response, the limbs' motor response and the eyes' opening. The scale has a maximum score of fifteen and a minimum score of three. A patient in coma scores seven points on the GCS. Usually, a patient has a good understanding of self and the surroundings when his score on the GCS is twelve and above and have an altered conscious level when the score is eleven and below.

There was little variation in the GCS of individual patients in all four areas of the right hemisphere. The mean score of Glasgow coma scale in each area was close to fifteen and the standard deviation's value was also small. The chances of obtaining a GCS of eleven and below in focal infarctions of the right MCA for a patient at random were quite negligible. Therefore, the individual areas of the right hemisphere were less prone to cause an impaired conscious level. Many patients of individual areas of the left hemisphere also showed scores of normal GCS. The GCS of a few patients approached close to eleven. However, focal infarctions in all four areas of the left MCA did not produce a significant number of patients with altered conscious level to suggest that consciousness would be a function of one of the left hemisphere's focal areas. We observed a disorder of interpretation in a few patients with infarctions of the left MCA4. It was mainly due to the parietal lobe's dysfunction. They had impaired cognition and were not able to interpret simple questions like where is your home town? Who is standing to your left? Where are you now? They would utter a simple answer to every question, "I cannot do it". This particular area of MCA4 has Wernicke's area of speech that helps us understand the written and spoken language. It is situated at the junction of parietal, occipital and temporal lobes (Lesser et al, 1986). A similar disorder of cognition was not found in the ischemic infarctions of the corresponding area of the right hemisphere. The motor component of speech was frequently affected in patients with involvement of the left MCA1 and MCA3 areas. They usually had slurred speech but the content of conscious meaning of the speech remained intact. Once these functions are lost due to ischemic infarctions of the left hemisphere, they are not restored by the contralateral hemisphere (El Hachioui et al, 2013).

If focal infarctions of different areas did not cause altered conscious level then consciousness would be very likely produced by the function of the whole brain. It seems consciousness evolves from the activity of neuronal network of coordination in the deep white matter of the two hemispheres as infarctions of different cortical areas have spared consciousness and only produced focal neurologic deficits in the form of hemiplegia, dysphasia, dysphagia and irrelevant talk. The neuronal network of coordination links different parts of the brain and makes communication between the hemispheres. The coordination of activity in different parts of the two hemispheres develops our cognition and influences our thinking, reasoning and the appropriate motor response for a stimulus. The hemispheres can exchange information through the corpus callosum (McKeever et al, 1981). The left hemisphere being dominant in most individuals probably governs the process of coordination of the two hemispheres (Knecht et al, 2000). It sounds reasonable because consciousness as a single entity should govern actions and decisions from one hemisphere and collaborate with the other hemisphere for any information if needed. It will be difficult to take any action if both hemispheres have an equal opportunity to decide. Our study affirms that important aspects of cognition like comprehension, speech and appropriate motor response can get impaired with infarctions of the left dominant hemisphere. Therefore, the interpretation of critical aspects of conscious mind like thinking, reasoning, speech and the appropriate motor response to a stimulus will be governed by the left dominant hemisphere. It will be possible for the left dominant hemisphere to practice and own the decision of coordination if a greater part of the network of coordination exists in it. A simplified form of the neuronal network of coordination of the two hemispheres and its activity are illustrated in figure 3.

The idea of consciousness as an integral part of the activity of the neuronal network of coordination is supported by the observation of altered conscious level in disorders that cause gross dysfunction of the brain. The altered conscious level due to gross dysfunction of the brain is usually observed in a generalized seizure, subdural hematoma, subarachnoid haemorrhage, systemic shock and brain trauma (Fischer et al, 2006; Urbenjaphol et al, 2009; Hop et al, 1999). The observations of our study also substantiate the integrative brain theory of consciousness. It states that the conscious meaning of information develops when it is

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processed between the sensory and motor areas of a hemisphere (Adnan, Azam, 2015).

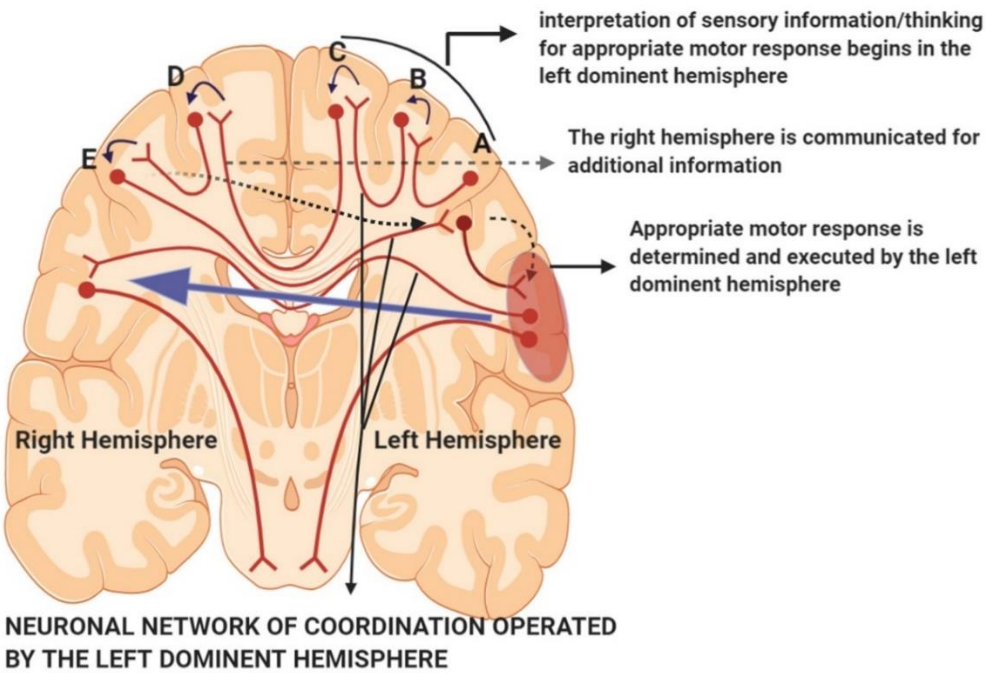

Figure 3. A simplified illustration of "Neuronal network of coordination"

Conclusion

Focal infarctions of the largest territory of the middle cerebral artery do not affect consciousness, and the finding of our study affirms it to evolve from the function of the whole brain. Focal ischemic infarctions produce limited neurologic deficit in the form of aphasia, hemiplegia, Visual and sensory hemineglect, and sometimes cognitive dysfunction. However, the quantitative feeling about self, that's more related to the function of the whole brain, remains intact.

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Not required
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Contributorship

Sohail Adnan: Conceived the study design, extracted the data, performed analysis and interpretation of data, and wrote the first draft. Mubasher Shah, Syed Fahim Shah: Extracted data, analyses of data, revised the manuscript and supervision of research work. Fahad Naeem, Akhtar Ali: Acquisition and analysis of data, obtained the images, illustrations, designed the tables, graphs and performed the calculations. Muhammad Hamid: Data acquisition, screened citations, collected appropriate papers, revision of the manuscript for the intellectual content and edited the final manuscript.

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