ANALYSIS OF CHANGES IN BRAIN MODEL PARAMETERS AFTER STROKE

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Abstract. The human brain consists of many structures, or so-called functional areas. Each area participates in the implementation of a certain function of the human organism (senses, vision, movements, thinking, etc.). Of course, these areas are not autonomous and are connected to each other, forming a network of brain connections, often called the connectome. Understanding how connectivity varies across nodes is an important step in analysing a network. These connections are of varying strength and importance and have various other important parameters that describe brain activity and its changes under the influence of external events (e.g. stroke, Alzheimer's disease, dementia and other neurological diseases). It turns out that functional regions and their connections can be represented as vertices and arcs of a graph, and elements of graph theory can be used to analyse such a model. The number of functional areas for graphing can vary and will depend on how detailed the brain structural model is. Previous studies have created a literature review, resulting in a knowledge base, and identified the consequences of injury or damage to each region resulting in different disfunctions. When the brain is affected by a stroke or any other abnormal neurological condition, the functional areas are damaged and the connections between them are altered. Consequently, the model of the brain - the graph, the parameters of its vertices and arcs - also changes. The purpose of this article is to look at what changes occur in the brain graph in order to use the changed model in future studies in the development of a system for predicting possible stroke consequences.

Keywords: connectome, graph theory, model analysis, brain regions.

Introduction

A stroke, a frequently occurring neurological condition, can lead to various complications afterward, with cognitive impairment being one of the most severe. Unfortunately, this state becomes more often due to unhealthy lifestyle, bad habits. A stroke is an acute disorder of cerebral circulation. It occurs due to blockage, compression or rupture of the vessels that carry blood to the brain. In this case, brain cells die due to lack of oxygen and nutrients. Any brain damage is always associated with severe consequences for a person. Of course, it depends on which important brain regions are injured.

Using different techniques, we can obtain the brain network, which shows connections and information flow between different brain regions. In the given article, the authors refer to the source [1], where 256 brain regions and their connections are reflected. In simpler terms, the networks within the brain can be categorized as either structural or functional. Next network can be visualized and analysed as a graph. In the previous studies the authors created a model of the brain injury process [2], summarising all the functions of brain regions and the possible effects of damage of functional regions.

Within several minutes of a stroke beginning, the connections between neurons are impacted by significant ischemic depolarization, followed by delayed cell death. While some connections can recover if blood flow is quickly restored, those linked to the dying area of tissue (infarct) may not be salvageable. In Fig. 1 there is an example how the brain network can be changed after stroke [3]. There are 2 situations described – normal brain network, where all regions are connected in small groups and then interconnected through the hubs – meaningful brain regions which are highly connected with the biggest part of nodes of the whole network.

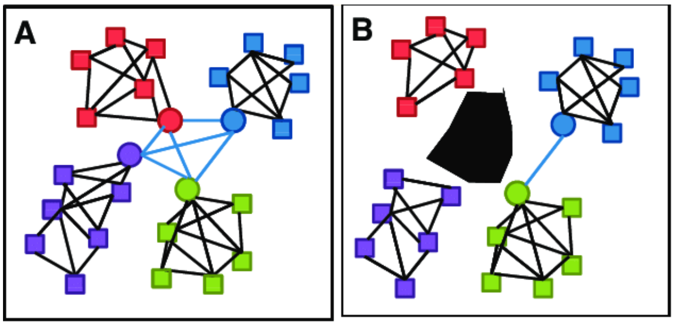

Fig. 1. **Degree distribution of the brain graph:** A – healthy brain graph;
B – two hub nodes are affected by a stroke

As we look at the brain model like the graph with nodes (brain regions) and edges (functional connections between regions), we can calculate different meaningful parameters, which can show the main characteristics of such brain model. In healthy brain, the networks are structured in what is known as “small-world” models, characterized by a high clustering coefficient and short characteristic path length. This arrangement offers significant advantages, including efficient global information transfer at a low cost in terms of connections. However, when there is functional or structural damage, severe clinical symptoms, or prolonged disease duration, the network organization deviates from this optimal small-world pattern, becoming increasingly pronounced as the damage worsens [4].

A small-world network maintains a high clustering coefficient while also having a few long-distance connections, allowing for efficient global information transfer with a low characteristic path length [5].

Although a stroke mainly affects a specific area, it also causes changes in other parts of the brain and alters how the entire brain network functions. So, instead of just focusing on where the stroke occurred, looking at the overall brain connectivity might be more helpful in predicting the behavioural problems caused by the stroke.

Materials and methods

How can we evaluate node connectivity? There are some main measures for summarizing the connectivity of each node in a network. They are shown in Table 1.

Table 1

Main parameters of connectivity in network

Parameter	Formula	Meaning
Node degree	$k_i = \sum_{j \neq i} A_{ij}$	Number of edged connecting node i with all other nodes
Mean degree of a network	$\langle k = \frac{1}{N} \sum_{i=1}^{N} k_i$	Average node degree of all node degrees
Degree centrality	$C_D(i) = k_i = \sum_{j \neq i} A_{ij}$	For an undirected network it is the same as the node degree
Closeness centrality	$C_C(i) = \frac{N-1}{{}_{j \neq i} l_{ij}}$	Inverse of node’s average shortest path length, where l_{ij} is the shortest path length between node i and j
Betweenness centrality	$C_B(i) = \frac{1}{(N-1)(N-2)} \sum_{h \neq i, h \neq j, j \neq i} \frac{\rho_{hj}(i)}{\rho_{hj}}$	Part of shortest paths between all pairs of nodes (j and h) in the graph that pass-through a given node i
Clustering coefficient	$C = \frac{N_{CT}}{N_T}$	Measures the degree to which nodes in the graph tend to cluster together. A triplet consists of three nodes that are connected by either two (open triplet) or three (closed triplet) undirected ties.
Characteristic path length	$L = \frac{1}{n(n-1)} \sum_{i \neq j} d(i,j)$	Average of all distances over all pairs of nodes in a network

The mentioned measures show that not all elements of the brain connectome are equal and with the same meaning in the brain connectivity analysis process. So, based on the graph theory parameters we can apply them in the context of brain connectivity analysis. Therefore, a very important moment is to correctly interpret the results of calculations.

Node degree is the simplest quantity of node connectivity but can give us a general impression about the most “connected” node – brain regions, which have links with almost all other brain areas, so we can put forward a hypothesis that the injury of these regions may cause even death of the connected regions too.

To get the full picture of the significance of individual graph nodes, we can also calculate a parameter, which shows the importance or influence of every brain region in the whole network functioning. The term “centrality” was introduced to analyze social networks, but then interpretated in neuroscientific applications [6]. Degree centrality, closeness centrality, and betweenness centrality are all measures used in network analysis to assess the importance or centrality of nodes within a network. Each measure provides a different perspective on how nodes are positioned within the network and their potential influence. Degree centrality is a measure of the number of connections a node has in a network. Nodes with high degree centrality are directly connected to many other nodes in the network. Closeness centrality measures how close a node is to all other nodes in the network. Nodes with high closeness centrality are close to many other nodes and can quickly interact with them. Betweenness centrality measures the extent to which a node lies on the shortest path between other nodes in the network. Nodes with high betweenness centrality act as intermediaries or connectors in the network. They control the flow of information or resources between other nodes.

To analyze how brain connectivity changes after any occurrences, like stroke, based on degree and centrality we can highlight highly connected nodes, which are called hubs [7]. Choice of the hubs also is a complicated process because there are some aspects that impact it. We will use different centrality measures to assign the label of “hub” to nodes.

The clustering coefficient measures the likelihood that if two nodes are both connected to a third node, they are also connected to each other. In other words, it quantifies the tendency of nodes to form clusters or groups of interconnected nodes. The characteristic path length is a measure of how closely connected nodes are in a network. It represents the average number of steps it takes to travel from one node to another. Specifically, it is the minimum number of edges needed to link any two nodes in the network, on average. In essence, while the clustering coefficient focuses on how tightly interconnected nodes are within local clusters, the characteristic path length gives us an insight into how efficiently nodes are connected on a global scale throughout the network [8].

Results and discussion

Using the adjacency matrix [9] that shows connections between 246 brain regions and Python package NetworkX, the authors have computed the previously mentioned parameters. In previous works of the authors a procedure of creating a brain connectivity graph from the adjacency matric was described [10] and some basic parameters were calculated.

First, a degree distribution – a frequency count of the occurrence of each degree – was computed. The results are shown in Fig. 2. The degree is the immediate risk of a node for catching whatever is flowing through the network. In the context of brain connectivity, the degree parameter would represent the immediate risk of a brain region for receiving or transmitting neural activity within the network.

Next visualisation is path distribution (Fig. 3) – a frequency count of the occurrence of each path distance in the brain graph. The average path distance of 1.52 means that, on average, the shortest path length between any two nodes in the brain graph is approximately 1.52. In terms of interpretation, a lower average path distance generally suggests a more tightly connected or efficient network, where information can travel relatively quickly between different regions of the brain. Also, the path is closely related to small-world phenomenon.

Understanding the clustering coefficient distribution provides insights into the local connectivity patterns within the brain graph and can help in characterizing its network structural organization (Fig. 4). An average clustering coefficient closer to 1 suggests a high level of local clustering or connectivity within the brain network. A value of 0.55 indicates that, on average, approximately 55% of a node’s neighbours are also connected to each other. This level of local clustering suggests a significant degree of organization or modularity within the brain network. The global clustering coefficient is a measure of the overall clustering or transitivity in the entire network. It quantifies how much the nodes in the graph tend to cluster together. A global clustering coefficient of 0.57 indicates a relatively high degree of local clustering within the brain graph, suggesting a structured and organized network architecture that supports efficient information processing and functional specialization.

Centrality measures of the brain graph nodes were also computed. For further research it is necessary to detect a ranking of nodes based on different types of centralities (Fig. 5). It will help find the most meaningful and highly connected nodes, which can influence others in case of damage. In Fig. 5 nodes with the highest centralities are shown. Decoding these nodes means that the brain regions of the subcortical nuclei area, such as basal ganglia and thalamus, and their subregions are most connected with other parts of the brain.

For overall conclusions about the centrality in the graph we can calculate average measurements of all nodes in graph:

- average degree centrality: 0.4738;
- average betweenness centrality: 0.0022;
- average closeness centrality: 0.6626.

The average degree centrality indicates that, on average, each node in the brain network is directly connected to about 47% of the other nodes. While the average betweenness centrality is low, the brain network likely still maintains efficient communication paths between different brain regions. The high average closeness centrality indicates that, on average, nodes in the brain network are relatively close to one another in terms of the shortest path distances.

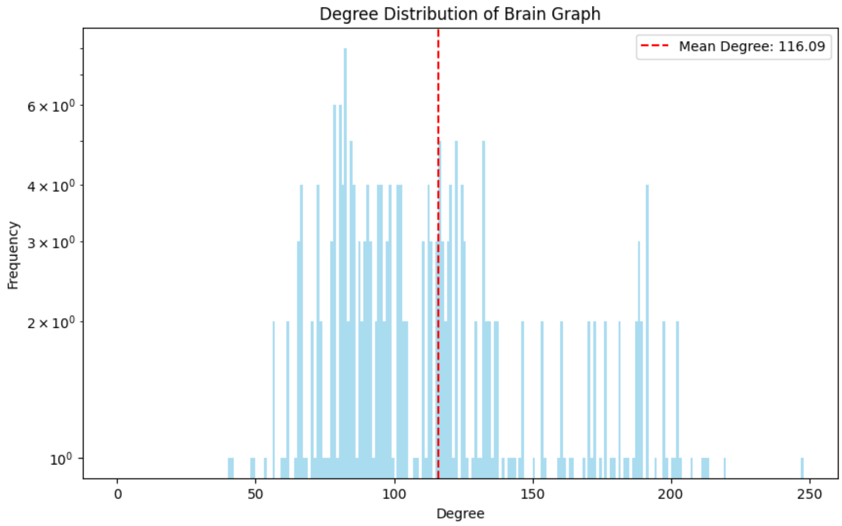

Fig. 2. **Degree distribution of the brain graph**

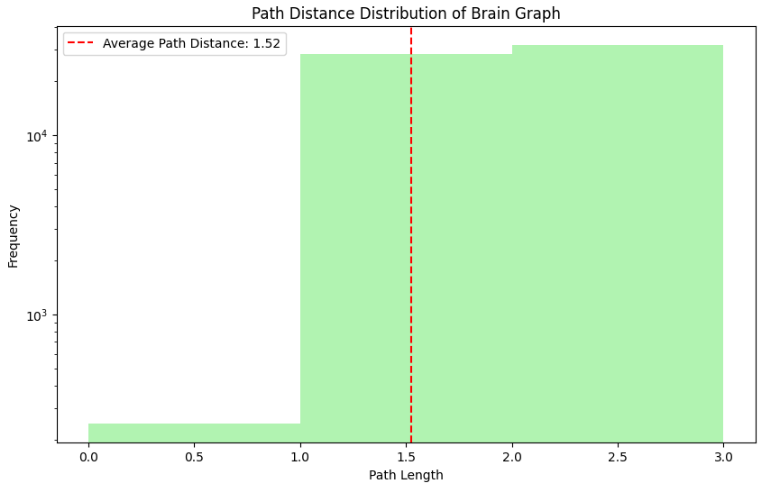

Fig. 3. **Path distance distribution of the brain graph**

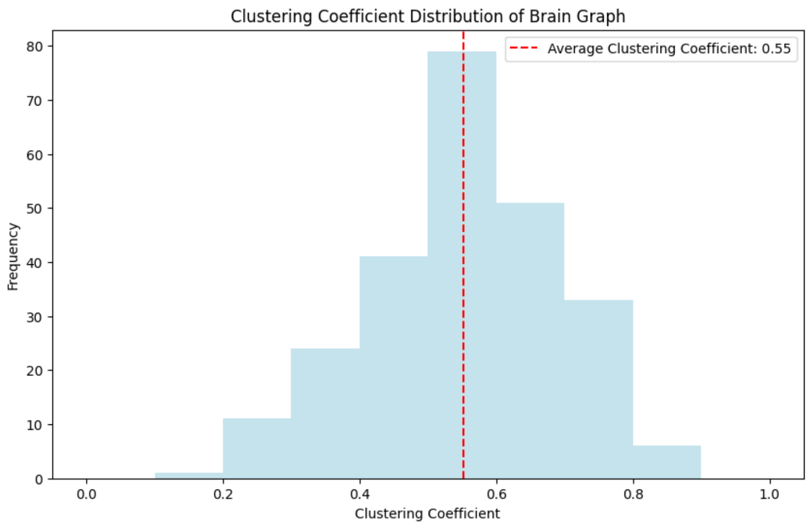

Fig. 4. **Clustering coefficient distribution of the brain graph**

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Degree Centrality:
Node 0: 1.0082
Node 242: 0.8939
Node 240: 0.8694
Node 239: 0.8653
Node 238: 0.8612
Node 241: 0.8449
Node 228: 0.8286
Node 222: 0.8245
Node 243: 0.8245
Node 230: 0.8204
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Betweenness Centrality:
Node 0: 0.0177
Node 242: 0.0097
Node 228: 0.0093
Node 239: 0.0089
Node 240: 0.0088
Node 238: 0.0081
Node 230: 0.0081
Node 222: 0.008
Node 241: 0.0078
Node 227: 0.0075
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Closeness Centrality:
Node 0: 1.0
Node 242: 0.8974
Node 240: 0.8781
Node 239: 0.875
Node 238: 0.8719
Node 241: 0.8596
Node 228: 0.8478
Node 222: 0.8448
Node 243: 0.8448
Node 230: 0.8419
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Fig. 5. **Nodes with the highest centralities**

This suggests that information exchange between different brain regions is efficient, with relatively short communication pathways.

But what changes in the brain structure if there are some neurological problems, for example, a stroke? In general, two major scenarios of graph parameter changes can be distinguished. The first type of graph reorganisation happens if hub nodes are affected by a stroke. This situation decreases the global functional integration among the communities in a graph. The second type is when community members are targeted which results in lower local integration inside of the modules or groups of brain regions.

If hub nodes of brain network are damaged, a big number of connections also is destroyed. Based on the degree and centrality, there are following hubs: basal ganglia, thalamus, and their subregions. These areas are crucial for advanced thinking processes so very meaningful [11]. In Fig. 6 the results of the graph parameter changes after injury of the brain hubs are shown.

So, damaging hubs leads to connectivity changes in the whole network. Removing hub nodes increases the average path length between pairs of nodes, reducing the closeness centrality of remaining nodes. Hub nodes usually have a high degree, meaning they are directly connected to many other nodes. Deleting hub nodes decreases the number of edges in the network and can change the relative degree centrality of other nodes. In summary, the removal of hub nodes can disrupt the flow of information or connectivity in the network, leading to changes in various centrality measures for other nodes.

It is important how big parts of hubs are damaged (deleted from the graph). In the given simulated scenario only some subregions of thalamus and basal ganglia (Fig. 7) [12] were damaged, and even in this situation we see how changes the connectivity of the network. Of course, if the stroke affects whole thalamus, connectivity of the network will almost be destroyed, and consequences can be tragic. Thalamus is responsible for sensory and motor functions, speech, sleeping, and basal ganglia subregions control our communication skills, emotions, behaviour, reactions, different skills, fatigue condition etc. [13].

Injury of nodes with the smaller significance (which are not hubs) also will impact information workflow in the network but in a less degree.

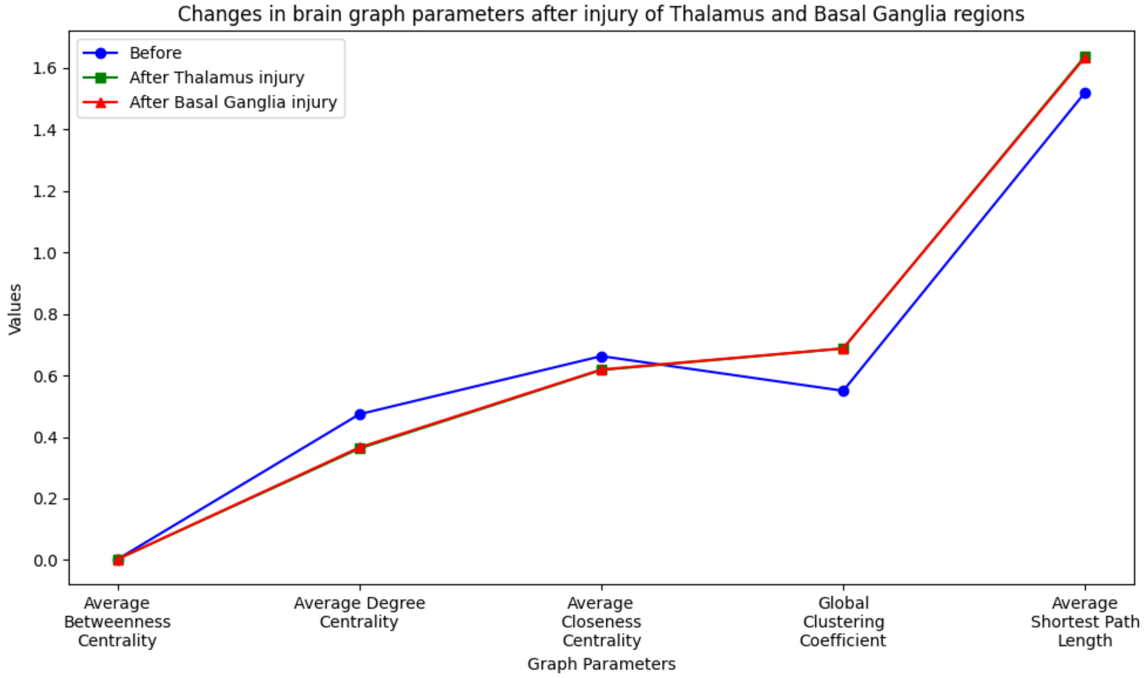

Fig. 6. **Changes of connectivity of a brain graph after damaging of hubs**

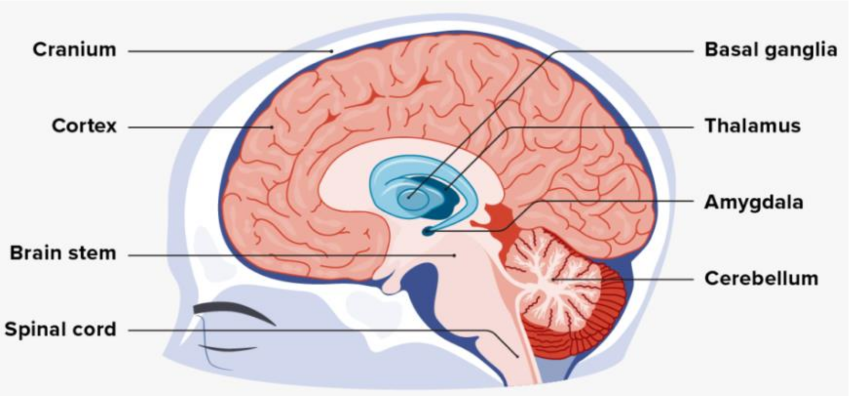

Fig. 7. **Regions of brain**

Conclusions

1. Using the graph theory, it is possible to determine the main parameters of brain connections.
2. The presence of hub nodes in brain networks, typically localized in areas of basal ganglia and thalamus, underscores their critical role in brain functions. These hubs serve as central points of integration and information exchange, coordinating communication across distributed brain regions.
3. Changes in centrality metrics, due to the damage of hub nodes, reflect alterations in information flow, integration, and efficiency within the network.
4. The average shortest path length in the brain network reflects the efficiency of information processing and transmission between different brain regions. Changes in the path length following alterations to the network structure provide clues about the impact on cognitive functions and behavioural outcomes.
5. Analysis of the brain network connectivity applying the graph theory has significant meaning for understanding the brain health and diseases.

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