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Weighted Leverage Centrality for Region Role Identification in Brain Networks

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Abstract: In recent times, the representation of brain as a network for understanding its complex structure and function are evolving tremendously. The identification of regions playing the key role is determined through the centrality measures. The changes in the brain connectivity exhibit the alterations in the brain and thus helpful in diagnosing the neurological disorders. Various centrality measures are employed to identify the central nodes in the brain network and leverage measure is one among them. Leverage centrality is a simple measure which finds the centrality score for a node based on the connectivity of its neighbours. To improve the scoring ability of leverage in the aspect of indirect neighbour's influence, a variant of leverage has been proposed. In addition to degree of a neighbour, the eigenvector measure is multiplied as a weight factor(i.e. connectivity of neighbour's neighbour). The weighted leverage measure is compared against other measures namely degree, betweenness, eigenvector and leverage centrality in the perspective of proper identification of network hubs. Experiments have been conducted on the group average functional connectivity matrix obtained from the resting state fMRI of the healthy people. The outcomes have projected the significant improvement in hub determination on comparison with other centrality measures.

Key words: Centrality · Brain Network · Leverage · Functional MRI

INTRODUCTION

Connectome analysis has received higher attention in the neuroscience research domain to appreciate the intriguing qualities of complex brain structure and function. The network representation of brain obtained from the neuroimages constitutes the connectome. The Region of Interest (ROI) or voxels in the image form the nodes of network. Edges depend on the type of neuroimage such as temporal correlations from functional MRI, white fiber bundles from structural MRI, etc [1]. These constructed network structures are analysed similar as related networks in other domains namely social network, World Wide Web, food webs, etc. Complex network analysis originated from the mathematical concept, graph theory has great implications in comprehending the characteristics of various networks. The network has different structure depending upon the connectivity patterns. Depending on the clustering coefficient and characteristic path length of the network, it could be classified into regular, random and small-world network [2-4]. With few changes in the connectivity, random network could be converted into small-world network. In random network, nodes have almost equal number of connections in contrast to small-world network. Brain networks are found to be scale-free networks, where fewer numbers of nodes have high number of connections and rest of the nodes have limited number of connections. Degree probability distribution follows power law function in scale-free networks. These brain networks are analysed using different graph theoretical measures. Network measures involved in the analysis can be commonly classified into segregation, integration and centrality. Segregation measures concentrates on the aspect of clustering the nodes which are tightly-connected in the network [5]. Clustering coefficient and modularity are most predominantly applied metrics to determine the cluster of nodes. The former utilizes the structure of triangle formed by the node which indicates the neighbourhood connectivity and the later measure analyses the network to group the nodes based on the connectivity between the nodes within the same group and other groups [1, 6]. These measures are further optimised to address various issues and identify the well-formed groups in the network.

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Integration measures investigate the flow of information in the network by understanding the connectivity between the nodes [5]. Characteristic path length is the most populous measure that elucidates the shortest path between all pairs of nodes and the inverse of this measure is known as global efficiency. Small world network connectivity and network motif are the measures involved in the detection of patterns that are formed with the equal proportion of segregation and integration metrics in the network. Centrality measures are widely applied in the network analysis to determine the importance of a particular node [5-12]. Hundreds of measures are developed for determining the role of a node with the examination of node distribution and connectivity of a network. The highly influential nodes can be called as hubs and non-hubs in the case of vice-versa. The contributions of the node can be assessed through other measures like motif and resilience.

It is well known that the identification of influential regions in the brain at different health conditions is really fascinating and necessary too. In the network view of brain, nodes which play major role to contribute for some functional or structural changes can be pointed through the computation of centrality measures.

The most common centrality measures derived from the literature are degree, betweenness and eigenvector centrality. These measures are applied on different types of network to identify central nodes at different context. In addition to these, multiple numbers of centrality measures are developed specific to particular field that analyses topological properties of a network and could also be used for networks in other domains. Leverage centrality is such a kind of measure devised for brain network analysis but is easily applicable for other kinds of networks as well.

Degree is the basic measure that specifies the number of neighbours of each node. This centrality orders the node based on the number of connections [7, 8]. Even though it ends in identification of crucial nodes, it does not consider other aspects of the network in their calculation. Yet, this measure is simple and hence, frequently involved in the estimation of variety of measures. Betweenness centrality utilizes the geodesic path to know the central node in the network [9]. The node which is highly involved in the geodesic path of other nodes is known to be hub. These hubs act as a bridge between two different parts of the network. However, the measure assumes the flow of information in sequential paths of the network. Since, brain network is dynamic and some paths become active on the fly, it follows parallel information processing. Another interesting measure which is widely used and has been modified based on particular application is eigenvector centrality [10, 11]. In spite of its complex computation, it has been applied in the network to identify the central nodes depending on the centrality of surrounding neighbour nodes. Eventhough eigenvector measure considers neighbour's activity in an attempt of identification of hubs, it does not involve degree of the neighbour directly.

Leverage centrality measure has been proposed to understand the network's assorative or disassorative character [12]. It utilises the degree of the neighbours to evaluate the centrality measure of each node. Leverage could able to detect the appropriate nodes as hubs significantly on comparison with similar centrality measures, There are several other measures are available to detect the influential nodes in the network based on different perspectives namely PageRank centrality, closeness centrality, knotty centrality, subgraph centrality, LeaderRank, ClusterRank, etc. In this research, we introduced the improvised version of the leverage centrality measure. To enhance the identification of hubs in the network, eigenvector measure is multiplied as a weight factor to the leverage centrality. The commonality between these measures is both of them involves the surrounding neighbours influence. However, leverage directly utilises the degree of immediate neighbour nodes to understand the local assortative behaviour whereas eigenvector includes the centrality values of the neighbours. In the weighted leverage measure, different viewpoint on assortative nature of the network is combined to determine the influential nodes.

To understand the implication of weighted leverage measure on the brain network, functional connectivity network of healthy human brain is utilised. The outcomes of the measure is compared with related measures namely degree, betweenness, eigenvector and leverage centrality. Functional cartography is used to detect the hubs based on the modularity factor and is defined to be gold standard for comparison. In this research, a weighted leverage has been proposed that incorporates the network's assortativity addressed by eigenvector and leverage measure as well. This facilitates the identification of some regions as network's central node which may or may not be revealed by either of those measures and provide new insight on the distribution of network and the behaviour of nodes.

MATERIALS AND METHODS

Participants: To experiment with the proposed weighted leverage measure, two different datasets has been utilized. The functional connectivity matrix obtained from the resting state functional magnetic resonance images (rs-fMRI) of the healthy individuals has been analysed. The sample from Nathan Kline Institute – Rockland (NKI-RS) is chosen to determine the regional roles of each node in the perspective of different measures.

The connectivity matrix of NKI-RS data has been obtained from the UCLA connectivity multimodal database online repository for sharing of brain network data developed by different users [13]. The RS-fMRI based connectivity matrix has been considered in this study. The dataset consists of information from images that has undergone global signal regression procedure and another group of images without performing regression. The twenty-five subjects with age ranging from 7 to 76 with mean age of 29.2 ± 19.8 are included in the group which has been performed global signal regression (GSR). The GSR group consists of eight female and seventeen male subjects. The sequence of interviews and tests has been conducted to conform the mental healthiness of the individual.

MRI Scanning Parameters: The images of NKI-RS have been acquired from the scanner Siemens Trio 3T. The RS-fMR images are obtained when the subjects are in rest and wont perform any significant cognitive tasks with TR (Repetition time) = 2500 ms, TE (echo time) = 30 ms and voxel resolution = 3×3×3 mm.

Data Preprocessing: The following preprocessing steps has been carried out to construct network from the RS-fMR images: FSL's slicetimer is utilized for differential slice timing, FMRIB's Linear Image Registration Tool (MCFLIRT) is employed for rigid-body motion correction, FSL Brain Extraction Tool (BET) is used for skull stripping, the images have been spatially smoothed with Gaussian kernel of 5 mm with FWHM, mean scaled the complete 4D dataset, filtering is performed to extract the data from 0.08 to 0.009Hz, FSL FAST is applied for tissue specific delineation from MPRAGE, CSF and WM masks are registered to the initial fMRI, Core WM mask and ventricular mask extracted from the MNI152 atlas applied to determine mean time courses from the core CSF, core WM and whole brain to construct the model. Then, linear regression is performed on the model which contains CSF, WM, 6 motion parameters and all temporal derivatives to acquire residuals and proceeded with motion scrubbing to identify significant motion changes or BOLD signal alterations. Then the image is registered with MNI152 brain atlas using FSL FLIRT. Further, the image is parcellated by applying the spatially constrained spectral clustering method [14] on the BOLD data to obtain 188 ROIs. These regions include cortical, subcortical and cerebellar structures which are spatially continuous and similar in functions across subjects. Then, the average time courses are estimated and followed with the determination of correlation between all pairs of regions and leads to the construction of resting state functional connectome.

Sparsity Selection: The constructed functional connectome consists of pearson correlation values between the pair of regions which may contain positive or negative values. To perform analysis on the network, the matrix is thresholded in order to derive the binarized functional connectivity matrix [1]. The threshold value is chosen to specify the significance of connection. The connection between the region-pair is considered to be significant if the value is greater than the threshold otherwise it is considered to be non-significant. The binary value 1 is assigned to the important connections which could be included to the network and others are assigned to the value 0 in the binary form of matrix. The heuristic has to be applied to achieve the threshold value instead of blind choice of some values. In this study, sparsity is estimated that defines the ratio of actual edges to the maximum number edges. The distinctive edge values are chosen and arranged from largest value to the smallest. For example, if the sparsity value is defined to be 10% then the minimum value among the top 10% values is selected as threshold. In this investigation, sparsity value of 10%, has been considered[15,16]. The weighted individual matrices are thresholded to obtain the sparse network. The binary functional connectivity is utilized for analysis of the centrality measures in the efficiency of determination of influential regions in the human brain under the resting state condition.

Modularity Analysis: To evaluate the outcome of the centrality computations in the identification of influential nodes in the brain network, the utilization of functional cartography is generally practised. The community structure is used for the calculation of two metrics namely within-module degree and participation coefficient which is involved in the estimation of central nodes in the network. The regions with similar functions are grouped in single community and thus form set of communities from the given network. The nodes within the module have increased number of connections on comparison with nodes in other modules or communities. The optimal number of communities is determined based on the partition parameter. The identification of parameter is an approximation problem where the partition value has to be maximized to determine the appropriate modular structure. The spectral partitioning algorithm has been engaged to cluster the regions that indicate the community structure of the brain network [17,18]. Mathematically, Modularity Q of a network G can be defined as follows.

$$Q(G) = \frac{1}{2m}\sum_{i \neq j}(a_{ij} - P_{ij})\delta(M_i, M_j) \quad (1)$$

where, m = number of links in the network; a_{ij}=1 if node i and j are connected;; a_{ij}=0 if there is no connection between node i and j; $\delta(M_i, M_j)$=1 if i and j are intra-modular nodes; $\delta(M_i, M_j)$=0 if the nodes are in different modules; P_{ij} is the probability of a presence of connection in a random network similar to the given network G.

P_{ij} can be mathematically derived as follows:

$$P_{ij} = N_{dc}(i)N_{dc}(j)/2m \quad (2)$$

where, $N_{dc}(i)$ is the number of connections of the node i. The modularity parameter value is adjusted in order to achieve the thickly connected modules together in the network. With the identification of modules for each node in the network, within-module degree z-score (Z_i) and participation coefficient (PC_i) has to be derived to identify the regional role as specified by functional cartography. Within-module degree z-score, the measure which indicates intra-modular connections define whether the given region plays a role of hub or non-hub in the network can be estimated as follows:

$$Z_i = \frac{k_{s_i} - \bar{k}_s}{\sigma k_s} \quad (3)$$

where, k_{si} is the number of connections of the node i within the module s; $\bar{k}_s$ and σ_{k_s} is the mean and standard deviation of intra-modular connections of module s respectively [19, 20].

The higher z value of a node indicates the most influential in the network with strong intra-modular connections. Node with Z value greater than zero are considered as modular hubs and node with Z value lesser than or equal to zero are considered as modular non-hubs in this investigation.

To further classify the role played by the nodes, participation coefficient is calculated which is mathematically represented as follows.

$$PC_i = 1 - \sum_{s=1}^{N_s}\left(\frac{k_{s_i}}{N_{dc}(i)}\right) \quad (4)$$

where, k_{si} is the number of connections of a node i in module s; $N_{dc}(i)$ is the total number of connections in the network regardless of module. N_s is the identified modules in the network. This measure could depict the between-module connections of a particular node in the network. If a hub or non-hub node is almost equally connected with nodes in other modules then it could be called as kinless hub or kinless non-hub respectively. If the hub has high level of intramodule connections then it is known to be provincial node. If the hub has high number of intermodule connections then it is said to be connector hubs as they connect the node from different modules. Similarly based on the connectivity, the non-hub nodes are classified as ultra-peripheral, peripheral, non-hub connector nodes. The thresholds for participation coefficient defined in the functional cartography technique are followed to define the regional roles for each node.The classification of hub using within-module degree z-score is used for the evaluation of the hubs identified through centrality measures.

Centrality Measures: The importance of a particular node in the network can be identified in different perspectives through centrality measures. If the node is found to be very efficient in communication then it is said to be hub. If a node does not play major role in the information transfer between the nodes then it is known to be non-hub. The efficiency of the node can be concluded through different centrality computations. In this study, a hybrid measure has been proposed that utilizes the eigenvector and leverage centrality measure. These two measures estimates the centrality value based on the degree distribution but in different aspects. Eigenvector centrality determines the centrality of a node based on the centrality score of neighbours whereas leverage measure calculates based on the connectivity of neighbours. The leverage measure estimates the regional role significantly better than other centrality measures. To further improve the measure, a weighted leverage centrality measure has been proposed. The outcome of the measure is compared with traditional centrality measures namely degree, betweenness, eigenvector and with leverage also.

Degree is a common measure that approximates the connectivity of the node with its neighbours. In terms of degree centrality, node with dense connections is considered to be hub which lead to the quick communication of the information among the nodes and the node with sparse connections is defines as non-hub of the network [7].

Mathematically, degree centrality is calculated as follows:

$$N_{dc}(i) = \sum_{j \in N} a_{ij} \tag{5}$$

where, i represents node and j represents it's neighbours, a_{ij} is the connectivity between node i and j, if a_{ij} = 1 and 0 indicates the presence and absence of connection respectively, N is the total number of nodes, $N_{dc}(i)$ is the degree measure of node i.

Betweenness measure could find the important middle nodes that could participate in the information transfer between the nodes in different modules. These nodes are commonly found in the path between various nodes in the network [9].

Mathematically, betweenness centrality (b_i) is defined as follows:

$$N_{bc}(i) = \frac{1}{(n-1)(n-2)} \sum_{h,j \in N, h \neq j, h \neq i, i \neq j} \frac{p_{hj}(i)}{p_{hj}} \tag{6}$$

where, h, i and j start node, middle node and destination node respectively, $N_{bc}(i)$ is the betweenness measure of node i, p_{hi} and $p_{hj}(i)$ indicates the number of shortest paths between h and j and between h and j through node i respectively.

Eigenvector centrality determines the importance of node based on the connectivity with the neighbours in the network. The node is said to be influential if it has connection with highly connected neighbours. Mathematically, it can determined as follows:

$$N_{ec}(i) = \frac{1}{\lambda} \sum_{j \in N} (a_{ij} e_j) \tag{3}$$

where, λ is the largest eigenvalue and e is the corresponding eigenvector, $N_{ec}(i)$ is the eigenvector measure of the node i [10, 11].

Leverage measure is based on the degree distribution of the nodes in the network. The measure is dependent on the degree of the immediate neighbours and does not consider the indirect neighbour's effect [12]. The measure can derive positive or negative value. Mathematically, Leverage measure is determined as follows:

$$N_{lc}(i) = \frac{1}{N_{dc}(i)} \sum_{n_i} \frac{N_{dc}(i) - N_{dc}(j)}{N_{dc}(i) + N_{dc}(j)} \tag{4}$$

where, $N_{dc}(i)$ and $N_{dc}(j)$ is degree of node and immediate neighbour respectively and n_i is the total number of neighbours of node i. The positive value means the node influences the neighbours and the negative value shows the influence of neighbours on the node.

In this study, weighted leverage measure is introduced which not only considers the degree of the immediate neighbours but also the effect of indirect neighbours. Eigenvector measure identifies a node as central if the node has more number of connections with neighbours. Hence, to improve the influential node identification in the aspect of understanding the effect of indirect neighbours influence, eigenvector measure of neighbour node is included as the weightage factor to degree of each node.

The eigenvector value of the node and its neighbours has been summed and the weightage factor of the particular neighbour is obtained. The weightage value has been multiplied with the degree measure of the particular node in the estimation of leverage centrality. The weighted leverage measure is calculated as follows:

$$N_{wl}(i) = \frac{1}{N_{dc}(i)} \sum_{n_i} \frac{W(i) * N_{dc}(i) - W(j) * N_{dc}(j)}{W(i) * N_{dc}(i) + W(j) * N_{dc}(j)} \tag{5}$$

$$W(i) = \frac{N_{ec}(i)}{TOTAL} \tag{6}$$

$$TOTAL = N_{ec}(i) + \sum_{n_i} N_{ec}(j) * a_{ij} \tag{7}$$

where, $N_{dc}(i)$ is a degree of a node i, $N_{dc}(j)$ is degree of immediate neighbour node and n_i is the total number of neighbours of node i. $N_{ec}(i)$ is a eigenvector measure of a node i, $N_{ec}(j)$ is a eigenvector measure of a neighbours of node i, a_{ij} indicates the connectivity between the nodes, TOTAL is sum of the eigenvector of a node i and its neighbours. W(i) is the weight factor of the node obtained from the fraction of contribution among its neighbours. The implication of value is similar to the leverage measure where positive value represents the influence of node on its neighbours and vice versa in the case of negative value. The weighted leverage value refines the measure to identify whether the node is influential or not and thus improves the leverage centrality.

Performance Metrics: The role identification of a particular node is based on the threshold fixed for the centrality measure. If the node has value greater than the threshold, then those nodes are known as hub. Otherwise, the nodes are said to be non-hub. Generally, the threshold for detection of hub in the network is assigned to the sum of the average and standard deviation of the centrality measure. The identified role is compared to the role designated by the functional cartography technique. The performance of the measure is evaluated using the measure accuracy, sensitivity and specificity[]. Accuracy is the ratio of total number of true positives and true negatives to the total number of samples as given in the formula below.

$$Accuracy = \frac{TP + TN}{TP + TN + FP + FN} \quad (8)$$

$$Sensitivity = \frac{TP}{TP + FN} \quad (9)$$

$$Specificity = \frac{TN}{TN + FP} \quad (10)$$

where, TP is the number of nodes regarded as hubs by the centrality measure as well as functional cartography technique (ground truth). TN is the number of nodes regarded as non hubs by the centrality measure as well as by the ground truth. FP is the number of nodes identified as hubs by the centrality whereas those nodes are identified as non-hubs by the ground truth. FN is the number of nodes identified as non-hubs by the centrality whereas those nodes are identified as hubs by the ground truth. The experimental analysis on the outcomes of the centrality measures are presented in the next section.

RESULTS AND DISCUSSIONS

The network representation of brain could be analysed exhaustively to discover unknown information to the world. In this research, resting state functional MRI of the healthy individuals from NKI rockland study have been considered. The functional connectome of those subjects which has undergone global signal regression have been involved in this work. Initially, the weighted connectome has been thresholded with sparsity level of 10% to form binarized network structure. Further, various centrality metrics namely degree, betweenness, eigenvector, leverage and the proposed weighted leverage have been estimated.

To understand and evaluate the regional role identification in the brain network, functional cartography is employed. The thresholded network is involved in the clustering of regions into modules. Spectral partitioning algorithm is utilized to form the modules which enable to calculate within module degree z-score. The regions which have within module degree z-score greater than zero are considered as hubs and other regions as non-hubs.

Then, the common centrality measures namely degree, betweenness, eigenvector are calculated. In addition to this, leverage centrality which has been proposed to determine hubs in the brain network is also determined. Leverage has slightly lower value if the nodes are highly interconnected in comparison with other measures. It involves the degree of the node and its immediate neighbours. In this work, we attempted to improve the ability of leverage to appropriately find the hubs in the brain network. Leverage measure utilizes the degree distribution of the network. Similarly, eigenvector measure also understands the assortative nature of the network in a different perspective. Eigenvector identifies the node as a influential if the neighbours of the node also found to be influential in the network whereas leverage considers only the immediate neighbour's connective structure.

However, leverage is computationally easier as they involve only simple calculation from the degree measure whereas eigenvector involves intensive computation. In the aspect of identifying hubs, the appropriate determination of region role rather than computation is important. The NKI Rockland study consists of 25 healthy individuals whose resting state functional connectivity values are obtained after the global signal regression is performed on the images. These subjects are considered for analysis of the proposed measure. If the node has eigenvector value greater than its neighbour, eventhough its degree value is lesser than neighbours, it may be recognised as influential region as the eigenvector values are lower than the node. According to eigenvector, a node is said to be influential, if the neighbour's are also influential in the network. Hence, the proposed measure not only looks into the degree of the neighbours but also analyses the influential nature of each node for computation of the measure. If the node is

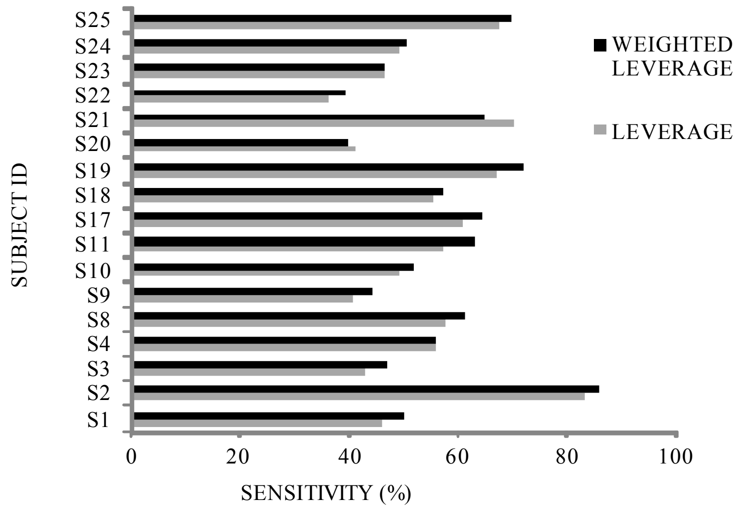

Fig. 1: Performance of Leverage and Weighted Leverage Measure

Table 1: Average Performance Evaluation Metrics of the Centrality Measures

Metrics Vs Centrality	Degree	Betweenness	Eigenvector	Leverage	Weighted Leverage
Accuracy (%)	80.53	74.38	82.04	84.51	84.91
Sensitivity (%)	40.85	19.67	45.78	55.95	56.36
Specificity (%)	99.93	99.97	99.61	99.35	99.55

highly influential and the number of neighbours is lower when compared to their neighbours, it may be regarded as hubs in the case of less influential neighbours.

In this study, to determine hubs the threshold for each measure has been fixed. The regions which have value greater than the threshold are considered as hubs and others as non-hubs. The threshold value is assigned to sum of the average value and the standard deviation of the measure. The regions identified as hubs are compared to the hubs determined by the functional cartography. The mean value of accuracy, sensitivity and specificity of each measure is presented in the Table 1.

From the Table 1, it could be found that overall the sensitivity value has increased significantly by the proposed measure which indicates that the hubs and non-hubs are identified appropriately on comparison with other measures. The improvement in accuracy and specificity is also evident from the result analysis. The identified number hubs in each subject against the total number of hubs are depicted in Figure 1. It is clearly evident that in most of the subjects, weighted leverage could able to find the influential regions better than other measures.

Leverage measure attempted to understand the information diffusion in the network. It reveals the regions with low connectivity which has neighbours with very minimal number of connections. Since, those regions are core in the network as they are connected to very low degree regions. On other hand, the regions with high interconnections and if their neighbours also has increased connections, then such a regions have low leverage. The cingulate and precuneus region were identified as the highly connected and significant region in the brain network of healthy individuals[22]. Thus, in few subjects, leverage has missed to identify the cingulate regions as influential region. The regions with high connectivity have to be considered as influential, as the removal of those nodes may affect the degree distribution of the network.

To improve the leverage measure, the eigenvector of the node is multiplied as a factor. Eigenvector decides on the region's significance based on the neighbour's connectivity as similar to leverage. Eigenvector finds the region influential if the neighbour regions are also influential in the network. To determine the trade-off between the regions with higher and lower degree to recognise as hubs, weighted leverage is proposed. At sparsity level of 10%, the weighted leverage performs better than the degree, betweenness and eigenvector measure to find the most central regions. The proposed measure comparatively performs better than the leverage measure. The regions that could be correctly classified as hubs by the weighted leverage measure are found to be influential in the literature also. The cingulate regions which have not been identified by the leverage as hubs are determined by the proposed measure.

The regions which have been most commonly identified as hubs in brain networks are caudate, thalamus, insula, paracingulate, precuneus, frontal pole region of both hemispheres. The middle frontal, superior frontal, frontal orbital, superior frontal of left and right hemispheres of brain also found to have higher scores in the identification of healthy subjects. Few regions from occipital and temporal lobes, lingual and Supramarginal region are recognised to act as hubs in the network. Caudate region determined to be highly central node in the brain network. Earlier studies also show that the caudate region has increased connectivity with the regions in the default mode network in the healthy individuals. The decreased connectivity between the caudate and those regions indicate the presence of disorder in the brain [23]. Similarly, the regions found to be influential by the proposed measure is in accordance with the previous studies.

The analysis has been done by varying the threshold to determine the hubs from the centrality measures. It has been found that the degree, betweenness and eigenvector measure have lower accuracy in correct identification of the region role in the network. Leverage measure concentrates on the determination of high number of hubs and thus leads to increased number of non-hubs to be wrongly identified as hubs. Weighted leverage measure attempts to bring the trade-off in the correct determination of hubs and non-hubs in the resting state fmri brain network of the healthy individuals. From, the experimental outcomes, it is well known that the weighted measure performs comparatively better than other centrality measures. The limitation of the measure is the inclusion of eigenvector increases the computational complexity in the very large brain networks. In future, different factors have to be analysed to replace the measure that greatly improves the functionality of leverage for correct classification of brain regional roles.

CONCLUSION

With the advancement in the functional network analysis, the different graph theoretical measures are employed to reveal the hidden patterns in the brain network. Among those measures, centralities are commonly involved in the identification of central nodes in the network. Various centrality measures are formulated to address the different issues in many real world networks namely transportation networks, protein networks, social networks, World Wide Web, etc. Leverage measure has been developed to determine the hubs in the brain networks of healthy individuals. It involves the connectivity measure of the network and addresses the degree distribution of the network. The node with lower degree could also identified to be hub if has connected to other extremely lower degree nodes. However, the highly interconnected nodes may have low leverage value and thus to improve the leverage measure along with degree measure, influential factor of the neighbours are included. Hence the brain region is recognized to be central node depending upon the connections of immediate neighbours as well as the eigenvector measure of them. The experiments reveal that the regional role identification of the weighted leverage measure is comparatively better than other existing measures.

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REFERENCES

1. Bullmore, E. and O. Sporns, 2009. Complex brain networks: graph theoretical analysis of structural and functional systems. Nat Rev. Neurosci., 10: 186-198.
2. He, Y. and A. Evans, 2010. Graph theoretical modeling of brain connectivity. Curr Opin Neuro., 23: 1-10.
3. Van den Heuvel, M.P. and H.E. Hulshoff Pol, 2010. Exploring the brain network: A review on resting-state fMRI functional connectivity. Eur. Neuropsychopharmacol., 20(8): 519-534.
4. Rubinov, M. and O. Sporns, XXXX. Complex network measures of brain connectivity: uses and interpretations, Neuroimage, 52(3): 1059-1069.
5. Meunier, D., R. Lambiotte and E.T. Bullmore, 2010. Modular and hierarchically modular organization of brain networks. Front. Neurosci., 4: 200.
6. Kashtan, N. and U. Alon, 2005. Spontaneous evolution of modularity and network motifs. PNAS. 102(39): 13773-13778.
7. Sabidussi, G., 1966. The centrality index of a graph. Psychometrika., 31: 581-603.
8. Barabasi, A.L. and R. Albert, 1999. Emergence of scaling in random networks. Science, 286: 509-512.
9. Freeman, L.C., 1979. Centrality in networks: I. Conceptual clarification. Social Networks, 1: 215-239.
10. Bonacich, P., 1972. Factoring and weighting approaches to status scores and clique identification. Journal of Mathematical Sociology, 2: 113-120.
11. Ruhnau, B., 2000. Eigenvector centrality-a node centrality? Social Networks, 22: 357-365.

12. Joyce, K.E., P.J. Laurienti, O.H. Burdette and S. Hayasaka, 2010. A New Measure of Centrality for Brain Networks. PLoS One., 5(8): e12200.
13. Nooner, K.B., S.J. Colcombe, R.H. Tobe, M. Mennes, M.M. Benedict, A.L. Moreno, *et al*., 2012. The NKI-Rockland Sample: A Model for Accelerating the Pace of Discovery Science in Psychiatry. Front Neurosci, 6: 152.
14. Craddock, R.C., G.A. James, P.E. Holtzheimer, X.P. Hu and H.S. Mayberg, 2012. A whole brain fMRI atlas generated via spatially constrained spectral clustering. Hum Brain Mapp, 33(8): 1914-1928.
15. Sun, Y., Q. Yin, R. Fang, X. Yan, Y. Wang, A. Bezerianous, *et al*. Disrupted Functional Brain Connectivity and its Association to Structural Connectivity in Amnestic Mild Cognitive Impairment and Alzheimer's disease. PLoS One, 9(5): e96505.
16. Zheng, G., L. Zhang, L.J. Zhang, Q. Li, Z. Pan, X. Liang, *et al*., 2014. Altered Modular Organization of Functional Connectivity Networks in Cirrhotic Patients without Overt Hepatic Encephalopathy. BioMed Research International., 2014(2014): 727452.
17. Newman MEJ. Finding community structure in networks using eigen vector of matrices. Phys Rev E 74:036104. 2004.
18. Reichardt, J. and S. Bornholdt, 2006. Statistical mechanics of community detection. Phys. Rev. E, 74: 016110.
19. Guimera, R. and L.A. Amaral, 2005a. Cartography of complex networks:modules and universal roles. Journal of Statistical Mechanics: Theory and Experiment. 2005a.
20. Guimera, R. and LA. Amaral, 2005b. Functional cartography of complex metabolic networks. Nature 433: 895-900.
21. Baldi, P., S. Brunak, Y. Chauvin, C.A. Andersen and H. Nielsen, 2000. Assessing the accuracy of prediction algorithms for classification: an overview. Bioinformatics, 16: 412-424.
22. Andrews-Hanna, J.R., J. Smallwood and R.N. Spreng, 2014. The default network and self-generated thought: component processes, dynamic control and clinical relevance. Ann N Y Acad Sci., 1316: 29-52.
23. Bluhm, R., P. Williamson, R. Lanius, J. Théberge, M. Densmore, R. Bartha, *et al*., 2009. Resting state default-mode network connectivity in early depression using a seed region-of-interest analysis: Decreased connectivity with caudate nucleus. Psychiatry Clin Neurosci, 63(6): 754-761.