

# Volume entropy and information flow in brain networks: in case of tinnitus in subjects with hearing loss

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## ABSTRACT

Brain regions send and receive information through neuronal connections in an efficient way. However, when these brain networks are organized in an abnormal way, a symptom-generating pathologic network may be generated. In this regard, based on the fact that only some of subjects with hearing loss develop tinnitus, we conjecture that subjects with hearing loss and tinnitus (HL- T) may be different from subjects with hearing loss without tinnitus (HL-NT) with regard to the cortical network property. This assumption prompted us to conduct the current study comparing the HL-T group and the HL-NT group with regard to volume entropy and inflow using a relatively large quantitative electroencephalography (qEEG) data.

We use volume entropy and the weights on vertices and edges, as well as other type of entropy-like invariants in modeling the brain networks of various populations including tinnitus and hearing loss using EEG. Volume entropy of a metric graph, a global measure of information, measures the exponential growth rate of the number of network paths. On the other hand, weight vectors of nodes and edges, which are local measures of information, represent the stationary distribution of information propagation in brain networks.

## METHOD

### 0.1 Subjects and qEEG data

From the qEEG database of Seoul National University Bundang Hospital, we have selected 65 qEEGs of HL-T subjects and 104 qEEGs of HL-NT subjects. QEEGs were measured in these subjects with a 19-channel EEG amplifier in the sitting position with the eyes closed for 5 minutes.

### 0.2 Metric graph

We choose 84 ROIs among the Brodmann areas as in [2] and define the connectivity between ROIs by lagged coherence. Analogous to the relation between conductance and the re-

sistance, we define the distance between two ROIs as the multiplicative inverse of the lagged coherence. The brain network is a complete graph whose nodes are ROIs and whose edges have the length described above. Throughout the talk, we regard the brain network as a complete metric graph with 84 nodes.

### 0.3 Volume entropy

Let  $X$  be a connected finite acyclic metric graph without any terminal vertex. The volume entropy of the metric graph  $X$  is defined by

$$h_{\text{vol}} = \lim_{r \rightarrow \infty} \log \text{vol}(B(x, r)) / r,$$

where  $\text{vol}B(x, r)$  is the sum of the lengths of edges or part of the edges in the ball of radius  $r$  centered at a vertex  $x$  in the universal covering tree of the graph. In other words, the volume entropy is the exponential growth rate of the volume of a ball in the universal covering tree.

Note that the volume entropy on a metric graph is also equal to the exponential growth rate of the number of paths in the ball of radius  $r$  as  $r \rightarrow \infty$ . It is known that the limit exists and the volume entropy is independent of the vertex  $x$  [1]. If we consider the growth of the number of paths as the amount of information spreading out, the volume entropy measures how well information spreads along the edges of a graph so volume entropy plays a role of global network invariant in dynamics.

### 0.4 Inflow

In the process of calculating the volume entropy using Perron-Frobenius theorem, we obtain a vector in  $\mathbb{R}^{|EX|}$ , that is, weights on the directed edges of the metric graph.

If a weight is large, then the corresponding edge is more likely to be contained frequently in a family of growing balls. So the weight represents how the corresponding edge affects the spread of information. Furthermore, we also observe that for complete graphs, such as brain networks, distinct directed edges with same terminal vertex have similar weights. Summing over weights on the directed edges with same terminal vertices, we obtain a vector of weights on vertices and we call it the inflow [3].

We remark that the value of the inflow is similar to the eigenvector centrality. The eigenvector centrality is based on the random walk on the nodes of a graph whose transition probability is connectivity between two nodes. Its value on a node represents the ratio of the number of times the random walk has passed the node. The concept of the eigenvector centrality and its value are similar to inflow but the main difference and advantage of inflow are that inflow is associated with global invariant which is volume entropy. Another difference is that the inflow does not allow backtracking of the information flow, whereas the eigenvector centrality does. Thus, the inflow is computed based on a better model of the information flow on the brain and is the local invariant that takes into account the global characteristics of the graph.

### 0.5 Statistical Inference

To make a statistical inference, we performed a permutation test: first, for each node, let  $w_v^1$  and  $w_v^2$  be the sets of inflows of the two groups and let  $\delta$  denote the difference between the averages of  $w_v^1$  and  $w_v^2$ . Then two groups were combined in a set and this set was randomly split into two subsets  $\overline{w_v^1}, \overline{w_v^2}$  with cardinality the same as those of  $w_v^1$  and  $w_v^2$ , respectively.

The difference between the averages of  $\overline{w_v^1}, \overline{w_v^2}$  is denoted by  $\delta$  and is compared to  $\delta$ . This described process is repeated 100,000 times. The value equals the proportion of cases in which the difference between the averages of and is greater than  $\delta$ . If there were a significant difference between the two groups, then the  $p$  value is small. We set the significant level as 0.05 and make statistical inference, then the  $p$ -value is small. We set the significant level as 0.05 and make statistical inference.

## RESULTS

In summary, as compared with the HL-NT group, the HL-T group showed significantly increased inflow to the retrosplenial cortex/hippocampus and parahippocampus for the alpha 2 and beta 3 bands, sgACC for the theta band, PCC for the alpha 2 band, and to the insula for the beta 3 bands. Since the retrosplenial cortex/hippocampus and parahippocampus are known as the generators of tinnitus, sgACC/PCC as the core components of the perception network, and the insula as the core of the salience network, we surmise that previously alleged tinnitus generators, perception network, and salience networks, that were revealed by whole-brain activity comparisons or functional connectivity analyses, are also areas that receive significantly increased information from other distant cortical areas of brain, and thus pathologic networks are formed to generate and perceive tinnitus.

## CONCLUSIONS

Taken together, we conclude that subjects with hearing loss develop tinnitus when the tinnitus generator, perception and salience networks are receiving significantly increased inflow from other brain nodes. These areas may serve as future therapeutic targets to ameliorate or abate tinnitus in subjects with hearing loss.

## REFERENCES

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