Contribution ID: **75** Type: **not specified**

Linking hubs, embryonic neurogenesis, transcriptomics and diseases in human brain networks

Monday, 19 December 2022 10:35 (25 minutes)

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I. Diez1, F. Garcia-Moreno2,3, N. Carral-Sainz4, S. Stramaglia5, A. Nieto-Reyes4, M. D'Amato3,6, J. Maria Cortes3,7, P. Bonifazi3,7
1Gordon Center for Medical Imaging, Department of Radiology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA.
2Achucarro Basque Center for Neuroscience, Scientific Park of the University of the Basque Country (UPV/EHU), Leioa, Spain.
3IKERBASQUE: The Basque Foundation for Science, Bilbao, Spain.
4Departamento de Matemáticas, Estadística y Computación, Facultad de Ciencias, Universidad de Cantabria, Santander, Spain.
5Dipartimento Interateneo di Fisica, Università degli Studi di Bari Aldo Moro, and INFN, Sezione di Bari, Italy.
6Department of Medicine and Surgery, LUM University, Casamassima, Italy.
7Computational Neuroimaging Lab, Biocruces-Bizkaia Health Research Institute, Barakaldo, Spain.

corresponding author Paol.bonifazi@gmail.com - paolo.bonifazi@osakidetza.eus

The most characteristic anatomical property of brain networks is their organization across multiple spatial scales. A key challenge is to decipher the rules of connectivity that shape brain networks in order to understand how the brain works and how traumatic or neurological damage may affect brain functionality[1]. The general structure and function of the human brain, and its internal connectivity are all the result of its developmental history, which is at the same time the product of evolution[2].
Small-world, scale-free or heavy-tailed distribution network organizations have been identified at the structural-functional level in microcircuits, and in meso- and macro-scale networks[3].
Inspired by the Barabasi-Albert model [4] which showed that the principle "the rich gets richer"(a.k.a. "preferential attachment") led to scale-free networks and hubs in real-world networks, in this work we test the hypothesis that the topology of brain networks could be shaped according to the rule that "the older gets richer", i.e. the evolutionary older circuits or those generated earlier in embryogenesis are most central in the organization of the adult brain network[5].
As a consequence, we expect that quantification of the hubness of brain nodes (i.e. circuits) based on metrics of centrality from complex networks should be correlated with circuits'embryogenic age.
We identified eighteen macro-circuits (MACs) according to their first (i.e. earliest) neurogenic time (FirsT) during embryogenesis. Since MACs'volumes span across multiple scales, we studied the brain networks with two different spatial resolutions: a low resolution parcellation corresponding to the eighteen MACs, and a high resolution parcellation composed of approximately two and half thousand regions of interest (ROI) of similar volumes.
Structural and functional brain networks were obtained using 7 Tesla MRI images acquired within the Human Connectome Project[6]. At high resolution level, we observed that FirsT reversely shaped the nodes' centrality in the structural and functional networks, where highly central nodes displayed respectively early and late FirsT. Distinctly, the structural and functional nodes'centrality of the low-resolution MACs similarly correlated with FirsT, with higher centrality displayed in the early born MACs. In addition, we observed that FirsT-lags reversely correlated with wiring probability and connection weight, so ROIs and MACs connected more and stronger with those at similar age. Finally, brain transcriptomic analysis revealed also high association between genes'expression, FirsT and nodes'centrality, in respect to physiological nervous system development and synapse regulation, and to neuropathological conditions. Notably, a significant rate of genes involved in major neurological diseases such as epilepsy, Parkinson's, Alzheimers'and autism spectrum disorder displays extreme correlation values with nodes'centrality (we especially mention high correlation for highly studied genes such as SCN1A, SNCA and APOE). The results [7] provide a new multi-scale evidence on how neurogenesis time shapes structural and functional networks, brain nodes'centrality and their transcriptomics in patho-physiological conditions and underlie two main neurogenesis preferential wiring principles: "the older gets richer"and "preferential age attachment".

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Primary author: Prof. BONIFAZI, Paolo (3IKERBASQUE: The Basque Foundation for Science, Bilbao, Spain)

Presenter: Prof. BONIFAZI, Paolo (3IKERBASQUE: The Basque Foundation for Science, Bilbao, Spain)

Session Classification: Session 1