Characterising the structural organization of the whole-brain: encompassing the cortex, subcortex, and cerebellum

Julian Schulte[1], Xenia Kobeleva[2] , Mario Senden[3] and Gorka Zamora-López[1]

[1] Computational Neuroscience Group, Center for Brain and Cognition, Universitat Pompeu Fabra, Barcelona, Spain.

[2]German Center for Neurodegenerative Diseases (DZNE), Bonn, Germany.

[3]Department of Cognitive Neuroscience, Faculty of Psychology and Neuroscience, Maastricht University, Maastricht, Netherlands

The white matter is made of anatomical fibers that constitute the highway of long-range connections between different parts of the brain. This network is referred to as the brain's structural connectivity and lays the foundation of network interaction between brain areas as it has been shown to constrain functional connectivity and to also relate to various psychiatric and neurological disorders. When analyzing the architectural principles of this global network most studies have mainly focused on cortico-cortical and partly on cortico-subcortical connections. Here we show, for the first time, how the integrated cortical, subcortical, and cerebellar brain areas synergistically shape the structural architecture of the whole brain. Considered individually, the cortical, subcortical, and cerebellar sub-networks show distinct network features despite some similarities, which underline their individual structural fingerprints. Whereas the three sub-networks are characterized by a nearly optimal short-average pathlength and capacity to transmit information, they differ regarding their degree distribution, clustering, and assortativity. Taken together, the global structural network displays a modular and hierarchical organization – similar to the one typically described for the cortex alone. However, (i) community detection reveals a modular organization that transcends the classical – cortical, subcortical, cerebellar – subdivision pointing to functional communities that encompass regions of the three parts. Also, we find that (ii) the most prominent hubs of the global rich-club correspond to subcortical regions whose lesioning leads to a major disruption in network efficiency and signal propagation, more so than lesions to cortical hubs. Our results, exposing the heterogeneity of internal organization across cortex, subcortex and cerebellum, and the crucial role of the subcortex for the integration of the global anatomical pathways, highlight the need to overcome the prevalent cortex-centric focus towards a global consideration of the structural connectivity.

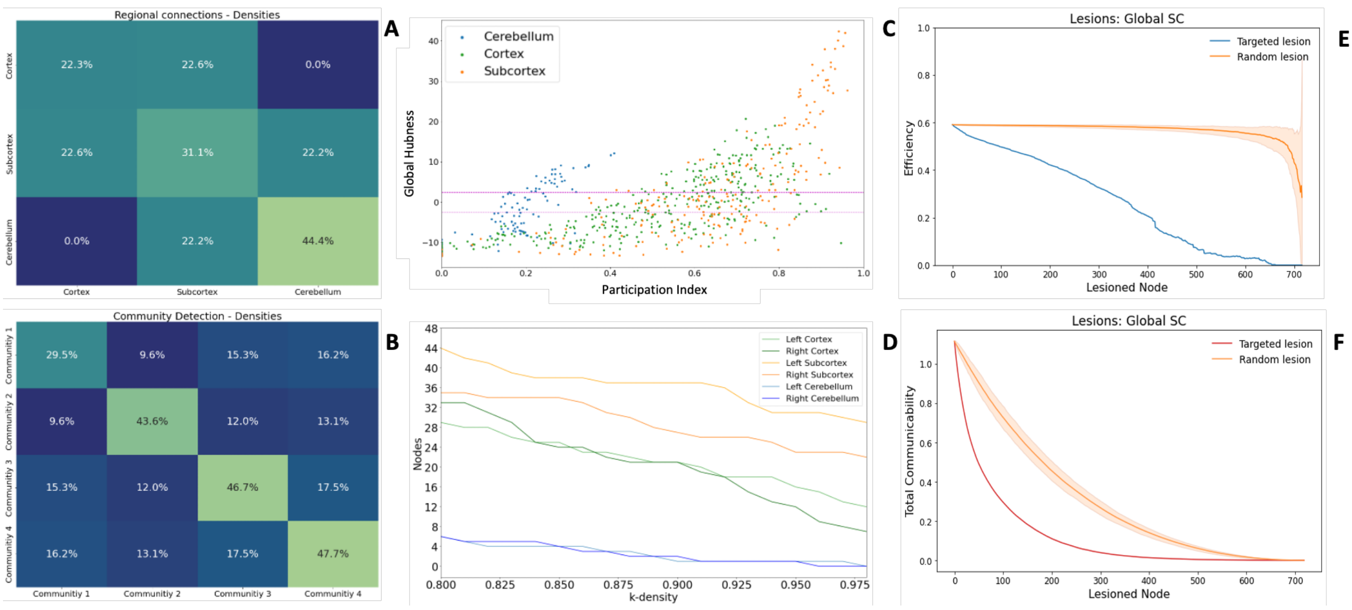

Figure 1. The cortex, subcortex, and cerebellum show a hierarchy of connection densities, however, high between-areal densities can be observed (**A**). This lead us to perform a community detection, where four highly segregated communities were found (**B**). These communities stretch over cortical, subcortical and cerebellar brain regions. Hubs can be found in the cerebellum, cortex, and especially in the subcortex, with the later two acting as integrators between the communities (**C**). Overall, these communities are centralized by a global rich-club, which is dominated by subcortical nodes independent of its internal density (**D**). Targeted lesions starting with subcortical hubs are detrimental for global efficiency (**E**) and signal propagation (measured with flow propagation; **F**) along the global network.