Novel subgroups of attention-deficit/hyperactivity disorder identified by topological data analysis and their functional network modular organizations.

Kyeong S, Kim JJ, Kim E.


Abstract

Attention-deficit/hyperactivity disorder (ADHD) is a clinically heterogeneous condition and identification of clinically meaningful subgroups would open up a new window for personalized medicine. Thus, we aimed to identify new clinical phenotypes in children and adolescents with ADHD and to investigate whether neuroimaging findings validate the identified phenotypes. Neuroimaging and clinical data from 67 children with ADHD and 62 typically developing controls (TDCs) from the ADHD-200 database were selected. Clinical measures of ADHD symptoms and intelligence quotient (IQ) were used as input features into a topological data analysis (TDA) to identify ADHD subgroups within our sample. As external validators, graph theoretical measures obtained from the functional connectome were compared to address the biological meaningfulness of the identified subtypes. The TDA identified two unique subgroups of ADHD, labelled as mild symptom ADHD (mADHD) and severe symptom ADHD (sADHD). The output topology shape was repeatedly observed in the independent validation dataset. The graph theoretical analysis showed a decrease in the degree centrality and PageRank in the bilateral posterior cingulate cortex in the sADHD group compared with the TDC group. The mADHD group showed similar patterns of intra- and inter-module connectivity to the sADHD group. Relative to the TDC group, the inter-module connectivity between the default mode network and executive control network were significantly increased in the sADHD group but not in the mADHD group. Taken together, our results show that the data-driven TDA is potentially useful in identifying objective and biologically relevant disease phenotypes in children and adolescents with ADHD.