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Structural brain network of gifted children has more integrated and versatile topology

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Abstract

Gifted children learn more rapidly and effectively than others, presumably due to neurophysiological differences that affect efficiency in neuronal communication. Identifying the topological features that support its capabilities is relevant to understanding how brain structure relates to intelligence. We proposed the analysis of the structural covariance network to assess which organizational patterns are characteristic of gifted children. Graph theory was used to analyse topological properties of structural covariance across a group of gifted children. The analysis was focused on measures of brain network integration, such as, participation coefficient and versatility, which quantifies the strength of specific modular affiliation of each regional node. We found that the gifted group network was more integrated (and less segregated) than the control group network. Brain regional nodes in the gifted group network had higher versatility and participation coefficient, indicating greater inter-modular communication mediated by connector hubs with links to many modules. Connector hubs of the networks of both groups were located mainly in association neocortical areas (which had thicker cortex), with fewer hubs in primary or secondary neocortical areas (which had thinner cortex), as well as a few connector hubs in limbic cortex and insula. In the group of gifted children, a larger proportion of connector hubs were located in association cortex. In conclusion, gifted children have a more integrated and versatile brain network topology. This is compatible with global workspace theory and other data linking integrative network topology to cognitive performance.

Keywords: structural covariance, gifted children, cortical thickness, connectome, module, magnetic resonance imaging.

1. INTRODUCTION

Intelligence is an attribute that is present in the most cognitively evolved species, etymologically derived from the Latin word *intelligentia,* which means the ability to learn and comprehend. Intelligence is related to the ability to solve problems, make decisions and adapt more efficiently to the environment. The neocortex of the brain is responsible for the implementation of intelligent cognitive processes, particularly in the associative areas, such as prefrontal and inferior parietal cortex.

The first tests of intelligence were created in the early twentieth century (Binet & Simon, 1916) and since 1926 the intelligence quotient (IQ) has been widely used as a measure of intelligence (Binet & Simon, 1948). Wechsler created the most famous and widely used intelligence test and proposed a general definition of intelligence as an “individual's ability to adapt and constructively solve problems in the environment” (Wechsler, 1939). Intelligence, therefore, is a very broad concept that involves the individual's ability to execute an action successfully. The concept includes cognitive intelligence and emotional intelligence. For cognitive intelligence we mean the reasoning, memorizing, or use of language to solve problems, while emotional intelligence is the set of skills that enable better adaptation to our social environment. Intelligence has also been sub-divided, based on its biological or cultural components, into fluid intelligence or crystallized intelligence (Davies et al., 2011). The development of intelligence is not static, since it depends on the processes of synaptic plasticity and axonal myelination of the brain, and these can be activated during life, provided that the brain has an appropriate stimulation (Chevalier et al., 2015; Fields, 2008; Goh et al., 2011). A recent review on human neuroimaging findings of structural plasticity can be found in Zatorre, Fields, & Johansen-Berg, 2012.

The term giftedness describes the combination of higher IQ and enhanced executive functioning with exceptional creativity and higher motivation (Navas-Sánchez et al., 2016). Gifted children have two important characteristics (i) their unique cognitive functioning that uses different strategies for problem solving and (ii) their differential mental maturity that reveals a way of thinking more characteristic of older children (Geake, 2008). Gifted children learn faster and in a more effective way, presumably because of neurophysiological differences (Gross, 2006). They have greater interconnectivity between different areas of their brains, specifically between hemispheres across the corpus callosum, and between prefrontal and parietal associative areas (Navas-Sánchez et al., 2014). It has been found that the brains of math-gifted adolescents mature faster than age and gender matched subjects (Navas-Sánchez et al., 2016; Zhang, Gan, & Wang, 2017).

The study of structural covariance networks (SCNs) allows us to examine the anatomical connectivity of cortical regions, defined as the correlation of cortical thickness or volume between pairs of brain regions measured in a sample of magnetic resonance imaging (MRI) data (Alexander-Bloch, Giedd, & Bullmore, 2013; Evans, 2013). Structural covariance between regions can be used to construct graphs or connectomes representing the strongest correlations as edges drawn between regional nodes. Several studies have been carried out analysing structural covariance networks in healthy subjects (Khundrakpam et al., 2013; Zielinski, Gennatas, Zhou, & Seeley, 2010), and in groups of patients with disorders including autism, attention deficit hyperactivity disorder, schizophrenia or Alzheimer's disease (Bassett et al., 2008; Bethlehem et al., 2017; He et al., 2009; Sharda et al., 2016). These results are compatible with previous reports of a positive association between the global efficiency of functional brain networks and intellectual performance (van den Heuvel et al., 2009). Moreover, recently a study of the relationship between non-verbal intellectual ability and structural network organization showed a strong positive association between the network's global efficiency and intelligence: non-verbal higher intellectual ability children have brain networks that are more highly integrated at both global and local levels (Kim et al., 2016). And in a study of 14-25-year-old healthy young people, individual differences in the degree of association cortical hub nodes explained about 40% of the variance in verbal and non-verbal IQ (Seidlitz et al., 2018).

In the present study, we propose a new approach for understanding structural brain organisation of giftedness based on the graph theoretical analysis of structural covariance networks from gifted and control groups. We were hypothetically motivated by prior theory and experimental data indicating that giftedness should be associated with more integrative brain network topology (Kim et al., 2016). The analysis therefore focused on global measures of brain network integration, such as efficiency or path length, and nodal measures of connectivity between modules (participation coefficient) and affiliation to more than one module (versatility).

2. MATERIALS AND METHODS

2.1 Participants

The sample consisted of 29 healthy right-handed male subjects with no history of psychiatric or neurological disorder: a control group (CG, n=14, age=12.53±0.77, IQ=122.71±3.89) and a gifted group (GG, n=15, age=12.03±0.54, IQ=148.80±2.93). The groups were not significantly different in terms of age. Criteria for gifted children included having an IQ in the very superior range, and also having a performance above the 90th percentile in three of the following aptitudes: spatial, numerical, abstract reasoning, verbal reasoning and memory (Santamaría et al., 2005). After providing a complete description of the study to all participants, written and verbal informed consent was obtained from a parent and affirmed assent was obtained from the children. The research ethics committee Institutional Review Board (IRB00003099) of the University of Barcelona (Catalonia) approved the study.

The raw (anonymized) MRI data and the cortical thickness data are available in the *OpenNeuro* repository (https://openneuro.org/datasets/ds001988).

2.2 Magnetic resonance imaging

All participants were examined on a 3T MRI scanner (Magnetom Trio Tim, Siemens Medical Systems, Germany) at the Centre de Diagnòstic per la Imatge in the Hospital Clínic of Barcelona. High-resolution T1-weighted images were acquired with the MPRAGE 3D protocol (TR=2300 ms; TE=3 ms; TI=900 ms; FOV=244x244 mm2; 1 mm isotropic voxel). These images were pre-processed using FreeSurfer software v5.3 to estimate regional cortical thickness (CT) from a three-dimensional cortical surface model using intensity and continuity information (Fischl and Dale, 2000). Two experienced independent researchers checked cortical reconstructions to ensure that all images passed quality control criteria. Each individual brain was parcellated in 308 regions of approximately equal size (500 mm^2 each). This parcellation atlas was constructed in the standard FreeSurfer template (fsaverage) by a backtracking algorithm that subdivides the regions defined in the Desikan-Killiany atlas (Desikan et al., 2006), so that the final parcels were constrained by the original anatomical boundaries (Romero-Garcia et al., 2012). We warped the parcellation from the standard template to each individual's MPRAGE native space using surface-based (non-linear) registration (mri_surf2surf, implemented in FreeSurfer). According to Ghosh et al., 2010, this approach provides better alignment of cortical landmarks than volume-based registration. Moreover, registering children's brains to a common space does not result in an age-associated bias between older and younger children, making it feasible to accurately compare structural properties and patterns of brain activation in children (Ghosh et al., 2010). Cortical thickness (CT) was estimated for each of the 308 cortical regions in each subject.

Each region defined by the parcellation was assigned to a cytoarchitectonic class of cortex defined a priori by the von Economo classification (von Economo, 1929). Structural types were manually assigned to cortical regions based on visual comparison. The von Economo atlas subdivided the cortex into five types according to the laminar structure of the cortex and roughly corresponding to functional cortical specializations. Briefly, regions with poor laminar differentiation, particularly the primary motor cortex/precentral gyrus are structural type 1, regions generally considered to be association cortices are structural types 2 and 3, while secondary and primary sensory areas are types 4 and 5, respectively. The original classification of structural types does not discriminate between true six-layered isocortex and mesocortex or allocortex, which have markedly different cytoarchitectures and ontogenies. We therefore defined two additional subtypes: limbic cortex which included the entorhinal, retrosplenial, presubicular and cingulate cortices, and thus primarily constitutes allocortex (type 6); and the insular cortex which contains granular, agranular and dysgranular regions, and is therefore not readily assigned a single structural type (type 7) (Seidlitz et al., 2018; Váša et al., 2018; Vértes et al., 2016).

2.3 Graph construction and modular decomposition

Using the cortical thickness estimates for the 308 cortical regions in each subject, we estimated the correlation between thickness of pairs of cortical regions in each group of participants (Figure 1A, regions arranged according to the modular community structure of each group's network). The structural covariance matrix is the {308×308} matrix of Pearson's correlations between each possible pair of regions *i* and *j* in a sample of N=14 (control group) or N=15 (gifted group).

The minimum spanning tree (van Wijk et al., 2010) was used as the starting point for graph construction to ensure that all graphs were node-connected, even at the sparsest connection density. Additional edges were then included in order of decreasing inter-regional correlation until the graph had arbitrary connection density, defined as the number of edges divided by the maximum number of edges possible in a graph of N nodes, i.e., $(N^2-N)/2$. We mainly focused on graphs constructed at 10% connection density, but several metrics and results were also tested over a range of connection densities.

Each graph was decomposed into a modular community structure using the Louvain algorithm with arbitrary resolution parameter, γ. This algorithm finds the modules or sub-graphs of the network with maximum modularity. When the resolution parameter, γ, is small, the community structure is represented by a few large modules; as γ is increased the community structure becomes more fine-grained, comprising a larger number of smaller modules. The Louvain algorithm does not find exactly the same community structure on repeated analysis of the same data at the same level of resolution, i.e., there is a stochastic element to the process of modular decomposition. To define a stable modular partition, we used a consensus approach: we ran the community algorithm 1000 times and defined a consensus matrix {308×308} where the $\{i,j\}th$ element represents the number of times that nodes i and j have been assigned to the same module across multiple iterations of the stochastic algorithm for modular decomposition. Finally, the community structure of the consensus matrix was analysed, resulting in a modular decomposition based on consensus over multiple iterations.

2.4 Graph topology metrics

We focused on two classes of graph theoretical measures of network topology: global integration/segregation and nodal "hubness"; see Fornito et al., 2016, for an introductory text on graph theory and neuroscience.

Global integration was measured by mean participation coefficient and mean versatility. Global segregation was measured by clustering coefficient, and maximum modularity. All the measures were normalized by corresponding metrics estimated in 100 null-model networks in which the degrees of all nodes were strictly preserved (Maslov and Sneppen, 2002). We used Brain Connectivity Toolbox for global topological analysis (Rubinov and Sporns, 2010).

Nodal "hubness" was measured in several ways. The simplest metric was the degree centrality, i.e., the number of edges k that link it to the rest of the network. We used the cumulative degree distribution $P(k) = \sum_{k' \geq k} p(k')$ to summarise the probability of hub nodes in both the control and gifted group networks. High degree hubs are known to be important for integrative global topology of brain networks. But degree is not the only way of measuring a node's integrative role. In a modular network, by construction, connections are dense between nodes in the same module (intra-modular) but much sparser between modules (inter-modular). Communication between modules is thus a key challenge for modular network integration that can be addressed by a specific nodal topology. Nodes with high inter-modular degree compared to their intra-modular degree, or high participation coefficient, have been defined as characteristic of so-called connector hubs that mediate much of the inter-modular communication in complex spatial networks.

Versatility (V) of nodal affiliation to communities was recently introduced as a metric to quantify how reliably a node in a modular decomposition is associated to a specific module (Shinn et al., 2017). A node with low versatility, V ~ 0, will be very consistently assigned to the same module on repeated runs of the Louvain algorithm (or any other probabilistic algorithm for modular decomposition). Whereas a node with high versatility will be assigned to one of several different modules on repeated analysis, thus inconsistently assigned to any single module. The idea is to assign a low value of versatility to the pairs of nodes that, when repeatedly running the Louvain algorithm, are consistently affiliated to the same community or to a different community in a consistent way. These nodes are called provincial nodes. On the contrary, a high value of versatility must be associated to pairs that are assigned to different communities in different runs of the Louvain algorithm (Shinn et al., 2017). Versatility, V of node j is formally defined as:

$$V(j) = \frac{\sum_i sin\left(\pi \mathbb{E}\big(a(i,j)\big)\right)}{\sum_i \mathbb{E}\big(a(i,j)\big)} \tag{1}$$

where $\mathbb{E}$ is expected value, and $a(i,j)$ is equal to 1 if i and j belong to the same community and 0 otherwise.

2.5 Statistical inference

Between-group differences in topological metrics were tested using a non-parametric permutation test where each subject was randomly assigned to one of the two groups. Metric differences between the resulting two random groups were used to create a reference distribution for each metric (1000 permutations) to reject or retain the null hypothesis of no difference between groups (*P*-value < 0.05). Due to the large number of comparisons entailed by hypothesis testing nodal statistics (like degree, versatility and participation coefficient) at each of 308 regional nodes in each network, *P*-values were corrected using the false discovery rate (FDR) with $\alpha<0.025$.

3. RESULTS

Gifted children showed a cognitive profile that differed from the control group. Gifted children scored in the very superior range in the WISC's indices and had a better performance in the aptitude's assessment (Table 1).

(Table 1 goes about here)

In relation to the brain structure, the structural covariance matrix for each group is shown in Figure 1A. Both groups had strongly positive pair-wise inter-regional correlations of cortical thickness that formed topological clusters or modules. This is emphasised by the block diagonal representation of the matrices and is consistent with a modular community structure of the networks.

Structural correlation strength decreased with increased anatomical distance between regions in both groups (Figure 1B). In other words, the strongest positive correlations of cortical thickness tended to be between regions that were anatomically located in close proximity to each other. The strength of structural correlation was generally weaker between regions that were separated by longer anatomical distances. This dependence of structural correlation on connection distance was significantly stronger in the gifted group network than in the control group network. The strength of correlation was significantly dependent on the interaction between group and anatomical distance ($P<10^{-4}$, ANCOVA, $F_{1,308}=66.05$).

There was some hemispheric asymmetry in structural covariance. In the control group, the mean correlation between regions in the left hemisphere was significantly greater than the mean inter-regional correlation in the right hemisphere ($r=0.534$ for the CG, $r=0.467$ for the GG; $P=0.023$, non-parametric permutation test, FDR corrected; Figure 1C). However, in the gifted group, this pattern was reversed: right hemisphere regions had stronger intra-hemispheric correlation in the gifted group ($r=0.457$ for the CG; $r=0.543$ for the GG; $P=0.023$, non-parametric permutation test, FDR corrected; Figure 1C).

3.1 Global network topology

Standard measures of network segregation, i.e., normalized clustering coefficient and modularity, were significantly higher for the control group compared with the gifted group when both networks were thresholded at sparse connection densities, 5% to 8% ($P<0.05$ two-tailed, non-parametric permutation test, FDR corrected; see appendix, Figure S2).

3.2 Nodal topology

Figure 1D shows the cumulative degree distribution of each group network thresholded at 10% connection density. There was a higher probability of very high degree nodes in the gifted group. Degree and connection distance were significantly positively correlated in the control group network ($r=0.21$, $P=0.0002$, t-test) (Figure 1E); but not in the gifted group ($r=0.0008$, $P=0.99$, t-test). In other words, high degree hubs in the control group network entailed more long-distance connectivity than high degree hubs in the gifted group network. The difference between groups in the strength of the relationship between distance and degree was significantly different (*P*=0.0085, ANOVA, $F_{1,612}$=6.98).

(*Figure 1 goes about here*)

3.3 Intra- and inter-modular degree

Degree was calculated for both networks as the sum of connections within the module of the index node (intra-modular degree) and the connections between the index node and nodes in other modules (inter-modular degree). The control group had higher intra-modular degree (mean=12.42) compared to the gifted group (mean=11.59), while inter-modular degree was higher for the gifted group (mean=19.11) compared with the control group (mean=18.28) (Figure 1F). The ratio of inter-modular:intra-modular degree was significantly different between groups (*P*=0.0179, Mann-Whitney *U* test, *df* = 307), with the gifted group having the higher ratio (see appendix, Figure S3).

Topological maps of the modular organization are presented in Figure S4. Brain networks have a hierarchical modular community structure which can be resolved at many levels; here we focus on the community structure defined when the resolution parameter γ=2. In both groups, the inner circle contains all the nodes with at least one connection to nodes in other modules. The outer ring contains nodes that have connections only to other nodes in the same module (same colour). We can see that the control group network has more intra-modular connections and fewer inter-modular connections than the gifted group.

3.4 Participation coefficient and versatility

The role of the nodes in the community structure was analysed using two different measures: participation coefficient and versatility, a recently proposed measure to assess the consistency of which each node is affiliated to a specific module (Shinn et al., 2017). Interestingly, both participation coefficient and versatility were significantly higher for the gifted group than for the control group (*P*=0.0061 for participation coefficient and $P<10^{-10}$ for versatility, Mann-Whitney *U* test, *df* =307; Figure 1G). Similar results were obtained at 5% and 15% connection densities (Figure S5). Moreover, mean versatility and mean participation coefficient were always higher for the gifted group compared to the control group over a range of modular resolution parameters ($1<\gamma<3$) and over a range of connection densities (5%-15%) (Figure 2). Specifically, the between-group difference of mean versatility at connection density 10% was statistically significant when integrated over a range of modular resolution parameters, $1.5<\gamma<3$ ($P=0.045$, two-tailed, non-parametric permutation test, FDR corrected). Cortical maps of the nodal versatility are depicted in Figure 3. High versatility nodes were mainly located in association cortical areas for the gifted group but not for the control group (Figure 3A).

(*Figure 2 goes about here*)

3.5 Cytoarchitectonic analysis

To further investigate the neurobiological substrate of versatility, we defined a subset of highly versatile nodes as those nodes with versatility at least one standard deviation greater than the network mean (at 10% connection density and $\gamma=2$). We tested the hypothesis that highly versatile nodes were concentrated in areas of association cortex, as defined a priori by the cytoarchitectonic atlas of von Economo.

In the gifted group network, we found that 76% of highly versatile nodes were located in association cortex (von Economo classes 2 and 3); whereas, in the control group, only 55% of highly versatile nodes were located in association cortex. This difference was statistically significant ($P=0.0147$, χ^2 test) (Figure 3B). The highly versatile nodes in the gifted group network also had significantly thicker cortex than the less versatile nodes ($P<10^{-5}$, unpaired two-sample t-test); whereas in the control group the more versatile nodes had thinner cortex ($P=0.027$, unpaired two-sample t-test). This difference was statistically significant ($P<10^{-5}$, ANOVA; $F_{1,54}=27.18$) (Figure 3C).

Similarly, when we defined a set of high degree hubs in each network as the nodes with degree at least one standard deviation greater than the network mean, we found that 75% of the hubs in the gifted group network were located in association cortex (von Economo classes 2 and 3) whereas only 55% of hubs in the control group network were located in association cortex. This difference was statistically significant ($P=0.028$, χ^2 test) (Figure S6).

(*Figure 3 goes about here*)

4. DISCUSSION

Evidence supports the hypothesis that integrative topology of structural brain network organization may be an important biological basis for intelligence (Bullmore and Sporns, 2012; Colom et al., 2010). The aim of our study was to identify the brain connectivity features characteristic of gifted children using structural covariance network analysis. We found that the structural covariance network of gifted children was more globally integrated and had more high degree hubs, with high participation coefficients and high versatility of modular affiliation, than the comparable network of the control group.

The reduced segregation of the gifted group structural covariance network indicates a more random topology of the human connectome in association with higher IQ. Similar results have recently been described by Khundrakpam et al., 2016, consistent with the idea that intelligence depends on more integrated, less segregated network topology. Likewise, Li et al., 2009, showed that higher IQ scores corresponded to a shorter characteristic path length and a higher global efficiency of DTI-based structural networks. And cognitive effort in performing a working memory task at variable levels of difficulty has been related to greater efficiency and reduced clustering of functional networks derived from MEG data (Kitzbichler et al., 2011). Similar results have been found recently, relating a higher performance on working memory and cognitive control to a higher level of global brain integration (Shine et al., 2016).

We found that the ratio of inter-modular degree to intra-modular degree was higher for the gifted group compared to the control group. The gifted group network nodes also had significantly higher participation coefficient, indicating a greater number of inter-modular edges, and higher versatility, indicating a less consistent affiliation to any single module. The association of high IQ with these integrative features of nodal topology, which will facilitate information transfer between anatomically distributed and otherwise segregated modules, is consistent with the global workspace theory (Dehaene and Changeux, 2011) which predicts that consciously effortful processes will depend on network architectures that "break modularity". Likewise, results from Wang et al., 2011 indicate that intelligence involves multiple brain regions throughout the brain, which requires efficient integration capabilities. And Naghavi and Nyberg, 2005, showed that even less demanding cognitive tasks can reflect a high level of multimodal integration across distributed representations that may be mediated by sensory and association areas associated with working memory, episodic retrieval and conscious perception. Our results are also aligned with the parieto-frontal theory (P-FIT) of intelligence (Jung and Haier, 2007). The majority of structural neuroimaging studies show a relationship between intelligence and/or reasoning and specific Brodmann areas, which are (mostly) in associative areas of the von Economo atlas. The fact that the high versatility nodes and the hubs in the gifted group are located in these associative areas can be interpreted as a structural requirement for having a gifted brain. As detailed in Jung and Haier, 2007, many of the areas implicated by the P-FIT have been related to fundamental cognitive processes including working memory and attention (Cabeza and Nyberg, 2000; Chabris, 2007; Naghavi and Nyberg, 2005).

Our results could contribute to better understand the modular organization of the brain. As it has been described, modular organization allows to execute discrete cognitive functions in each module, being each module relatively autonomously from the other modules (Meunier, Lambiotte, & Bullmore, 2010). Results of functional analysis of brain modularity have showed the existence of connector nodes integrating across or coordinating connectivity between task-relevant modules to maintain modular function of the brain. Connector nodes have been found in brain areas where activity is associated with many different cognitive components, and its role is related to the cognitive performance (Bertolero, Yeo, & D'Esposito, 2015). In agreement with that, our results showing that brain regional nodes in the gifted group network had higher versatility and participation coefficient indicate greater inter-modular communication mediated by connector hubs with links to many modules.

In short, the results we have reported –indicating that gifted children have brain networks associated with less segregation, less modularization, and more global integration– are thus compatible with the general hypothesis that integrative network topology is important for higher cognitive performance.

This is the first study using versatility to compare nodal properties between groups. Versatility can be useful in identifying nodes that do not fit very well with any specific module. In our context, these nodes can be relevant because they could be playing different roles depending on the brain's processing demands, which could perhaps explain the greater problem-solving adaptivity of the more topologically versatile and cognitively gifted group. Our results suggest that high versatility nodes in the gifted group network are predominantly located in association areas because they play important roles, probably collaborating with several different communities at different times depending on the cognitive demands, and hence helping the network to be more reconfigurable.

Versatility was highly correlated with participation coefficient (Figure 7S). However, the two metrics are measuring different aspects of nodal topology because participation coefficient assumes that there exists a fixed community structure, while versatility measures how reliably each node is affiliated to a specific module of the community structure. Our results using participation coefficient were similar to those with versatility, with higher mean participation of nodes in the gifted group network. This result is also in agreement with prior reports (Wu et al., 2011) that nodes with overlapping affiliation to more than one module usually showed higher nodal efficiency, degree and participation coefficient, suggesting that high versatility nodes play a key role in the flow of information through the structural brain network.

Previous studies have reported that cortical thickness is thicker in associative areas compared with primary areas (Vuoksimaa et al., 2016; Whitaker et al., 2016). We also found that cortex is thicker for the highly versatile nodes concentrated in the associative areas (von Economo regions 2 and 3) of the gifted group network. Accordingly, it has previously been reported (Karama et al., 2011; Menary et al., 2013) that CT was positively associated with general intelligence in a wide range of associative areas. Interestingly, CT of low versatility nodes was notably thinner in the gifted group compared with control group, resulting in a lower global mean cortical thickness in the gifted group. Recent findings have revealed that math-gifted adolescents have a thinner cortex and a bigger surface area in key regions of the fronto-parietal and default mode networks, pointing to an above-age neural maturation of these networks in math-gifted individuals (Navas-Sánchez et al., 2016; Schnack et al., 2014; Yang et al., 2013).

Our study has some limitations. In this sense, we prioritized the homogeneity of the sample (including only right-handed males) at the expense of reduced sample size (N=29). This sample size limits the power and generalizability of our results. The limited number of MRI scans is particularly problematic for a network approach based on structural covariance of cortical thickness across subjects. Moreover, the nature of morphometric covariance is not fully understood. It is generally regarded as a proxy for anatomical connectivity between cortical areas. Thus we have interpreted topological differences in structural covariance networks as indicative of between-group differences in the pattern of anatomical connectivity to association cortical areas, which are more often “wired” as connector hubs in gifted children. This interpretation underpins our use of graph theoretical parameters, like participation coefficient, as descriptors of large-scale brain network connectivity in these data. Interpreting structural MRI covariance as a marker of anatomical connectivity is supported by prior data (Alexander-Bloch et al., 2013). For example, structural covariation between brain regions was associated with high levels of co-expression of genes that are specific to supragranular layers of human cortex and known to be important for large-scale, long-distance, cortico-cortical connectivity (Romero-Garcia et al., 2018). Structural covariance networks have also been corroborated by comparison to other MRI-based techniques, such as diffusion-weighted tractography or morphometric similarity (Seidlitz et al., 2018). However, not all recent studies are consistent with the interpretation of structural covariance as a marker of anatomical connectivity (Gong et al., 2009; Irimia & Van Horn, 2013). Further work is needed to secure the biological interpretation of structural covariance and other candidate MRI markers of human brain anatomical connectivity. Between-group differences in between-subject variability of cortical thickness could bias within-group estimates of covariation of cortical thickness, which would have implications for all subsequent graph theoretical parameters. However, we did not find evidence of significant differences in standard deviation of cortical thickness between the groups (see Supplemental Information, Figure S1). Additionally, we used the correlation coefficient as an estimator of structural covariation, which scales the between-subject covariance by the between-subject variance. A fundamental limitation of tractography-based approaches to structural network modelling is the underestimation of long-distance white matter tracts between spatially distributed cortical areas. Long-distance connections are typically important for topologically integrative aspects of brain network organization (Bullmore & Sporns, 2012; Mukherjee, Chung, Berman, Hess, & Henry, 2008). And we hypothesised a priori that the higher cognitive capacity of gifted children might be related to more integrative brain network topology (Seidlitz et al., 2018). Therefore, we preferred to use structural covariance analysis as an alternative to DTI-based tractography on the grounds that it might be more sensitive to measurement of long-distance, topologically integrative connections that were of hypothetical interest. Both gifted and control groups had a mean IQ significantly above the normal range. Thus, the relationship between intelligence and structural brain organization across the full range of IQ is not encompassed by our results and the future study of brain network versatility and centrality in relation to a broader IQ range will be important. Finally, our sample had an average age of 12.3 years and it is possible that the relationship between IQ and structural network topology may be conditioned by age, meaning that our results should not be automatically generalised to a wider age range.

In summary, the present study shows that gifted children have a less segregated and less modular structural brain network with more high versatility nodes mainly located in associative areas. We propose that this difference in the connectome is related to the more adaptive cognitive performance of gifted children.

COMPLIANCE WITH ETHICAL STANDARDS

Conflict of Interest: The authors declare that they have no conflict of interest.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

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TABLE 1 Cognitive profile of the sample. Statistical analyses of the cognitive profile were performed with the Statistical Package for the Social Sciences (SPSS v250, SPSS Inc, Chicago, USA). Non-parametric methods (Mann–Whitney U-test) were used to compare gifted and control groups

	Gifted group (mean±SD)	Control group (mean±SD)	Z	p	Effect size (*d*)
Full-scale IQ	148.80±2.93	122.71±4.41	-4.605	<0.001	6.97
Verbal comprehension index	146.33±4.50	122.86±10.24	-4.358	<0.001	2.97
Working memory index	137.60±9.70	115.07±8.88	-4.072	<0.001	2.42
Perceptual organization index	142.40±6.56	121.29±8.74	-4.072	<0.001	2.73
Processing speed index	120.60±12.57	106.57±15.45	-2.298	0.020	0.99
Aptitudes					
Spatial	130.00±5.43	109.79±9.99	-4.070	<0.001	2.51
Numerical	134.07±3.615	109.36±13.34	-4.258	<0.001	2.52
Abstract reasoning	124.33±10.69	112.14±6.72	-2.924	0.003	1.36
Verbal reasoning	133.53±5.68	114.86±10.90	-4.047	<0.001	2.15
Memory	122.80±7.07	99.07±11.98	-4.341	<0.001	2.41

SD: standard deviation; (*d*): Cohen's d

FIGURES

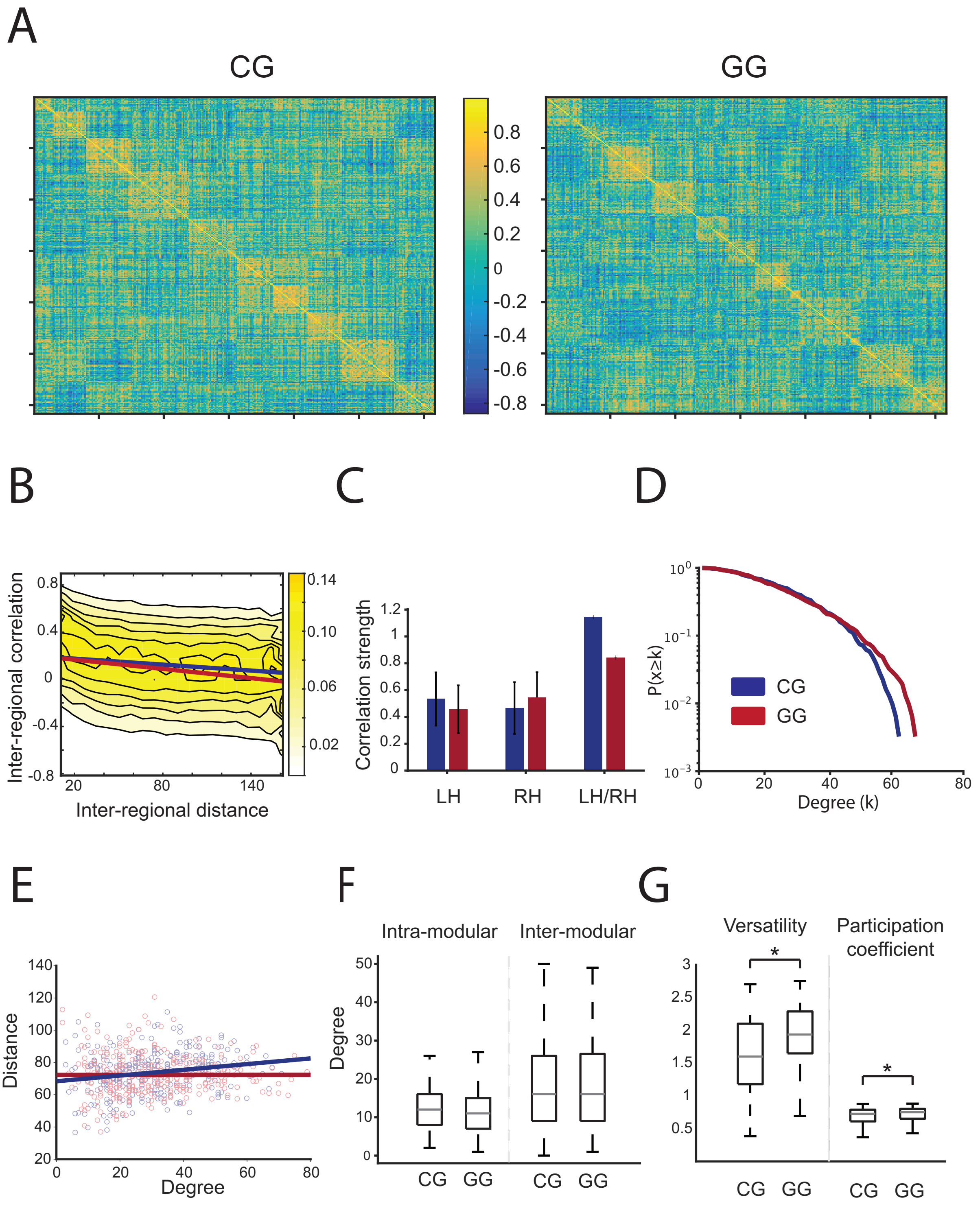

FIGURE 1 (A) Cortical thickness correlation matrix with rows and columns ordered according to modular affiliation, left panel for control group (CG) and right panel for gifted group (GG). (B) Inter-regional correlation strength as a function of Euclidean distance. (C) Barchart of intra-hemispheric correlation in left hemisphere (LH), right hemisphere (RH), and the ratio between them (LH/RH) in gifted (red bars) and control groups (blue bars). (D) Cumulative degree distributions. (E) Scatterplot of nodal degree versus connection distance (mm) for

gifted (red line) and control children (blue line) (F) Boxplots of intra-modular and inter-modular degree for CG and GG. .(G) Boxplots of versatility and participation coefficient for CG and GG; * denotes P<0.05.

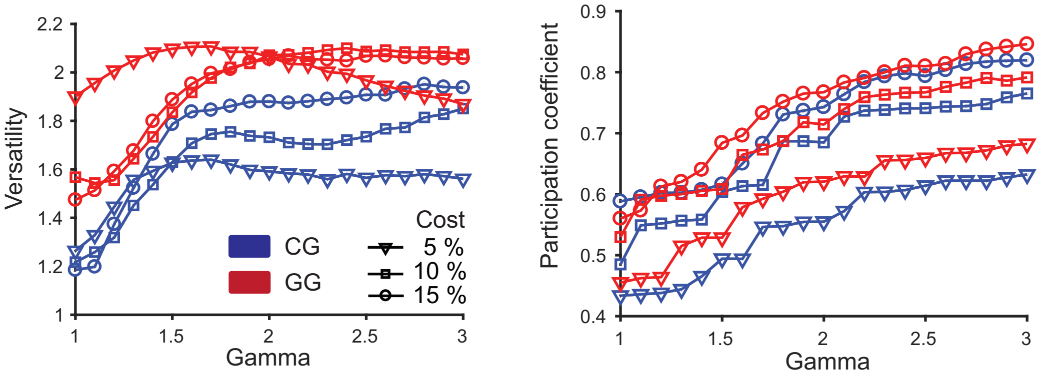

FIGURE 2 Evolution of global mean versatility (left) and global mean participation coefficient (right) for 1≤γ≤3 and connection densities 5%, 10% and 15% for the gifted group (GG) and the control group (CG).

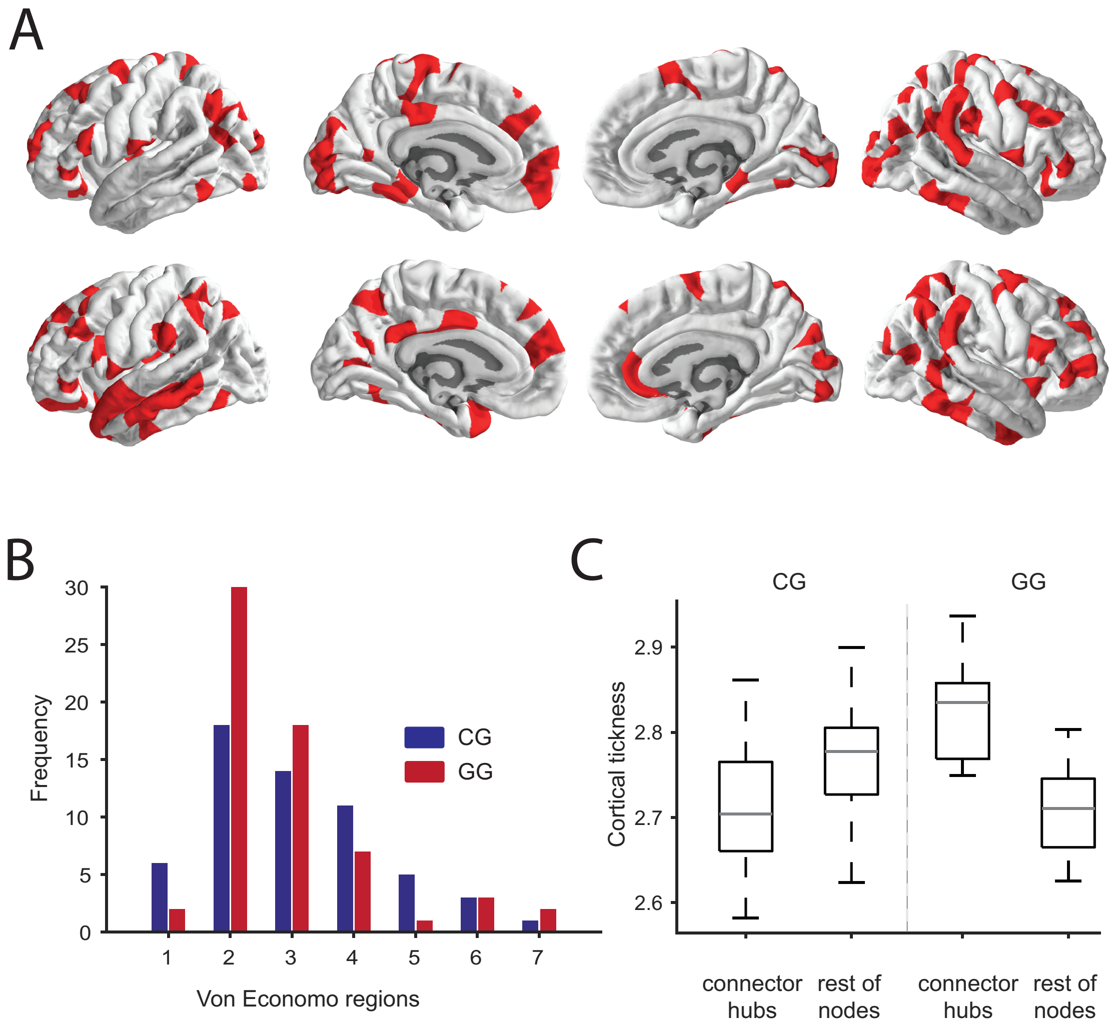

FIGURE 3 (A) Cortical map of the high versatility nodes (V > mean(V) + 1 SD(V)) at $\gamma=2$, for the control group (CG; upper row) and gifted group (GG; lower row). (B) Barchart of the number of high versatility nodes in each von Economo region in gifted and control groups. (C) Boxplots of the mean cortical thickness for the high versatility nodes (denoted connector hubs) and the rest of the nodes at $\gamma=2$.