



Anatomical connectivity changes in the bilingual brain

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ABSTRACT

How the brain deals with more than one language and whether we need different or extra brain language sub-networks to support more than one language remain unanswered questions. Here, we investigate structural brain network differences between early bilinguals and monolinguals. Using diffusion-weighted MRI (DW-MRI) tractography techniques and a network-based statistic (NBS) procedure, we found two structural sub-networks more connected by white matter (WM) tracts in bilinguals than in monolinguals; confirming WM brain plasticity in bilinguals. One of these sub-networks comprises left frontal and parietal/temporal regions, while the other comprises left occipital and parietal/temporal regions and also the right superior frontal gyrus. Most of these regions have been related to language processing and monitoring; suggesting that bilinguals develop specialized language sub-networks to deal with the two languages. Additionally, a complex network analysis showed that these sub-networks are more graph-efficient in bilinguals than monolinguals and this increase seems to be at the expense of a whole-network graph-efficiency decrease.

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Introduction

Bilingualism is an extended phenomenon in the world and an interesting condition for investigating brain plasticity. Modern educational models often now include bilingual teaching from earliest childhood as societies become aware of the advantages of multilingualism for social communication and job opportunities. However, little is yet known about the brain implications of learning more than one language and so a key topic in recent brain research is the nature of the biological bases of bilingualism. It seems plausible that dealing with two languages instead of one should result in anatomical brain changes, especially when the languages concerned are typologically distant. Some previous studies have shown functional brain changes associated with bilingualism: i.e. the left inferior frontal gyrus (pars opercularis and triangularis), insula, anterior cingulate, dorsolateral prefrontal cortex, superior temporal cortex and the planum temporal (Kim et al., 1997; Parker Jones et al., 2012; Perani et al., 2003; Rodriguez-Fornells et al., 2002; Wartenburger et al., 2003). However, evidence for structural changes related to bilingualism is scarce and structural connectivity changes have not been documented so far. Here, we investigate whether the structural connectivity of the bilingual brain differs from that of

the monolingual brain by using DTI (diffusion tensor imaging) and complex network analysis.

Several studies have shown specific brain changes related to experience and expertise in different cognitive skills (Carreiras et al., 2009; Draganski et al., 2004; Gaser and Schlaug, 2003; Lee et al., 2007; Maguire et al., 2012; Mechelli et al., 2004). Particularly in bilingualism, increased gray matter (GM) density has been reported in the left inferior parietal cortex in bilinguals as compared to monolinguals and this effect was stronger in early than in late bilinguals (Mechelli et al., 2004). In addition, Abutalebi et al. (2012) found a higher positive correlation for bilinguals as compared to monolinguals between GM volume in the anterior cingulate cortex (ACC) and the conflict effect that they found using an fMRI/behavioral paradigm in the same region. Stein et al. (2012), studied GM density changes in a group of second language (L2) learners after 5 months of L2 learning. They showed a correlation between the increase of L2 proficiency and increase of volume in the left inferior frontal gyrus and anterior temporal lobe. However, if bilingualism produces structural changes in GM, it is quite likely that these changes are also reflected in WM, due to changes in axonal characteristics such as myelination, density or caliber, axonal fiber wiring and synaptic connectivity during plasticity allowing faster and more efficient transmission of the information (Fields, 2008; Hursh, 1939; Tang et al., 2012; Thiebaut de Schotten et al., 2011; Waxman and Bennett, 1972). There are three prior studies showing higher WM density in the left parietal regions (Golestani et al., 2002) and in the left Heschl's gyrus (Golestani and Pallier, 2007) for faster learners as compared to slower

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learners of nonnative speech sounds, as well as in the left insula/prefrontal cortex and the bilateral inferior parietal cortex for people who accurately produce foreign sounds, compared to poorer producers (Golestani and Pallier, 2007; Golestani et al., 2007); suggesting that WM differences across individuals could predict behavioral differences in some aspects of language learning. More recently, Luk et al. (2011) compared the WM integrity in older bilinguals who regularly used both languages from childhood with their monolinguals peers. To do so, they used fractional anisotropy (FA), an index that can reflect variations in axonal density and myelination in WM tracts. Using a TBSS (tract-based spatial statistics) approach (Smith et al., 2006), they found higher FA values for older bilinguals as compared to those for monolinguals in the corpus callosum, in the superior longitudinal fasciculi, in the right inferior fronto-occipital fasciculus and uncinate fasciculus. Moreover, Mohades et al. (2012) extracted the mean FA values from 4 major tracks that are well known to connect language regions (i.e. the left arcuate fasciculus/superior longitudinal fasciculus, the left inferior fronto-occipital fasciculus and the bundles arising from the anterior and middle part of the corpus callosum) to compare children who were simultaneous bilinguals, sequential bilinguals and monolinguals. They found higher mean FA values in the left fronto-occipital fasciculus for simultaneous bilinguals as compared to those for other groups and lower values in the bundle arising from the anterior part of the corpus callosum in bilinguals as compared to those for monolinguals. Also, Schlegel et al. (2012) showed that brief linguistic immersion experience in L2 produced an increase in FA in the genu of the corpus callosum, in left tracts that connect language regions and in the right temporal regions for L2 learners as compared to that for non-learners.

Nonetheless, modifications in the axonal connectivity of the whole brain associated with bilingualism are still unknown. In particular, the relationship between bilingualism and topological properties of the brain anatomical network has never been investigated. There are many studies modeling the human brain as a complex network (Bassett et al., 2009; Iturria-Medina et al., 2007, 2008; Li et al., 2009; Zalesky et al., 2010a). From this perspective, the brain is modeled as a graph whose nodes (structural/functional brain regions) are interconnected by edges (structural/functional connections) (Bullmore and Bassett, 2011). This brain graph has complex network topological properties that are important for its performance. Conversely, functional performance can impact these topological properties (Sporns et al., 2000). As structural changes have been associated with increased language demands (Abutalebi and Green, 2007), we investigate whether, when two languages are acquired simultaneously early in life as compared with only one: a) whether brain structural network connections between GM regions are modified and b) if the network's capacity of management and integration of information differ or not. Taking into account the convergences between previous functional and structural findings, we expect structural connectivity in bilinguals to show higher axonal connection density among regions that have previously shown increased GM density and/or different functional demands in bilinguals or between regions that are connected by bundles of fibers with higher FA values, as previously demonstrated in bilinguals. These regions may have required a different configuration to increase their processing capacity in order to fulfill the increased language demands, thus we expect changes in some topological properties of the brain structural network in bilinguals.

We investigate the brain network structural changes associated with early bilingualism by using DTI-based anatomical connectivity analysis, where the connection density between pairs of GM regions is estimated by a tractography algorithm (Gong et al., 2009; Hagmann et al., 2008; Iturria-Medina et al., 2007, 2008). More specifically, we investigate brain network connectivity differences in 13 early Basque–Spanish bilinguals as compared to those in 13 Spanish monolingual participants, using a probabilistic fiber tractography algorithm. To determine differences in connectivity patterns between both groups we employ a network-based statistic (NBS) approach (Zalesky et al., 2010a, 2010b). The NBS identifies differences between groups; isolating

sets of more highly interconnected regions (i.e. sub-networks) instead of just pairs of regions, thus providing information about whole-brain structural organization. Previous studies have used this methodology to identify impaired connectivity in subjects with different disease conditions as compared to that in healthy subjects (Bai et al., 2012; Verstraete et al., 2011; Zalesky et al., 2010b; Zang et al., 2011). To assess for the spatial configuration properties of the whole brain network and possible differential sub-networks we use a graph theoretical approach (Costa et al., 2007; Latora and Marchiori, 2001; Watts and Strogatz, 1998). This allows us to explore differences between networks in terms of quantitative parameters that can be structurally and, by inference, functionally interpreted. So, we also use here a graph theory approach in order to investigate differences in the topological parameters associated with the structural networks of bilinguals and monolinguals. In particular, we focus on graph network efficiency, a measure of the intrinsic capability of the network to guarantee high information exchange between nodes/regions. In general, we expect to detect the presence of more interconnected and graph-efficient sub-networks to accomplish the processing of two languages. Our results will provide new evidence of how the brain deals with physical constraints in adapting to a challenging functional behavior (Bullmore and Sporns, 2012), something that could have advantages and/or disadvantages for the functioning of the brain network.

Methods

Participants

13 native Spanish monolinguals (7 females, age range from 20 to 40 years, mean age, 29.07 years, 6.60 std) and 13 early Spanish–Basque bilinguals (9 females, age range from 20 to 36, mean age, 24.08 years, 4.62 std) took part in the experiment. Mean age was not statistically significantly different between groups (Z -value = -1.77 , P -value = 0.076). Eleven of the bilinguals acquired Spanish and Basque simultaneously from birth and 2 of them started to acquire the second language before or at age three. Thus, all bilingual participants had acquired both languages before preschool. They used both languages everyday and rated themselves as very highly proficient in both languages (mean rates: 9.86, 0.26 std for Spanish and 9.38, 0.71 std for Basque) on a scale from 1 (very poor level) to 10 (perfectly fluent). The ratings were based on reading, writing, listening and speaking skills. The monolinguals used only Spanish for daily life and had no/little knowledge of any other language. Only 5 monolinguals had been in contact with Basque but they had received little exposure and rated themselves as very poorly proficient in Basque (mean rate: 1.20, 1.78 std) or any other language (see Table 1 for participants' language profile). Information about language profile was obtained by means of a questionnaire before the experiment. Because handedness can influence language laterality, the study contained only right-handed participants as assessed by the Edinburgh Handedness Inventory (Oldfield,

Table 1
Language profile of monolingual and bilingual groups.

Variables	Mean (\pm SD)	
	Monolinguals (N = 13)	Bilinguals (N = 13)
AoA of Spanish	0	0.23 (\pm 0.44)
AoA of Basque		0.46 (\pm 0.96)
% daily exposure to Spanish	97.13 (\pm 3.44)	61.8 (\pm 17.41)
% daily exposure to Basque	2.40 (\pm 3.30)	29.58 (\pm 14.42)
% daily exposure to other language		3.75 (\pm 8.76)
Spanish proficiency	9.92 (\pm 0.24)	9.86 (\pm 0.26)
Basque proficiency	1.20 (\pm 1.78)	9.38 (\pm 0.71)
Other language proficiency	0.53 (\pm 1.66)	1.35 (\pm 3.16)

AoA, age of acquisition (the age at which participants started to learn these languages). SD, standard deviation. Proficiency measures are means on a scale from 1 (very poor level) to 10 (perfectly fluent) of ratings based on reading, writing, listening and speaking skills.

1971). Handedness scores averages were not statistically significantly different between groups (Z -value = -0.443 , P -value = 0.685). All participants gave written informed consent and the Ethics Committee of BCBL approved the study.

Data acquisition

All images were acquired on a 3-T Magnetom Trio Tim scanner (Siemens AG, Erlangen, Germany). DW-MRI was recorded using a single-shot spin echo-planar imaging (EPI) sequence, along 64 gradient directions at b -value = 1500 s/mm^2 and 1 unweighted ($b = 0$) image. Acquisition parameters used were: echo time (ET) = 99 ms, repetition time (RT) = 9300 ms, FOV = $1840 \times 1840 \text{ mm}^2$, matrix size 1024×1024 , 58 contiguous slices and an isotropic voxel resolution = $1.79 \times 1.79 \times 1.79 \text{ mm}^3$. The total scan time for the DW-MRI protocol was approximately 10 min. A high-resolution T1weighted scan was acquired with a 3D ultrafast gradient echo (MPRAGE) pulse sequence. Acquisition parameters used were: matrix size 256×256 ; 160 contiguous axial slices; voxel resolution $1 \times 1 \times 1 \text{ mm}^3$; TE/TR/TI = 2.97 ms/2300 ms/1100 ms, respectively; and flip angle 9° .

Image preprocessing

DW-MRI datasets were preprocessed using FMRIB's Diffusion Toolbox (FDT) as part of FSL 4.1.6 software package (available at <http://www.fmrib.ox.ac.uk/fsl/>). Eddy currents correction was applied to correct for the distortions induced by the application of the diffusion encoding gradients and for simple head motion, using affine registration to the $b = 0$ image (first volume in the dataset). After correction, individual diffusion parameters were estimated in each voxel (Fig. 1a) using as well FDT toolbox (Smith et al., 2004).

T1-weighted images of each participant were first co-registered to the participant's b_0 and then segmented in 3 tissue probability maps: GM, WM and cerebrospinal fluid (CSF) using SPM8 software package (available at <http://www.fil.ion.ucl.ac.uk/spm/>). The three tissue classes in native space and the matrix transformation to MNI space obtained from segmentation were then used to automatically parcellate the cerebral cortex of each participant into 90 GM regions taken from AAL atlas (Tzourio-Mazoyer et al., 2002), using IBASPM toolbox (available at <http://www.fil.ion.ucl.ac.uk/spm/ext/#IBASPM>) (Alemán-Gómez et al., 2006). The individual atlases in T1 native space (Fig. 1) were then resliced to DTI space using the nearest-neighbor interpolation in SPM8 to create seed points mask for tracking.

Voxel-region axonal connectivity estimation

For each participant, axonal connectivity values between each brain voxel and the surface of each of the 90 GM regions considered (voxel-region connectivity) were estimated using the probabilistic fiber tractography algorithm implemented in the FSL software (Behrens et al., 2003). For each brain voxel, an index of connectivity, representing the number of generated paths that passed through it from the seed region, was assigned (Fig. 1b). Tracking parameters used were 5000 as the number of generated paths from each seed point (defaults in the FSL software package as optimum to reach the convergence of the algorithm), 0.5 mm as the step length, 500 mm as the maximum trace length, and a curvature threshold of $\pm 80^\circ$.

Network construction

For each participant, the whole-brain undirected weighted network was created as follows: 1) A node was defined to represent each anatomic region considered (i.e. 90 gray matter regions of the AAL atlas template), 2) An undirected arc a_{ij} between nodes i and j was established if a nonzero connectivity value was found to exist between the boundary voxels of regions i and j , and 3) Arc weight $w(a_{ij})$ was

defined as the connection measurement (the output of the tractography algorithm) between regions i and j (Iturria-Medina et al., 2011), estimated by counting the “effective” number of voxels over the surface of both regions and weighting each voxel by its voxel-region connectivity value with the opposite zone, relative to the total number of considered superficial voxels (Fig. 1c).

Data analysis

Network-based Statistic (NBS) analysis

We used an NBS approach (Zalesky et al., 2010a, 2010b) to isolate the components of the 90×90 undirected connectivity matrices that differ significantly between the two groups ($N = 13$ for monolinguals, $N = 13$ for bilinguals). A component is a set of interconnected edges (i.e. sub-networks) in the connectivity matrix. The NBS analysis first performed a two-sample t -test at each edge independently to test the null hypothesis (H_0) that the values of connectivity between the two populations come from distributions with equal means. After that, a preselected T -value (T -threshold = 3.5) is used to threshold the statistical value calculated at each edge of the connectivity matrix to identify the set of supra-threshold edges. All interconnected components present in the set of supra-threshold edges are identified and their size (number of edges that the components comprise) is stored. Thus, a component is formed by interconnected supra-threshold edges at which the H_0 was rejected. To estimate the significance of each component, the NBS performed a nonparametric permutation test ($K = 5000$ permutations). A total of K random permutations are generated independently; for each permutation the group to which each subject belongs is randomly exchanged, and then the statistical test is recalculated in each permutation. After that, the same threshold is applied to create the set of supra-threshold links for each K permutation. Then, the size of the largest component in the set of supra-threshold links derived from each K permutation is stored, thus providing an empirical estimation of the null distribution of the maximal component size. Finally, the p -value of each observed connected component was corrected, calculating the proportion of the 5000 permutations for which the largest component size was greater than the observed connected component size and then normalized by K . This allowed us to control the family-wise error (FWE) associated with each connected component, based on its size.

In other words, the NBS tries to identify components (connected structures) that are formed by a set of links (connections) between regions that exceed an appropriately chosen supra-threshold link. The topological extent of these connected structures is then used to determine their significance. The first step is creating the set of supra-threshold links computed for each pair-wise association. Then any connected components present in the set of supra-threshold links are identified and the number of links that they are comprised of (their size: m) is stored. A non-parametric permutation test is used to assign a p -value controlled for the FWE to each connected component, based on its size. The p -value of each connected component of size m is estimated, looking for the proportion of permutations for which the maximal component size is greater than m , and then is normalized by K (for more details see Zalesky et al., 2010a and for applications and examples of the NBS approach see Bai et al., 2012; Verstraete et al., 2011; Zalesky et al., 2010b and Zang et al., 2011).

Graph analysis

Global efficiency. In terms of the information flow, the global efficiency (E_{glob}) of a network G reflects how efficiently information can be exchanged over G , considering a parallel system in which each node sends information concurrently along the network. It is defined as (Latora and Marchiori, 2001):

$$E_{glob} = \frac{1}{n(n-1)} \sum_{\substack{i,j \in G \\ i \neq j}} \frac{1}{d_{ij}},$$

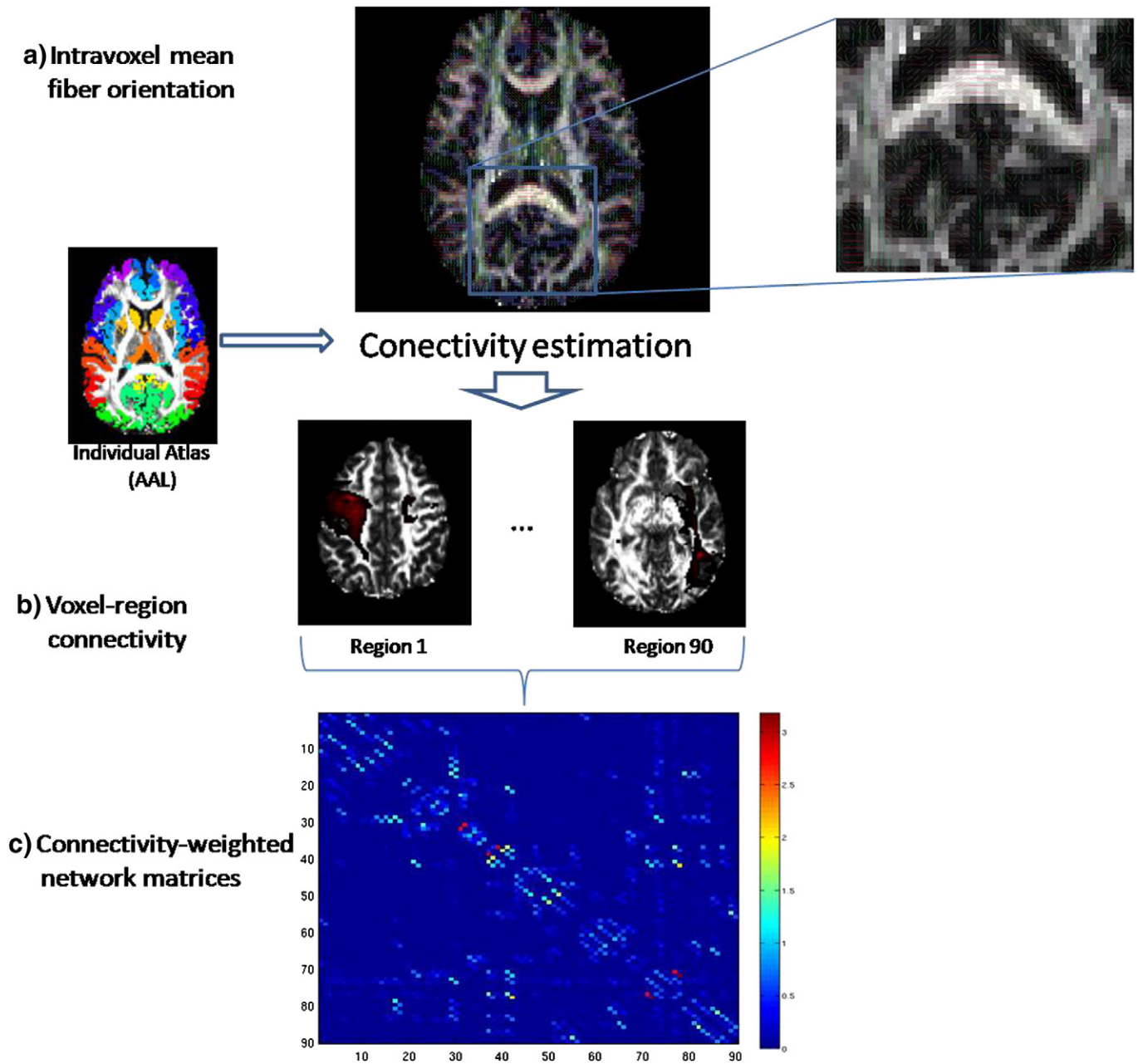


Fig. 1. A schematic representation of the connectivity estimation and network matrix construction in one participant as an example. a) Axial map representing intra-voxel mean fiber orientation (dyadic vectors) overlaid on the FA image; the inset figure provides details of the high fiber orientation coherence within the splenium of the corpus callosum. b) Axial voxel-region connectivity maps corresponding to region 1 (precentral gyrus) and region 90 (inferior temporal gyrus), overlaid on the FA image; voxels are color-coded according to whether the connectivity of each voxel is high (red) or low (black). c) Whole-brain structural network matrix derived from the tracking algorithm, as described in [Methods](#).

where n is the number of nodes, and d_{ij} is the geodesic length over all pairs of nodes. In the unweighted network context, the shortest path length d_{ij} is defined as the number of arcs along the shortest path connecting nodes i and j . In the case of weighted networks, the path with the minimum number of nodes is not necessarily the optimal d_{ij} and it is necessary to define a physical length associated with each arc (this should be a function of the characteristics of the hypothetical link among any nodes i and j). In this study, we assumed that the physical length of an arc connecting nodes i and j is inversely proportional to the strength of the analyzed connection ([Iturria-Medina et al., 2008](#)), i.e., $l_{ij} = 1 / w_{ij}$. Thus, the shortest path length d_{ij} is finally computed as the smallest sum of the arc lengths throughout all the possible paths from node i to node j . Note that for the particular case of unweighted graphs, $l_{ij} = 1$ for all arcs and the geodesic lengths d_{ij} reduce to the minimum number of arcs traversed to get from i to j .

Local efficiency. The local efficiency (E_{loc}) of G is defined as the average efficiency of the local sub-graphs ([Latora and Marchiori, 2001](#)):

$$E_{loc} = \frac{1}{n} \sum_{i \in G} E_{glob}(G_i),$$

where G_i is the sub-graph of the first neighbors of node i . This measure has been used to reveal how much a system is fault tolerant, showing how efficient the communication is among the first neighbors of i when i is removed.

In a physiological sense, the global efficiency of a structural brain network reflects the potential parallel exchange of neural information between the anatomical regions involved (a high global efficiency value, i.e., $E_{glob} \approx 1$, may indicate highly parallel information transfer in the brain system, in which each element node could efficiently send

information concurrently along the network). The local efficiency of a structural brain network reflects its potential tendency to present communities or clusters of anatomically and physiologically different regions that deal with common neural information (where regions connected to a same region tend also to link to each other). In addition, concurrent higher values of global and local efficiencies indicate a system with a high balance between local necessities (fault tolerance) and wide-scope interactions.

Statistical analysis of efficiency topological features. A Wilcoxon rank-sum test was used to investigate differences between both groups of participants ($N = 13$ for monolinguals, $N = 13$ for bilinguals). This is a non-parametric method to test the null hypothesis (H_0) that medians for each graph network measure are equal. We also computed Pearson's linear correlation coefficient (r -value) to evaluate the relationship between graph measures across all participants ($N = 26$). In order to minimize false positive findings (proportion of incorrectly rejected H_0) arising from the high number of tests performed in the topological analysis, we used FDR correction (at $q = 0.05$) to set a critic p -value (Benjamini and Hochberg, 1995; Groppe et al., 2011). All p -values less than or equal to the critic p were significant; suggesting that there is a group difference (reject H_0).

Results

NBS analysis

The NBS (T-threshold = 3.5, $K = 5000$ permutations) was used to detect any connected sub-networks that were significantly different between groups. Two sub-networks were found to be significantly more connected in bilinguals than monolinguals at $p < 0.01$ corrected (Figs. 2a and b). The first sub-network (sub-network I) interconnected frontal and parietal/temporal regions in the left hemisphere, comprising a total of 6 regions: the insula (INS), the superior temporal gyrus (STG), pars triangularis (PT) of the inferior frontal gyrus, the supramarginal gyrus (SMG), the pars opercularis (PO) of the inferior frontal gyrus and the medial superior frontal gyrus (MSF). All of these (Fig. 2a) are brain regions related to language processing (Binder and Desai, 2011; Price, 2010) and have been implicated in bilingualism (Kim et al., 1997; Parker Jones et al., 2012; Perani et al., 2003; Rodriguez-Fornells et al., 2002; Wartenburger et al., 2003). The second sub-network (sub-network II) involved 5 nodes (Fig. 2b), 4 of them in the left hemisphere: the left superior occipital gyrus (SOG), right superior frontal gyrus (SFG), left superior parietal gyrus (SPG), left superior temporal pole (STP) and left angular gyrus (ANG). Two of these (i.e. STP and ANG) are regions that have been associated with language processing (Binder and Desai, 2011; Price, 2010), while the others have been reported as involved in functions related to language, such as the SOG in high level visual processing of letters and words (Carreiras et al., 2009), the SFG in language control (Abutalebi and Green, 2007) and the SPG in visual-spatial processing during visual word processing (Sun et al., 2011).

Monolinguals did not show any set of regions more highly interconnected than bilinguals. Schematic representations of the sub-networks are depicted in Fig. 2 using BrainNet Viewer version 1.1 (available at: <http://www.nitrc.org/projects/bnv/>). The anatomical name by which each node is labeled was taken directly from the Anatomical Automatic Labeling (AAL) atlas (Tzourio-Mazoyer et al., 2002).

Topological features E_{glob} and E_{loc}

Global network efficiency is a measure of how much parallel information can potentially be exchanged over a network. The E_{glob} , of the differential sub-networks identified with the NBS, was compared between groups. The results show a significantly higher global efficiency of sub-network I and sub-network II for bilinguals as compared to

those for monolinguals at $p \leq 0.016^1$ (see Fig. 2c and Table 2 for comparisons between bilingual and monolingual participants).

In order to understand how the presence of these structural sub-networks influences or modifies the structure of the whole brain network, we also compared the global and local efficiency of the whole structural network (E_{glob} and E_{loc} , respectively) with the global efficiency of sub-network I ($E_{glob\ I}$) and sub-network II ($E_{glob\ II}$). The results show a clear linear inverse correlation between the global/local efficiencies of the whole network and the global efficiency of sub-network I and sub-network II (all significant at $p \leq 0.016$). Fig. 3 shows the Pearson correlation values and p -values between the global/local efficiencies of the whole network and the global efficiency of sub-network I and sub-network II. These results suggest that the development of these structural brain sub-networks might compromise the intrinsic capability of the whole brain system to transmit parallel information between its nodes/regions (i.e. the capacity of each node to send concurrent information along the network). In fact, we obtained a significantly higher global efficiency of the whole network ($p = 0.016$) for monolinguals as compared to that for bilinguals (see Table 2). This result is perhaps a general consequence of the higher demand implied in the development of these sub-networks, for example, in terms of additional axonal cost.

Additionally, in order to test the significance of the correlation results, the same correlation analysis that was performed on the sub-networks of interest was carried out again over 10,000 randomly-created sub-networks of 6 regions (i.e. over each sub-network composed by 6 arbitrary selected regions from 90 possible, being the same across subjects). From this procedure we obtained new correlation values that were used to create a null correlation distribution with which to compare the initial correlation values between $E_{glob\ I}$ and E_{glob} , and $E_{glob\ I}$ and E_{loc} . Once verified the Gaussian distribution of both empirically-created null correlation distributions, a z -test was performed to test if our initial correlation values were random samples of these null distributions. Results showed that the observed correlation effects had a very low probability of being random samples of these null distributions ($p = 0.0258$ for $E_{glob\ I}$ and E_{glob} ; $p = 0.0012$ for $E_{glob\ I}$ and E_{loc}). These complementary results indicate that the observed inverse correlation between the global and local efficiencies of the whole network and the global efficiency of the sub-networks (with the former decreasing when the latter increases) are not casual effects, but are robust facts highly specific of the networks described.

Finally, due to a limited statistical power because of the small sample size, a sensitivity power analysis was conducted to know the minimum effect size for which the tests are sufficiently sensitive with these small sample sizes (bilinguals, $N = 13$, monolinguals, $N = 13$), allowing a power ($1 - \beta$) of 0.8 and α of 0.05. Results showed that the effect size (d) between groups for the global efficiency measures ($E_{glob\ I}$: $d = 1.948176$; $E_{glob\ II}$: $d = 1.955$; E_{glob} : $d = 1$) is close to or larger than the expected minimum effect size ($d = 1.17$) for these small sample sizes. Thus, we can conclude that due to the high connectivity differences between groups the study was sensitive enough to capture these, even with relatively small sample sizes.

Discussion

The goal of the present study was to investigate brain network axonal connectivity differences in 13 early Basque-Spanish bilinguals as compared to those in 13 Spanish monolingual participants and to examine differences in the topological parameters of the brain network between both groups; in particular, we focus on graph network efficiency measures.

¹ FDR correction for multiple comparisons (at $q = 0.05$) sets a critic p -value of 0.016, and all p -values less than or equal to the critic p are significant (Benjamini and Hochberg, 1995; Groppe et al., 2011).

Bilinguals vs. Monolinguals

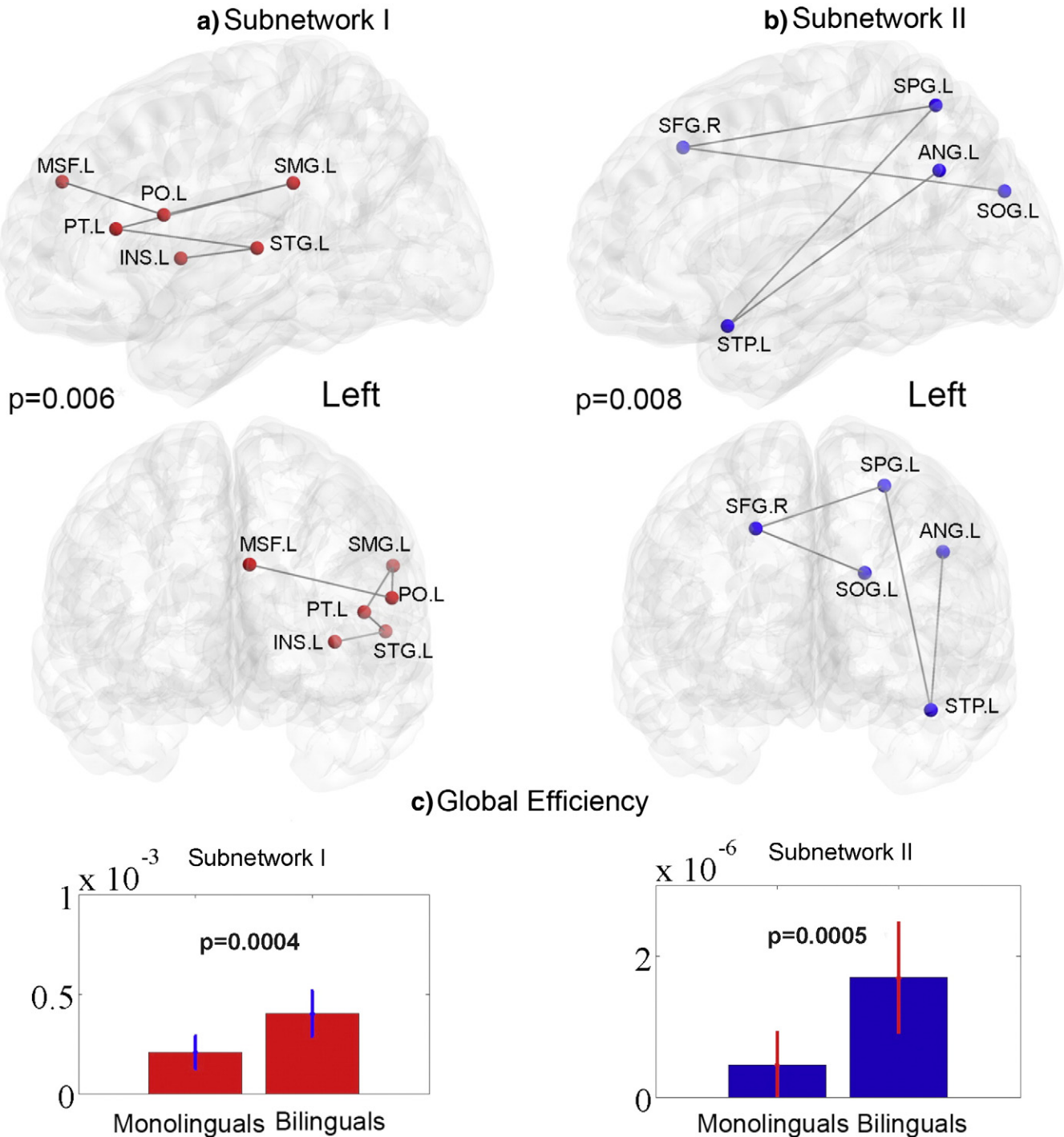


Fig. 2. The sub-networks showing increased structural connectivity and graph-efficiency in bilinguals ($N = 13$) compared with those in monolinguals ($N = 13$). Panels a–b show the NBS results (T -threshold = 3.5; $K = 5000$). a) Regions forming an individual component (sub-network I) with 6 nodes/regions and 5 edges/connections. b) Regions forming an individual component (sub-network II) with 5 nodes/regions and 4 edges/connections. c) Between-group differences in global graph-efficiency measure of sub-networks I and II. Bars represent mean-values. Whiskers represent standard deviation (SD) values. Abbreviations: L, left; R, right; INS, insula; STG, superior temporal gyrus; PT, pars triangularis of the inferior frontal gyrus; SMG, supramarginal gyrus; PO: pars opercularis of the inferior frontal gyrus; MSF: medial superior frontal gyrus; SOG, superior occipital gyrus; SPG, superior parietal gyrus; STP, superior temporal pole; ANG, angular gyrus.

The first finding of this study is the identification of two sub-networks of regions interconnected by anatomical tracts that were more strongly connected in early bilinguals as compared to those in monolinguals. These sub-networks contain the left frontal and parieto-temporal brain regions, most of them previously described in literature as language-relevant. The six left interconnected regions involved in

sub-network I (Fig. 2a) are: INS–STG–PT–SMG–PO–MSF. In turn, the left INS has been found more activated for bilinguals than for monolinguals (Parker Jones et al., 2012) and for high proficiency compared to low proficiency bilinguals (Chee et al., 2012) when performing language tasks. In general, the left INS has been implicated in articulatory planning and in the production of unfamiliar speech sounds (e.g. pseudowords)

Table 2

Global graph-efficiency comparison results between monolingual ($N = 13$) and bilingual ($N = 13$) groups for each sub-network obtained from the NBS analysis.

Groups	Global graph efficiency mean (\pm SD)		
	Eglob I	Eglob II	Eglob
Monolinguals	2.082×10^{-4} ($\pm 8.169 \times 10^{-5}$)	4.579×10^{-7} ($\pm 4.612 \times 10^{-7}$)	0.040 (± 0.002)
Bilinguals	4.014×10^{-4} ($\pm 1.140 \times 10^{-4}$)	1.694×10^{-6} ($\pm 7.658 \times 10^{-7}$)	0.038 (± 0.002)
z-Values	-3.5385	-3.4872	2.4103
p-Values	0.0004	0.0005	0.016

SD, standard deviation. Eglob I, global graph efficiency of sub-network I. Eglob II, global graph efficiency of sub-network II. Eglob, global graph efficiency of the whole network. The p-values correspond to the null hypothesis (H_0) that medians are equal. $p \leq 0.016$ suggests that there is a group difference (reject H_0).

compared to familiar speech sounds (e.g. words) (Price, 2010). In addition, structural imaging evidence shows higher WM density underlying the left INS when comparing good and poor producers of nonnative speech sounds (Golestani and Pallier, 2007). Thus, it is quite likely that this region develops stronger and additional connections with other language regions due to the greater demands of articulatory speech plans for two languages in bilinguals. The STG is implicated in pre-lexical processing of auditory speech and higher left STG activations have been related to top-down processing in noisy environments, words vs. pseudowords and in auditory-motor feedback during speech production (Price, 2010). Additionally, the left STG has also been shown more

activated in late bilinguals than monolinguals in language tasks, maybe because the processing of two languages could involve more demands either for pre-lexical or post-articulation processing (Parker Jones et al., 2012). The PT and PO are the classic left inferior prefrontal language regions and many functional neuroimaging studies have shown more activation in bilinguals than monolinguals when performing language tasks (Parker Jones et al., 2012; Rodriguez-Fornells et al., 2002) and more for late than early bilinguals (Wartenburger et al., 2003) and even for early bilinguals when they perform tasks with their L2 as compared to their first language (Perani et al., 2003). In this context of bilingualism, these regions have been associated with the control of verbal interference between languages (Parker Jones et al., 2012; Rodriguez-Fornells et al., 2002) and in general for lexical, phonological, syntactic (Price, 2010) and semantic effects (Binder and Desai, 2011). Our results are in line with the well-documented importance of these classic regions and show that they have stronger connections with other crucial regions for language processing.

Concerning the left SMG, structural studies have shown that in bilinguals GM density is increased in the posterior SMG (Mechelli et al., 2004). Moreover, WM underlying the left inferior parietal region has also correlated positively with the capacity of individuals to learn new speech sounds (Golestani and Pallier, 2007; Golestani et al., 2002). Furthermore, GM has correlated positively with increased vocabulary knowledge in monolinguals (Lee et al., 2007) and has been shown to be higher in late literates than illiterates (Carreiras et al., 2009). Interestingly, all these results fit with the bilingual findings (Mechelli et al., 2004) and with the fact that vocabulary knowledge in bilinguals is

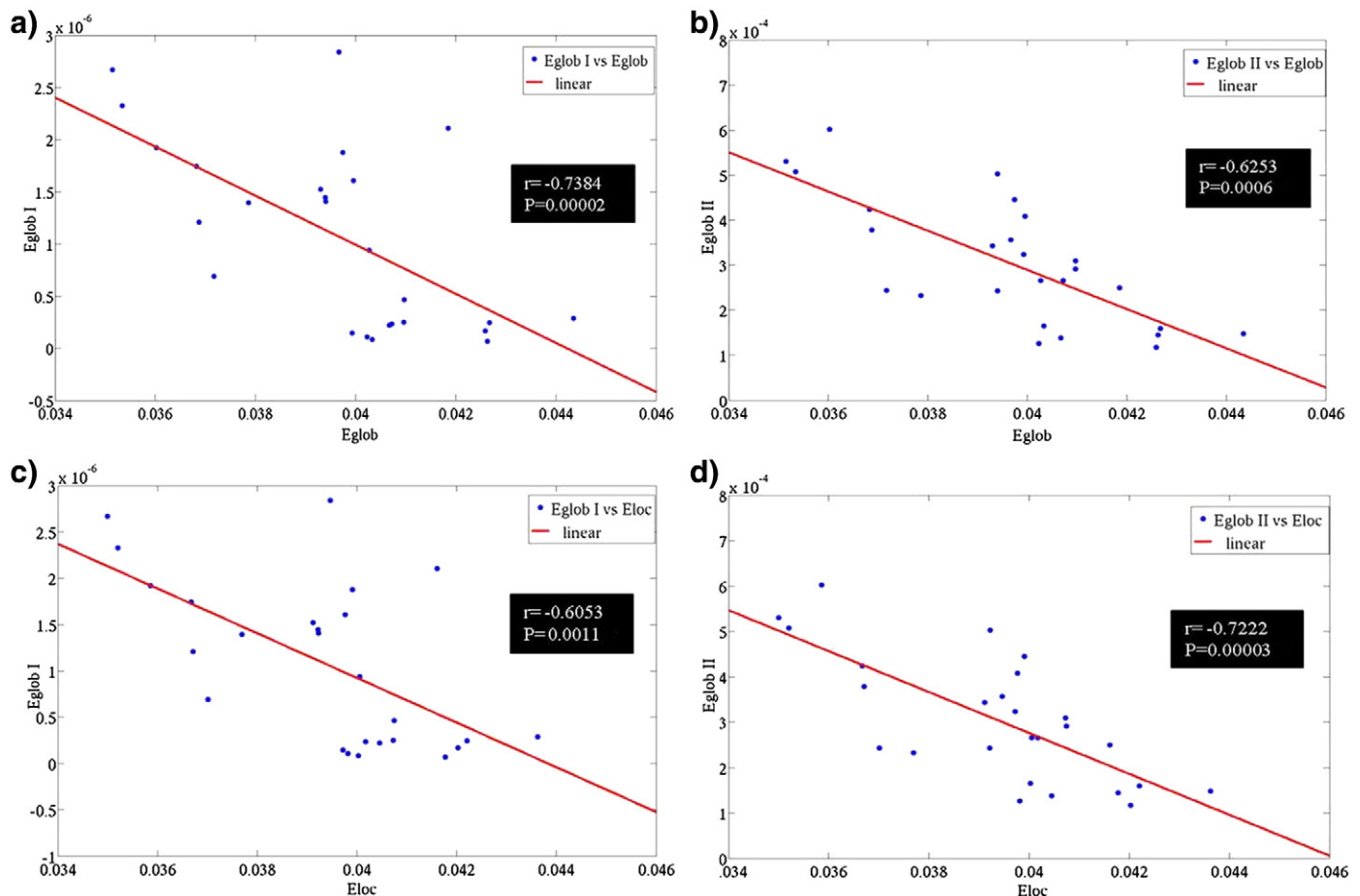


Fig. 3. Relationship between the graph-efficiency measures of the whole brain network and sub-networks obtained by NBS. (a–d) Graphics showing decrease of global/local efficiencies of the whole network with the increase of global efficiency of each sub-network. Pearson's linear correlation coefficient (r-value) was used to test the relation between efficiency measures. Abbreviations: Global efficiency of whole brain network (Eglob), Global efficiency of sub-network I (Eglob I), Global efficiency of sub-network II (Eglob II), Local efficiency of whole brain network (Eloc). Here we present correlations between measures across all participants ($N = 26$) without taking into account the differences between groups.

different, since they are dealing with two languages (Green et al., 2007). In functional studies, the SMG has been associated with phonological and semantic processing (Binder and Desai, 2011; Price, 2010) but seems to be more specific for subvocal articulation (Price, 2010). Finally, the MSF has been related to high level executive functions and decision-making processes (Talati and Hirsch, 2005) and has been found more activated in semantic than in phonological word retrieval and more for words than pseudowords (Price, 2010). Bilinguals need to manage interference between two languages, so they would need to use executive control mechanisms more often to make semantic or lexical decisions. There is considerable behavioral evidence that bilingualism has an impact on executive control mechanisms (Abutalebi and Green, 2007; Bialystok et al., 2012). In summary, all the regions involved in sub-network I seem to play an important role in facilitating language monitoring. Under challenging conditions the demands are greater in many different ways: phonetic/semantic/syntactic interference, articulatory speech planning, prelexical processing and auditory feedback. Since all these processes represent cognitive challenges for bilinguals, the brain network may have adapted by increasing the interconnectivity between these regions in early bilinguals.

Sub-network II (Fig. 2b) includes some brain regions that have also been extensively related to language processing (i.e. the left STP and left ANG) while others have been implicated in other cognitive processes related to language. These more interconnected brain regions for the bilingual group are: the left SOG—right SFG—left SPG—left STP—left ANG. Traditionally, neurological models of reading have proposed that visual information is transferred from the occipital cortex to the left ANG to converge with the auditory information coming from the posterior superior temporal sulcus (Richardson et al., 2011). The left ANG has been implicated in semantic processing (Binder and Desai, 2011) and this implication seems due to top-down processes that facilitate sentence comprehension (Price, 2010) and reading (Carreiras et al., 2009). Since the ANG has been reported to be involved in semantic processing, it possibly requires stronger connections with other phonological areas (e.g. STP) and other semantic areas. The STP is the most anterior part of the superior temporal lobe (Olson et al., 2007). Bilateral activations in this region have been related to phonemic processing of prelexical stimuli such as vowels, but higher left hemisphere activations are probably also reflecting top-down processing (Price, 2010). In the context of language processing, the temporal pole has been considered a high-level region for processing the emotional aspects of words and phrases (Binder and Desai, 2011), but in general has a crucial role in processing emotional significance of any type of stimuli (Olson et al., 2007). For its part, the left SPG has been involved in spatial orientation and receives sensory information from visual inputs and proprioception, which is why it is described as a site for integration of visual, auditory and somatosensory information (Gaser and Schlaug, 2003). It also seems to be important in letter-by-letter serial reading that involves more visual–spatial processing than automatic parallel reading (Cohen et al., 2008). For example, one study found that this region was more sensitive for Chinese degraded characters than English degraded words, which fits with the idea that Chinese depends more on visual–spatial processing during visual word recognition (Sun et al., 2011). In the case of the SFG, this region is part of the dorso-lateral prefrontal cortex, an area implicated in language control and important for the maintenance of relevant information in working memory (Elliott, 2003). Finally, the SOG might be related to high level visual processing (Carreiras et al., 2009) and to letter shape analysis that begins in the middle/inferior occipital gyri (Ellis et al., 2009). It is not clear what might be the role of sub-network II but it includes regions important for the integration of multimodal information (i.e. visuo-spatial, auditory, proprioceptive and somatosensory), which might be essential for visual word recognition, reading and semantic processing. It also includes a frontal executive control region that is crucial for dealing with increased working memory load and might help in the maintenance or monitoring of the information that comes from many modalities.

To summarize the impact of these two sub-networks in bilingualism: sub-network I seems to be involved in phonological, syntactic and to some extent semantic interference between languages, while the role of sub-network II in bilingualism is less clear but it seems to be important in facilitating word recognition, reading and semantic processing. Interestingly, both sub-networks also include one frontal region related to language control. This is important, since these bilinguals switch very often between both languages, depending on the characteristics of the interlocutor and the context of the interaction. In general, these results suggest that the brain structurally adapts to fulfill increased language demands and to control the use of two languages.

The second finding of this study concerns the use of the graph theoretical approach to examine global and local graph network efficiencies of the two sub-networks obtained in the NBS analysis and concerning the whole network. We found that both sub-networks, I and II, were more graph-efficient (i.e. higher capability of transferring information between nodes/elements) in bilinguals as compared to that in monolinguals (Fig. 2c, Table 2). We also found a linear inverse correlation between the global/local graph-efficiencies of the whole structural brain network and the global graph-efficiency of each sub-network (Fig. 3) and that the graph-efficiency of the whole network decreased for bilinguals as compared to that for monolinguals (Table 2). We interpret this result as an indication that the acquisition from early in life of two languages seems to result in the development of specialized structural brain sub-networks, not only in terms of higher connection density between regions in these sub-networks, but also in terms of a more graph-efficient flow of the information that these sub-networks are subserving. However, it seems that the consequence of the additional demands implied in the development of these sub-networks could be associated with a reduction in the graph-efficiency of the entire structural brain network (Table 2, Fig. 3), suggesting less efficient parallel information transfer between all nodes in the whole brain. In other words, the optimization in the configuration of the sub-networks correlates with a less optimized general configuration of the whole network in which these sub-networks are inserted – which resembles the functioning of other systems with limited resources.

In terms of functional principles, these connectivity changes seem to support the idea that demanding, highly specific processing in higher-level cognitive functions such as language might require more devoted specialized sub-networks. But they also seem to indicate that the existence of specialized sub-networks, bringing about the reduction of the global graph-efficiency of the whole network, could also affect higher-cognitive processes that might require greater efficiency in transferring parallel information across all regions in the entire network (Bassett et al., 2009; Bullmore and Bassett, 2011; Li et al., 2009). It has already been demonstrated that bilinguals have disadvantages in different language tasks. In particular, it has been found that bilinguals are less accurate and slower than monolinguals of each language in some linguistic tasks such as picture naming, word recognition and lexical decision (Gollan et al., 2011; Martin et al., 2012). Thus, it may be the case that the over-developed sub-networks allow bilinguals to deal with two languages but do not improve linguistic skills per se in each language. On the other hand, the fact that a few regions important in executive control mechanism are involved in the sub-networks might explain the over-training of bilinguals as compared to that of monolinguals in some executive control tasks (Abutalebi and Green, 2007; Bialystok et al., 2012; Costa et al., 2008, 2009, but see Duñabeitia et al., in press). Further complex topological studies are needed to understand how over-developed sub-networks and the entire network functioning correlate with bilingual advantages and disadvantages in executive control and behavioral linguistic tasks, respectively.

It should be noted that the participant samples used in this study only represent the extremes of a (fairly complex) distribution of bilingualism with multiple, admittedly interacting, factors. In order to avoid the potential impact of continuous factors such as age of first and second language acquisition or language proficiency, we carefully

selected a relatively homogeneous bilingual sample composed of individuals who had acquired both languages before age 3 and who were all highly proficient in the two languages (scores range from 8.5 to 10, in a 1-to-10 Likert-like proficiency self-rating scale). Given the fact that the sample of bilinguals tested clearly represents an extreme of the distribution (namely, balanced simultaneous bilinguals; see Duñabeitia et al., 2010), the reduced variability within this group of bilinguals does not allow for further correlation or regression analysis. Nonetheless, future studies that take into consideration the distributional factors which have been intentionally avoided in the current study (e.g., proficiency or age of acquisition) are needed. Also, additional studies are needed to explore the neuro-anatomical bases of the found sub-networks and the extent to which all or part of these sub-networks are reproducible across other groups of bilinguals with different linguistic backgrounds and properties.

In the present study, a whole-brain tractography approach was performed to construct axonal connectivity networks between 90 GM regions. Although the methodologies used here have the advantage of investigating brain differences by examining the brain as a whole, the results are sensitive to the limitations of the tractography algorithm, as probabilistic tractography may miss fiber crossing and fanning (false negative) or reconstruct spurious connections in the case of kissing and intertwining configurations (false positive), and these errors increase in longer tracts. Probabilistic tractography offers an estimate of the mathematical confidence we can have in the reproducibility of a given pathway for a given dataset but may be highly inaccurate (Jones, 2010). Therefore, further research is needed using other advanced techniques to alleviate this intrinsic limitation of the tractography algorithm used in this study. Future WM connectivity studies will benefit from multi-modal brain measurements to understand brain functioning better.

In conclusion, when two languages are simultaneously acquired early in life, more graph-efficient sub-networks are developed in order to accommodate extra language demands and the increase in the graph-efficiency of these sub-networks seems to be at the expense of decreased whole network graph-efficiency. These more developed sub-networks which are present in early bilinguals may be devoted to language monitoring, avoiding interference effects between languages and facilitating processing of both languages. However, an increase in demand on a physically constrained brain network, brought about by the need to deal with two languages, could give rise to some disadvantages for the entire network. In general, we maintain that early acquisition of more than one language seems to trigger brain plasticity, even modifying to some extent the structural organization of the brain network. Further studies are required to detail the neuroanatomical bases, extent and functioning of these sub-networks across other groups of bilinguals with different linguistic backgrounds and properties and to describe the impact of these neuroanatomical differences on cognitive and behavioral differences between bilinguals and monolinguals.

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