RESEARCH ARTICLE

Brain network profiling defines functionally specialized cortical networks

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Funding information

BIAL Foundation, Grant/Award Number: 195/16; McDonnell Center for Systems Neuroscience; NIH Blueprint for Neuroscience Research; University of Oxford; University of Minnesota; Fundação Bial

Abstract

Neuroimaging research made rapid advances in the study of the functional architecture of the brain during the past decade. Many proposals endorsed the relevance of large-scale brain networks, defined as ensembles of brain regions that exhibit highly correlated signal fluctuations. However, analysis methods need further elaboration to define the functional and anatomical extent of specialized subsystems within classical networks with a high reliability. We present a novel approach to characterize and examine the functional properties of brain networks. This approach, labeled as brain network profiling (BNP), considers similarities in task-evoked activity and resting-state functional connectivity across biologically relevant brain subregions. To combine task-driven activity and functional connectivity features, principal components were extracted separately for task-related beta values and resting-state functional connectivity z-values (data available from the Human Connectome Project), from 360 brain parcels. Multiple clustering procedures were employed to assess if different clustering methods (Gaussian mixtures; k-means) and/or data structures (task and rest data; only rest data) led to improvements in the replication of the brain architecture. The results indicated that combining information from resting-state functional connectivity and task-evoked activity and using Gaussian mixtures models for clustering produces more reliable results (99% replication across data sets). Moreover, the findings revealed a high-resolution partition of the cerebral cortex in 16 networks with unique functional connectivity and/or task-evoked activity profiles. BNP potentially offers new approaches to advance the investigation of the brain functional architecture.

KEYWORDS

brain functional architecture, clustering, Gaussian mixture model, parallel analysis, principal component analysis, resting-state fMRI, task fMRI

1 | INTRODUCTION

In the endeavor of deciphering the functional architecture of the brain, functional connectivity analysis supported the passage from an activation-localization approach toward a network perspective. In recent years, neuroimaging took an ambitious route of acquiring brain functional images during periods of time in which subjects are instructed to lay in the scanner, stay still, and keep their eyes open/closed without being involved in a specific task (Biswal, 2012; Greicius, Krasnow, Reiss, & Menon, 2003). The corresponding brain states, called resting-states, are informative about the brain's intrinsic organization (Buckner, Hrienen, & Yeo, 2013; Ding et al., 2011; Fox, Snyder, Vincent, et al., 2005). Analysis of resting-state functional connectivity using functional MRI led to the identification of brain

networks, defined as ensembles of brain regions that share similar patterns of variance in activity over time (Doucet et al., 2011; Hacker, Laumann, Szrama, et al., 2013; Power, Cohen, Nelson, et al., 2011; Rosazza & Minati, 2011; Smith, Fox, Miller, et al., 2009; Yeo et al., 2011).

Recent studies highlighted parallelisms between the intrinsic and task-related functional organizations of the brain. Meta-analytic approaches, based on the likelihood of brain regions to be recruited in different tasks or cognitive states, yielded task-related networks that closely resemble resting-state networks (Crossley, Mechelli, V´ertes, et al., 2013). The analysis of multi-task functional connectivity (Cole, Bassett, Power, Braver, & Petersen, 2014) and task co-activations (Laird et al., 2013) also showed similarities between task-related and resting-state architectures. However, these studies compared task-related with resting-state networks emphasizing similarities between

the two results, but they did not directly consider both intrinsic features and task-evoked activation proprieties when defining networks. As a drawback, previous studies may be biased by the inclusion of a greater amount of externally directed attention tasks, compared to other types of tasks. Moreover, meta-analyses are troubled by conversions between different templates (Fox, Lancaster, Laird, & Eickhoff, 2014; Laird, Robinson, Mcmillan, et al., 2010) and biases related to the selection and quality of the included studies (Greco, Zangrillo, & Landoni, 2013).

The topography of functional subsystems within classical networks as well as subtle differences between network functional properties is still unclear. For instance, the default mode network (DMN) is presumed to be divided into three functional subsystems (Andrews-Hanna, Reidler, Sepulcre, Poulin, & Buckner, 2010; Andrews-Hanna, Smallwood, & Spreng, 2014), but most studies on the functional architecture of the brain highlighted different partitions (Hacker et al., 2013; Power et al., 2011). Moreover, auditory and somatomotor systems may appear mingled with cingulo-opercular regions (Hacker et al., 2013), although the functional specialization of the cingulo-opercular network goes beyond somatomotor or auditory modalities (Dosenbach, Fair, Cohen, Schlaggar, & Petersen, 2008; Sadaghiani & Esposito, 2015). Another example concerns the dorsal attention network (DAN) which is usually considered as a unique system covering frontal, parietal, and occipital association cortices (Corbetta & Shulman, 2002), although its subregions are known to be differentially involved in motor planning (Burnod, Baraduc, Guigon, et al., 1999; Caminiti, Innocenti, & Battaglia-Mayer, 2015) and to express a different degree of effector-specificity (Heed, Leone, Toni, & Medendorp, 2016; Leonè, Heed, Toni, & Medendorp, 2014). This background suggests that the significance of brain networks may be multi-modal, relying both on intrinsic functional connectivity and on measures of brain activity in task-related states (Bolt, Nomi, Rubinov, & Uddin, 2017; Buckner et al., 2013; Di, Gohel, Kim, & Biswal, 2013; Smith et al., 2009). We hypothesize that certain subtle specializations within the classical networks may have been obscured by not directly integrating resting-state and task data.

In the attempt of combining resting-state and task fMRI data for the study of the functional organization of the brain, we here describe a novel method referred to as brain network profiling (BNP). BNP aims at considering similarities in both task-related activity and functional connectivity of biologically relevant brain subregions, to distinguish functional networks that would otherwise be blurred together.

For this purpose, group average data from the Human Connectome Project (HCP 500-subject release, July 2014) were used to obtain a consistent and reliable data structure. To analyze the network affiliation and functional profiles of biologically distinct brain areas, we adopted the parcellation in 360 brain parcels proposed by Glasser et al. (2016). To merge task-induced activity and functional connectivity, principal components were extracted separately for task-related beta values and for resting-state functional connectivity z-values from the 360 brain parcels. To compare clustering methods with different assumptions about the data structure, the clustering procedure was performed using the *k*-means approach and a Gaussian mixtures model (GMM).

We expected that this novel approach would yield peculiar functional networks with increased reproducibility. In accordance with our hypothesis, BNP provided a functional segregation of networks characterized by unique profiles of task-induced activity and functional connectivity. Moreover, addressing reliability issues in neuroscientific research (Poldrack et al., 2017), BNP improved the reproducibility as evidenced using both the parcellation and validation data sets provided by the HCP database. The functional profiles of the obtained networks are analyzed and discussed in the context of recent literature and past partitions.

2 | MATERIALS AND METHODS

2.1 | Data

fMRI data used in the analysis of this study were obtained from the Human Connectome Project (HCP) database (balsa.wustl.edu). We used group averages from the 210P data set including resting-state and task data from 210 subjects (130 females, 90 males), aligned using areal-feature based registration. This is the same data set used for the parcellation in Glasser et al. (2016).

There are several reasons for which we selected fMRI data from the HCP for our study.

First, these data come from a large sample of healthy participants in a controlled environment and with an extremely accurate preprocessing (Glasser et al., 2013; Glasser et al., 2016; Robinson et al., 2014; Salimi-Khorshidi et al., 2014).

Second, the 360-areas parcellation (Glasser et al., 2016) was created using multiple MRI modalities, including intrinsic functional connectivity, task activity, myelin density maps, and cortical thickness maps. This multi-modality enhances the likelihood that parcels will reflect effective biologically specialized areas that present sharp changes in architecture, function, connectivity, and topography. The markedly improved intersubject cortical alignment using cortical folding, myelin, and resting-state fMRI suggest that these parcels are likely to represent the typical subject's parcellation. As other studies indicated (Gordon, Laumann, Adeyemo, Huckins, & Kelley, 2016; Schaefer, Kong, Gordon, et al., 2017), the spatial extent of different subregions may not be uniform, possibly favoring spatial biases when defining networks. Thus, using the 360-areas parcellation allows us to inquire how biological sub-units of the brain are functionally associated in higher order systems, how these systems are intrinsically connected, and how they behave during task execution.

Third, this data set contains an independent validation sample (210 V). To validate our results, we performed the clustering also on this second data set. The two groups of 210 subjects (210P and 210 V) did not share family members between them, although they did within groups.

Fourth, the data set is publicly accessible for researchers.

The data used for this study consists of a 360-by-86 matrix of beta values for task activity and a 360-by-360 matrix of z-values for resting-state functional connectivity (calculated using full correlation). These matrices were extracted from the grayordinate dense maps of group averages, for task-related activation (7 tasks, 60 minutes total)

and resting-state functional connectivity (4 runs concatenated, 15 min each), using the parcellation above. The connectome was created by correlating the areal group PCA series after parcellating the dense group PCA series.

Given the repetition of information in the task matrix, we eliminated all the redundant data and maintained only 24 columns in the matrix. The redundant data consisted of activation levels with an inverted sign (negative copies), averages across task conditions and contrasts between conditions of the same task. The removal of redundant task data before the PCA is necessary because adjoining highly correlated variables increases the contribution of their common underlying factor to the PCA. This redundancy biases the evaluation of the eigenvalues and consequently also the clustering procedure. Furthermore, as task-related contrasts and task-related beta maps lie on dissimilar dimensions ($\Delta\beta$ in the first case, β in the second case), they should not be fused together into a single PCA. This would be incorrect because: (a) by construction, $\Delta\beta$ s have lower means and different variances; (b) it would be theoretically unsound (e.g., one would never fuse in the same analysis reaction times and differences in reaction times); (c) contrasts among conditions (as well as averages) were defined arbitrarily. However, most importantly, (d) task-related contrasts (and averages) represent redundant data in the analysis since they are derived from variables that already exist in the data.

The 24 columns retained for the PCA were the beta values that represented: activity in the four conditions of the 2-back and 0-back WORKING MEMORY tasks (*body*, *face*, *place*, and *tool*), activity in the *punish* and *reward* conditions of the GAMBLING task, activity in the six conditions of the MOTOR task (*cue*, *left foot*, *left hand*, *right foot*, *right hand*, and *tongue*), activity in the *maths* and *story* conditions of the LANGUAGE task, activity in the *random* and *theory of mind* conditions of the SOCIAL task, activity in the *match* and *relational* conditions of the RELATIONAL task, and the activity in the *faces* and *shapes* conditions of the EMOTION task.

Names of tasks and conditions are the same as those used in Glasser et al. (2016); for a detailed description of the task paradigms and classification, see the HCP reference manual (Wu-Minn Consortium HCP, 2014; see also Barch, Burgess, Harms, et al., 2013; Glasser et al., 2016). Data were processed using MATLAB 9.2 (The Math Works Inc., Natick, MA) and the HCP WorkBench (Marcus et al., 2013).

2.2 | Network profiling

2.2.1 | PCA and parallel analysis

The overall procedure is schematized in Figure 1. To reduce the dimensionality of the data sets and to merge task-induced activity and functional connectivity, principal components were extracted separately from the 360-by-24 task matrix and from the 360-by-360 resting-state matrix. As it has been already demonstrated, the use of PCA allows the extraction of neurally relevant latent variables (Baumgartner et al., 2000; Friston, Frith, Liddle, & Frackowiak, 1993). The number of components of interest was assessed using parallel testing (Horn, 1965; Ledesma & Valero-Mora, 2007) separately for task and rest data. The parallel analysis uses a Monte Carlo statistical simulation process to generate a distribution of simulated eigenvalues starting from random data sets with the same sample size and the

same number of variables of the original data set. Then, the eigenvalues of the main PCA are compared with those generated using parallel analysis to retain eigenvalues which fall within the 95% confidence interval.

Reducing the dimensionality of the data through parallel analysis is described as appropriate in many studies, because it aims at improving the clustering by estimating the number of principal components (or factors) to retain without biases related to arbitrary choices of the experimenter, to the existence of noise in the data, to the number of variables or to the sample size (Humphreys & Montanelli, 1975; Ledesma & Valero-Mora, 2007; Patil, McPherson, & Friesner, 2010; Silverstein, 1990; Zwick & Velicer, 1986).

Nevertheless, it can be argued that the selection of a restricted number of PCs may cause a loss of information during the analysis. To explore such a hypothesis, we performed a complementary analysis in which we retained all the possible information into the data structure. The results of this complementary analysis are reported and discussed in the Supporting Information (Text and Figures S1–S4, Supporting Information).

2.2.2 | Clustering

The resulting components of interest from the PCA are illustrated in Figure 1 (parcel component matrices) and were used as factors for a cluster analysis. To note, we are not applying transformations or re-weighting procedures on these PCs because we wanted to retain their relative importance for the clustering. The clustering procedure was performed using the *k*-means approach as well as a GMM implemented in MATLAB through the function *fitgmdist*.

Differently from *k*-means clustering, the GMM clusters as Gaussians (Scrucca, Fop, Murphy, & Raftery, 2016) avoiding the assumptions of (a) equal variance of clusters across factors (spherical distribution) and (b) similar cluster size. Figure 2 shows some example scenarios regarding clustering simulations using four different data structures, with three clusters. The four cases are: clusters have the same sample size and the same variance; clusters have the same sample size and uneven variances; clusters have uneven sample sizes and the same variance; clusters have uneven sample sizes and uneven variances.

As shown in the figure, whereas the *k*-means approach may work slightly better when clusters share the same circular shape, it biases the clustering procedure when its assumptions are violated. Such differences between clustering methods concerning the nature of the data have been already investigated in many research fields (Greve, Pigeot, Huybrechts, Pala, & Börnhorst, 2015; Lin, Tseng, Cheong, et al., 2008; Ward, Marvin, Halloran, Jacobsen, & Vogt, 2013). Given that there is no reason to presume that brain networks share neither the same degree of variability nor the same spatial extent across multiple dimensions of resting-state functional connectivity or task-induced activity, results from *k*-means and GMM are compared. The parcellation (210P) and the validation (210V) samples were clustered using both methods to assess any effective advantage of one method over the other.

The clustering procedure was repeatedly run with different *k* values ranging from 3 to 25, to select the appropriate *k* (number of

FIGURE 1 Illustration of the workflow used in the current study. Task (beta values) and rest (FC z values) input data were obtained from the HCP database (full correlation, shown in the lower half of the FC matrix, was used). After removing redundant data from the task matrix, principal components were extracted separately from both data sets. Components retained after parallel analysis are represented in the first parcel component matrix. The second parcel component matrix represents the parcels reordered after clustering (the horizontal red lines in separate clusters). Clustering was performed using both *k*-means and a Gaussian mixture model (GMM) and using both rest data alone and joint task and rest data. After comparing the clustering procedures, anatomical and functional profiles of each network were extracted and analyzed. Matrices of the parcellated task and parcellated functional connectivity are reproduced by permission from Springer Nature from “A multi-modal parcellation of human cerebral cortex” by Glasser et al., 2016, *Nature*, 536(7615), 171–178 [Color figure can be viewed at wileyonlinelibrary.com]

clusters). The optimal *k* for the *k*-means clustering was selected using the Davies–Bouldin index (Davies & Bouldin, 1979). This index represents the ratio of within-cluster and between-cluster distances and therefore accounts for both intra-cluster similarities and inter-cluster differences. Regarding GMM clustering, the appropriate *k* was selected as the one associated with the global minimum of the Bayesian information criteria (BIC; Schwarz, 1978). The BIC penalizes for the model complexity and is, therefore, a useful criterion to avoid data overfitting (Fraley & Raftery, 1998). An expectation–maximization (EM) iterative algorithm is implemented in the GMM to assign elements to clusters maximizing the posterior probability. At each step, the log-likelihood of the model is calculated, and the EM process stops when the log-likelihood of the model cannot be improved further. Once the GMM is constructed, each parcel is assigned to the mixture component showing the highest posterior probability.

2.2.3 | Validation of the procedure

To the best of our knowledge, this is the first attempt to define a multi-modal classification of brain networks. However, multimodality is not necessarily a better option than considering functional connectivity

alone. Furthermore, given the unbalance between the number of retained principal components of task and rest data (4 vs. 10), rest data may dominate the clustering and make the BNP essentially a resting-state approach. Thus, the network architecture was computed also using solely resting-state functional connectivity to assess the advantage of including both task and rest data. This approach allows to compare the reproducibility of the results obtained by both clustering methods (GMM, *k*-means) and through both input data structures (task + rest, rest-only). Given the high correspondence between the parcellations obtained through the 210P and the 210V data sets (Glasser et al., 2016), a stable clustering can be expected across the two data sets.

As clustering involving high numbers of clusters (or components) usually has multiple configurations which correspond to local minima of the log-likelihood, we considered it important to (a) avoid local minima related to sub-optimal clustering and (b) statistically compare the four methods. Hence, once the ideal number of clusters/components was estimated for each method, we repeated the clustering procedure for obtaining the functional architecture in 1000 clustering cycles. At each cycle, and for each clustering procedure, the adjusted Rand index (Hubert & Arabie, 1985) was calculated to assess the replication

FIGURE 2 The efficiency of clustering methods when assumptions of equal variance and cluster size are respected versus violated. Each column depicts a specific input data structure for clustering; in the first row, the true clusters are shown, while the second and the third row show results obtained using *k*-means and GMM, respectively. Red crosses represent the real mean values of each cluster along each dimension; black crosses represent mean values after clustering. *K*-means does perform slightly better when variances and sample sizes are equal, whereas GMM performs better when variances and/or cluster sizes are not even (last three columns) [Color figure can be viewed at wileyonlinelibrary.com]

between the parcellation and validation architectures. The adjusted Rand index represents a more appropriate index than classification rates because it accounts for the chance correlation between the two partitions (Steinley, 2004). Adjusted Rand indices were transformed to Fisher *z*-scores to avoid data skewness.

Finally, we compared the distributions of these values for the four clustering procedures using a 2×2 ANOVA with the factors *clustering method* (levels: GMM, *k*-means) and *data structure* (levels: task + rest, rest-only). As the Rand index is not the only measure for assessing clustering replication, the same analysis was performed using the adjusted mutual information criterion (Vinh, Epps, & Bailey, 2010). The architecture with the highest Rand index (which corresponded to the one with the highest mutual information index) was selected for subsequent network profiling.

2.2.4 | Profiling

After obtaining the clusters, cluster indices were translated into functional networks and visualized using the HCP WorkBench (Marcus et al., 2013). Mean values and standard deviations for task-related activity and cross-network functional connectivity were extracted to

obtain network profiles. To report a measure of within-cluster reliability, posterior probabilities maps were generated. The posterior probability describes the amount of evidence for each element (parcel) to belong to its component or cluster (network). As such, it provides a useful measure of consistency for future comparisons, in addition to the parcellation-validation comparison.

To obtain greater insight into the involvement of each network in different tasks, we performed multiple one-sample *t* tests to assess significance levels of their activation or deactivation in each task. Results were corrected within each network (24 comparisons) using the Bonferroni method. To evaluate cross-network differences in both task-activity and connectivity profiles, we performed contrasts between network pairs as follows. Task and functional connectivity data were fitted with a repeated measures model (using the MATLAB function *fitrm* from the Statistics and Machine Learning Toolbox). Task data consisted of the average activity of each parcel in each task condition, whereas FC data consisted of the average functional connectivity of each parcel with each other network. Differences in task-related activity and functional connectivity were assessed using multiple pairwise comparisons. *p* values were corrected using the Bonferroni method.

FIGURE 3 (a,b) Results for the parallel analysis of task data (a) and resting-state data (b). The red dotted lines indicate the confidence intervals for the results of the parallel analysis; the black line indicates the real eigenvalues obtained with the PCAs. The vertical lines indicate the number of PCs retained. (c–f) Davies-Bouldin (DB) and BIC values for each k tested using k -means and GMM clustering. The asterisks indicate the k associated with the optimal solution [Color figure can be viewed at wileyonlinelibrary.com]

2.2.5 | Principal components and cortical networks

As recently pointed out by Margulies, Ghosh, Goulas, Falkiewicz, and Huntenburg (2016), both human and macaque cortices show a principal gradient in functional connectivity, which dissociates regions associated with primary sensory processing (visual, somatomotor, and auditory regions) from “transmodal” DMN regions. A second gradient seems to dissociate between auditory/somatic and visual modalities (Margulies et al., 2016). To explore the relationship between principal components and brain networks, the normalized probability density of each network along principal components was calculated and plotted in two-dimensional (2D) scatter plots, together with single brain parcel scores. We generated the plots as follows: a 2D grid was created for each pair of principal components; for each network, the normalized probability density was calculated for each pixel of the grid (i.e., for each combination of principal component scores); networks with probability densities larger than 0.5 were plotted using corresponding network colors; single brain parcels were then plotted as black dots. This diagram would be more informative than a simple scatter plot of the 360 parcels.

3 | RESULTS

3.1 | PCA and parallel analysis

Figure 3a,b shows the results of the PCA and parallel analysis. For the PCA on task beta values, the first four components showed eigenvalues above the distribution generated by parallel analysis or near the 95% confidence interval. Regarding the PCA on functional connectivity

z-values, this was true for the first 10 components. We used these 14 components as inputs for the clustering procedure. The BIC and Davies-Bouldin values obtained for different values of k are represented in Figure 3c–f. Appropriate numbers of clusters were selected as the ones associated with the global minima among these values. Sixteen networks (clusters) were selected for the GMM clustering using task and rest data; 14 networks for the k -means clustering using task and rest data; 12 networks for the GMM clustering using only rest data; 14 networks for the k -means clustering using only rest data.

Significant effects for the factors *clustering procedure* and *data structure* were detected in the 2×2 ANOVA ($F = 13,063$, $p \ll .001$ for *clustering procedure*; $F = 1,264$, $p \ll .001$ for *data structure*). The interaction term *clustering procedure* $\times$ *data structure* was significant ($F = 526$, $p \ll .001$). Multiple comparisons (using Tukey's HSD) of marginal means revealed that GMM clustering led to a better replication, and that within both GMM and k -means clustering there was a significantly higher replication ($p \ll .001$ for all pairwise comparisons) when the data structure included both task and rest data (means and standard deviations of the adjusted Rand indices z-scores: GMM = 1.53 ± 0.17 ; GMM, rest only = 1.24 ± 0.21 ; k -means = 0.85 ± 0.12 ; k -means, rest only = 0.79 ± 0.11). Figure 4a shows the adjusted Rand indices obtained using the four clustering procedures (GMM, k -means, GMM using only rest data; k -means using only rest data) on the parcellation (210P) and validation (210V) data sets.

Given the high number of cycles used ($N = 1,000$), it can be argued that the significant differences between clustering procedures may be inflated by the sample size. To exclude this possibility, we repeated the procedure with different numbers of cycles for each clustering ($N = 100$, $N = 500$): results were equivalent to the case in

FIGURE 4 (a) Correspondence between parcellation and validation architectures with data reduction. Z-scores were analyzed (and reported) to avoid skewness in the data. (b) Anatomical correspondence between parcellation (left) and validation (center) architectures. The best clustering obtained in the whole procedure (GMM using both task and rest data) is illustrated. Parcels which were assigned to the same network for both parcellation and validation are depicted in yellow (right) [Color figure can be viewed at wileyonlinelibrary.com]

which 1,000 cycles were used (p values still $\ll 0.001$). The same results were obtained when using the adjusted mutual information index (Figure S5). Summarizing, the results indicated that the GMM clustering with an input data structure of joint task and rest data provided the highest replicability.

3.2 | Anatomical profiles

The 16 networks detected by BNP through GMM clustering are visualized in Figure 4c and included: two core default networks (DMN1 and DMN2), a lateral default network (IDMN), a limbic network (Limb), a language network (Lan), two DANs (proximal DAN, pDAN, and distal DAN, dDAN, named according to their spatial arrangement with respect to the central sulcus), a network located in the temporo-parietal-occipital junction (TPOJN), a frontoparietal network (FPN), a cingulo-opercular network (CON), three visual networks (Vis1, Vis2, and Vis3), two somatomotor networks (SM1 and SM2), and an auditory network (Aud).

3.3 | Functional profiles

For a clearer description of the results, we group the networks considering previous partitions of the cortex (Doucet et al., 2011; Hacker et al., 2013; Power et al., 2011; Yeo et al., 2011) and studies focusing on distinct brain subsystems (Andrews-Hanna et al., 2010; Corbetta & Shulman, 2002; Dosenbach et al., 2008; Heed et al., 2016; Sereno,

Lutti, Weiskopf, & Dick, 2013; Uddin, Kinnison, Pessoa, & Anderson, 2014).

The topographies of the 16 networks obtained through BNP are visualized in the first column of Figures 5–7 and their functional profiles are illustrated in the second and third columns of the same figures. The nomenclature adopted for brain parcels and brain sections follows the one used in Glasser et al. (2016). p values related to the one-sample t tests for task-related activity are also reported in these figures. When needed, we report results obtained through multiple pairwise comparisons of task activity and functional connectivity. Notably, all possible comparisons were carried out, but we report only those that are theoretically most relevant. All the p values reported in the text below are Bonferroni corrected for the total number of performed comparisons.

3.3.1 | Default networks

The task profile of DMN1 showed only negative values: this was the only network which was significantly deactivated in all tasks. DMN2 was significantly activated during the *cue* presentation of the motor task. In line with previous studies (Shulman et al., 1997), the deactivation of DMN regions was particularly strong in the language tasks. However, DMN1 was significantly less deactivated than DMN2 during the *story* condition of the language task ($p < .001$), while we observed the opposite trend in the *math* condition of the same task ($p = .10$). Furthermore, DMN2 was less deactivated than DMN1 in

FIGURE 5 Functional profiles of default, limbic, and language networks. In each row, a network's anatomical profile is represented (left column), together with mean beta values in the considered tasks (central column) and the mean connectivity with other networks (z-values, right column). Bars represent the SE of the mean. Asterisks indicate activity levels significantly different from zero (*** $p < .001$, ** $p < .01$, * $p < .05$ after correction for multiple comparisons). For a detailed list of parcels affiliated to each network, see Table S1 [Color figure can be viewed at wileyonlinelibrary.com]

both conditions of the gambling task ($p < .001$ for the *punish* condition, $p = .004$ for the *reward* condition), in the *tongue* condition of the motor task ($p < .001$) and in the 2-back task (*body*: $p = .001$; *place*: $p = .07$; *tool*: $p = .002$).

The functional connectivity profiles of DMN1 and DMN2 showed the following differences: DMN1 was more connected with IDMN than DMN2 ($p < .001$), while DMN2 exhibited higher connectivity with CON ($p < .001$), FPN ($p < .001$), SM2 ($p = .04$), and dDAN ($p = .002$).

Unlike DMN1 and DMN2, the IDMN exhibited significant activations in both conditions of the social tasks (especially in the *theory of mind*, *ToM*, condition) and in the *LFoot*, *RFoot*, and *RHand* conditions of the motor task. Furthermore, while the IDMN was deactivated in most visual tasks, it was slightly activated in the *face* and *body* conditions of the 0-back task.

In comparison with both DMN2 and DMN1, IDMN was more connected with Lan ($p < .001$ for both contrasts). When compared to DMN1, IDMN was more connected with DMN2 ($p < .001$) and with CON ($p = .01$) whereas DMN1 was more connected with Limb ($p < .001$). Comparing IDMN and DMN2, the latter was more connected with both CON and FPN ($p < .001$ for both contrasts).

3.3.2 | Limbic network

The Limb was significantly activated in the *place* conditions of both the 2-back and the 0-back working memory tasks, in the *body* condition of the 0-back task, and in the *ToM* condition of the social task. It was significantly deactivated in both conditions of the language task, in both conditions of the gambling task, and in the *LHand* and *tongue* conditions of the motor task.

FIGURE 6 Functional profiles of attentional and control networks. In each row, a network's anatomical profile is represented (left column), together with mean beta values in the considered tasks (central column) and the mean connectivity with other networks (z-values, right column). Bars represent the SE of the mean. Asterisks indicate activity levels significantly different from zero (*** $p < .001$, ** $p < .01$, * $p < .05$ after correction for multiple comparisons). For a detailed list of parcels affiliated to each network, see Table S2 [Color figure can be viewed at wileyonlinelibrary.com]

A distinctive functional connectivity profile was detected for Limb: it exhibited a relatively low functional connectivity with all networks, including itself. However, this does not mean that this network is not coupled with any other network. For example, Limb showed a stronger coupling with DMN1 and IDMN compared to CON, pDAN, and dDAN ($p < .001$ for all contrasts), and a stronger coupling with sensory networks compared to FPN ($p < .001$ for Vis1, Vis2, Vis3, SM1, and SM2; $p = .003$ for Aud).

3.3.3 | Language network

Lan was activated in both conditions the language task and of the social task. In addition, it was activated in the *cue*, *LFoot*, *RFoot*, and *tongue* conditions of the motor task, in the *face* condition of both the 2-back and the 0-back tasks, in the *body* condition of the 0-back task, and in the *match* condition of the relational task. Lan showed a high

functional coupling with TPOJN, IDMN, and Aud, and revealed a differential connectivity with DMNs, being more connected with IDMN than with DMN1 and DMN2 ($p < .001$).

3.3.4 | Attentional networks

Among attentional networks, pDAN exhibited a significant positive modulation during motor (*cue*, *LFoot*, *RFoot*, and *tongue*) and social tasks (both conditions). In addition, it was significantly activated in the *shapes* condition of the emotion task, whereas it was significantly deactivated during the language tasks. Instead, dDAN was significantly engaged in all tasks, but not in the motor tasks (except for the *cue* presentation). DDAN also showed a differential modulation by the language tasks, being activated in the *maths* condition (n.s. after Bonferroni correction) but deactivated in the *story* condition. Compared to pDAN, dDAN showed higher activity in all the conditions of working memory,

FIGURE 7 Functional profiles of sensory and motor networks. In each row, a network's anatomical profile is represented (left column), together with mean beta values in the considered tasks (central column) and the mean connectivity with other networks (z-values, right column). Bars represent the SE of the mean. Asterisks indicate activity levels significantly different from zero (** $p < .001$, ** $p < .01$, * $p < .05$ after correction for multiple comparisons). For a detailed list of parcels affiliated to each network, see Table S3 [Color figure can be viewed at wileyonlinelibrary.com]

gambling, relational and emotion tasks ($p < .001$ for all contrasts) and in the *math* condition of the language task ($p = .04$). Regarding differences in functional connectivity, pDAN was more connected with the two somatomotor networks ($p < .001$ for SM1, $p = .002$ for SM2), while dDAN was more connected with FPN ($p < .001$).

The TPOJN was significantly involved in both conditions of the social task, in the *body* condition of both working memory tasks, in the *face* condition of the 2-back task, in both conditions of the gambling task, in the *match* condition of the relational task, and in both conditions—especially in *face*—of the emotion task. It was also

recruited in the motor task (*cue*, *LFoot*, *RFoot*, and *tongue*). It was deactivated during the language task.

DDAN was more engaged than TPOJN in working memory, gambling and relational tasks ($p = .02$ for *face* in the 2-back task; $p = .03$ for *face* in the 0-back task; $p < .001$ for the remaining conditions), during the *math* condition of the language task ($p = .01$), and during the *shapes* condition of the emotion task ($p < .001$). On the other hand, TPOJN was more connected than dDAN with sensory networks (Vis1, $p = .01$; SM1, $p = .002$; SM2, $p < .001$; Aud, $p < .001$), with default networks (DMN1 and IDMN, $p < .001$), and with Lan ($p < .001$).

The task profile of pDAN and TPOJN did not show significant differences, although two differential modulations can be noticed: first, concerning the emotion task, TPOJN is more activated in the *faces* condition, whereas pDAN is recruited only in the *shapes* condition; second, in the social task, pDAN is more engaged during the *random* movement of objects on the screen, while TPOJN is more engaged in the *ToM* condition. In addition, TPOJN was more connected than pDAN with Aud ($p = .01$), LAN ($p < .001$), and IDMN ($p < .001$).

3.3.5 | Fronto-parietal and cingulo-opercular networks

FPN and CON activation profiles were similar, being both activated in the working memory, gambling, social, and relational tasks. Furthermore, they were both significantly deactivated in the *story* condition of the language task. However, FPN showed higher activity in all the conditions of the 2-back task ($p < .001$ for *face* and *place*, $p = .001$ for *body*, and $p = .004$ for *tool*), but not in the 0-back task ($p > 1.00$ for all conditions). On the other hand, CON showed higher—and significant—activity during all the conditions of the motor task ($p < .001$ for all conditions).

Regarding functional connectivity, CON had higher connectivity with sensory, attentional, and language networks ($p = .004$ for LAN, $p < .001$ in all the remaining comparisons), whereas FPN showed higher connectivity with the default networks ($p < 0.001$ for the three comparisons). The functional connectivity of CON and FPN with Limb was not different ($p > 1.00$).

Together with Limb and SM2, CON and FPN included most parcels of the insular lobe. Remarkably, these networks differed not only in their task profiles but also regarding their functional connectivity patterns. Compared to CON, Limb was more connected with default networks (DMN1, IDMN: $p < .001$ for both). Compared to Limb, CON was more connected with attentional (dDAN and pDAN: $p < .001$), somatomotor (SM1: $p = .001$; SM2: $p < .001$), and Auditory ($p < .001$) networks. Comparing SM2 and CON, SM2 exhibited higher connectivity with every other network ($p < .001$), except FPN, dDAN, pDAN, and DMN2 ($p > 1.00$). FPN was more connected than SM2 with DMN2 ($p < .001$). In contrast, SM2 was more connected than FPN with every other network except dDAN ($p = .13$), DMN1 ($p > 1.00$), and IDMN ($p > 1.00$). Similarly, compared to Limb, SM2 was more connected with most other networks ($p < .001$), but not with DMN2, IDMN, and FPN ($p > 1.00$).

3.3.6 | Sensory and motor networks

The visual networks (Vis1, Vis2, and Vis3) were positively modulated during visual tasks and deactivated in both conditions of the language task. In addition, Vis1 and Vis2 were significantly deactivated in the motor task, except for the *cue* presentation. However, Vis2 showed higher activation than both Vis1 and Vis3 in many tasks ($p < .001$ for all conditions of the working memory, relational, gambling, and emotional tasks). Moreover, activity in Vis3 was higher than in Vis1 for the *face* and *body* conditions of working memory tasks ($p < .001$ for *body*, $p = .003$ for *face* in the 2-back task, $p = .001$ for *face* in the 0-back task), in the *LHand* and *RHand* conditions of the motor task ($p = .002$ for both), in both conditions of the social task ($p < .001$ for both), and in both conditions of the emotion task ($p < .001$ for both). Activity in

Vis3 was higher than in Vis2 in the *LHand* and *RHand* conditions of the motor task ($p = .04$ for *LHand*, $p = .001$ for *RHand*), and in the *random* condition of the social task ($p = .008$).

Functional connectivity with Aud and SM2 was higher for Vis1, compared to Vis2 and Vis3 (contrasts with Vis2: $p = .01$ for Aud, $p < .001$ for SM2; contrasts with Vis3: $p = .007$ for Aud, $p = .003$ for SM2). In addition, in comparison with Vis3, Vis1 was more connected with DMN2 ($p = .005$). Finally, Vis3 was more connected with pDAN than Vis2 ($p = .005$).

The two somatomotor networks SM1 and SM2 were activated during the motor and social tasks. Both networks were significantly deactivated in the gambling and language tasks. Furthermore, SM1 was deactivated in the *face* and *place* conditions of the 2-back task, in the *relational* condition of the relational task, and in the *shapes* condition of the emotion task. SM2 showed stronger deactivations in all the working memory tasks and in the emotion task. However, there were no significant differences in the task-related activity between SM1 and SM2. Nevertheless, the two networks had distinguishable FC profiles, with SM2 showing a stronger connectivity with CON ($p < .001$), and with Aud ($p < .001$). Notably, activity in SM1 during the *LHand* and *RHand* condition was not significant, and the standard errors related to this network during conditions of the motor task are particularly high. This is because hand motion causes strong deactivations in the ipsilateral motor cortex, whereas this effect is less conspicuous for lower limb movements.

Aud was significantly activated in language, emotion, and motor (*cue*, *LFoot*, *tongue*) tasks. It was generally deactivated during visual tasks. Although Aud expressed a task profile which is profoundly different from SM2, these two networks share a very similar FC profile. Only two differences are noticeable: first, functional connectivity with Lan was higher for Aud than for SM2 ($p < .001$); second, functional connectivity with CON was higher for SM2 than for Aud ($p = .01$).

3.4 | Principal components and cortical networks

The probability density of each network along principal components is shown in Figure 8. The first principal component associated with FC data (fcPC1) distinguished between sensory networks (visual, somatic, and auditory) and *transmodal* networks (default, frontoparietal, and limbic). The third principal component associated with FC (fcPC3) discriminated sensory modalities, dividing visual networks from somatic/auditory networks. These two PCs reflect the results from the first two principal gradients in Margulies et al. (2016), and we labeled them *internal-external* and *visual-audiosomatic*, respectively. The second principal component associated with FC (fcPC2) discriminated networks associated with higher-order cognitive functions (FPN, CON, and dDAN) from sensory and default networks. We labeled this component as *high-low*.

The first principal component associated with the task data (tPC1) identified networks strongly activated during externally oriented visual tasks at one extreme, and networks deactivated by such tasks on the other end. Instead, the second principal component (tPC2) essentially distinguished networks related to auditory/linguistic tasks from networks involved in other modalities (which were mainly visual).

FIGURE 8 Scatter plots of the first three FC principal components (a) and of the first two TASK principal components (b). The normalized probability density of each network is plotted using corresponding colors. Each black dot represents a single parcel. Axes for fcPC1 and fcPC3 are reversed to match the figure from Margulies et al. (2016). Higher color intensity indicates higher probability density. We report here only the first three PCs for FC because of the drop in the eigenvalues after the third component; see Figure S6 for the scatter plots of the further components. Cortical representations of the principal components are illustrated in Figures S7 and S8 [Color figure can be viewed at wileyonlinelibrary.com]

We labeled these two task principal components as *activations-deactivations* and *visual-linguistic*, respectively.

3.5 | Posterior probabilities

Most brain parcels showed a high posterior probability of belonging to their own network: 97% of the parcels (348 out of 360) had a posterior probability above 0.95; 98% of the parcels (353 out of 360) had a posterior probability above 0.90. Brain parcels that showed a relatively low posterior probability (<0.90 ; $N = 7$) were mostly located in the cortical midline, particularly in the anterior and posterior cingulate cortices (right 23c, right 7m, left d32, left d23ab), but also included the right frontal pole (a10p), the left anterior temporal cortex (left TE1a), and the left dorsolateral prefrontal cortex (8Ad). Among these seven regions with a relatively low posterior probability, one parcel belonged to the CON (right 23c), whereas the remaining six were included in default networks (right 7m, left d23ab and left 8Ad: DMN1; right a10p and left d32: DMN2; left TE1a: IDMN; see Figure S9).

4 | DISCUSSION

BNP detected a high-resolution brain architecture consisting of 16 nonoverlapping cortical brain networks with distinct functions. To the best of our knowledge, this is the first study of the functional architecture of the brain including at the same time task-related activity and resting-state functional connectivity through the extraction of latent features from biologically representative subregions. Results show that the GMM clustering granted a higher replicability across the HCP parcellation and validation data sets. Furthermore, using both resting-state and task data remarkably improved the replication, compared to including only resting-state data. The reproducibility of the *rest + task* based architecture is also corroborated by the high posterior probabilities among parcels for their network and by the low number of nonreplicated parcels (4 out of 360, $\approx 1\%$ for the high-

resolution architecture). We describe in detail our findings considering previous insights in the brain functional architecture and studies of task-related activity and connectivity as follows.

4.1 | The diversified organization of the DMN

The DMN has been defined as an evolutionarily conserved network (Mantini et al., 2011) that is deactivated during most goal-directed behavior (Raichle, Macleod, Snyder, et al., 2001). However, recent evidence suggests that the DMN is not always uniformly suppressed (Buckner, Andrews-Hanna, & Schacter, 2008; Spreng, 2012), suggesting the existence of functional subsystems within this network. On the one hand, there is evidence for an anterior-posterior segregation, where the two partitions could be related to autobiographical and episodic memory, respectively (McDermott, Szpunar, & Christ, 2009; Sestieri, Corbetta, Romani, & Shulman, 2011). On the other hand, there is evidence for a division in medial and lateral networks, which could be associated with the processing of self-relevant constructs and of social information, respectively (Andrews-Hanna et al., 2014; Braga, Buckner, Braga, & Buckner, 2017).

BNP identified three networks within classic DMN regions: DMN1, DMN2, and IDMN. DMN1 and IDMN largely overlapped with the core DMN and the dorsal subsystem described in Andrews-Hanna et al. (2014) and Yeo et al. (2011). LDMN encompassed dorsomedial and inferior prefrontal cortex, lateral temporal cortex, and the angular gyrus. Coherent with previous studies, this network was actively recruited in social tasks (Nicholson, Roser, & Bach, 2017; Wheatley, Milleville, & Martin, 2007). LDMN was also activated by motor tasks, whereas it showed deactivations in most other tasks. Differently, DMN1, which incorporated midline components of the classic DMN, was deactivated in all tasks. DMN2, which comprised the cingulate cortex and inferior parietal lobule, also showed consistent deactivations, but not during the cue presentation in the motor task.

Although the default networks shared similar functional connectivity profiles, we found IDMN to be more connected with Lan, while

DMN1 was more connected with Limb, and DMN2 was more connected to CON and FPN. Recent studies reported the involvement of DMN regions in narrative comprehension (Simony, Honey, Chen, et al., 2016) and, together with limbic regions, in creative processes (Beaty, Benedek, Silvia, & Schacter, 2017; Shi, Cao, Chen, Zhuang, & Qiu, 2017) as well as in the decoding of emotions conveyed by music (Bashwiler, Wertz, Flores, & Jung, 2016). Considering this evidence, we suggest a prominent role of IDMN in social and linguistic tasks (see also "Insights into the language system" section), and a stronger involvement of DMN1 in autobiographical, imaginative, and emotional/affective functions. Through its connection with higher-order networks CON and FPN, the DMN2 may regulate the participation of the individuality in conscious experiences monitoring, for example, the balance between perceptual and memory functions (retrosplenial cortex, Vann, Aggleton, & Maguire, 2009) and the disengagement of the self from the external world (mid-cingulate and inferior parietal cortices: Singer et al., 2004; Vogt, 2016).

4.2 | Attentional networks

BNP detected three networks including regions associated with attentional processes, namely, pDAN, dDAN, and TPOJN. DDAN was strongly activated in most tasks. Moreover, together with Aud and Lan, dDAN was the only network activated in the *maths* condition of the language task. TPOJN and pDAN were mainly recruited by the motor and social tasks. In addition, pDAN showed higher activity during the *random* condition of the social task and the *shapes* condition of the emotion task, while TPOJN showed higher activity in the *ToM* and the *faces* conditions of these two tasks.

Fronto-parietal regions ascribed to pDAN and dDAN are involved in the planning of eye and limb movements (Colby & Goldberg, 1999; Filimon, Nelson, Huang, & Sereno, 2009), in visual attention (Gillebert et al., 2011; Shulman et al., 2003), in mental rotation of objects and calculation (Amalric & Dehaene, 2016; Dehaene, 1999). The primate parietal cortex is suggested to be organized according to a functional-to-effector gradient from the posterior to the anterior end (Heed et al., 2016; Leonè et al., 2014). This organization is thought to have a correspondence in the frontal lobe, symmetrically with respect to the central sulcus (Burnod et al., 1999; Caminiti et al., 2015). Our findings support the existence of (a) a general dorsal attention network (dDAN) which encompasses non-effector-specific regions related to visual attention, motor planning, and calculation, and (b) a second network proximal to the primary motor cortex (pDAN) and specifically involved in sensorimotor processes and shape detection. According to Heed et al. (2016), and differently from dDAN, pDAN may carry effector-specific information. The evidence listed above led us to label these two networks according to their spatial arrangement with respect to the motor cortex.

With respect to TPOJN, regions in the temporoparietal junction are involved in attentional reorienting both following external stimulation and during the processing of memory-based information (Cabeza, Ciaramelli, & Moscovitch, 2012), suggesting a general role of these regions in contextual updating (Geng & Vossel, 2013). Indeed, there are several sub-processes of executive working memory that probably rely on the differential interactions of many networks depending on

the ongoing task (Cole et al., 2013; Di Plinio et al., 2018). Thus, through a flexible interplay with other systems (Mars et al., 2012; Vossel, Geng, & Fink, 2014), TPOJN may be involved in the reorientation of attention when external or internal information is interfering with the ongoing behavior. The development of an attentional system connected with both default and executive systems during human evolution (Kaas, 2013; Patel, Yang, Jamerson, Snyder, & Corbetta, 2015) may have favored the conscious control over an increased repertoire of internal/external triggers that guide the behavior.

4.3 | Insights into the language system

Lan was consistent with the language network described in Hacker et al. (2013), enclosing auditory association regions, premotor cortex, and areas in the left temporoparietal junction. Lan was engaged in language and social tasks and was strongly connected with both TPOJN and Aud. Moreover, it was significantly more connected with IDMN than with other default networks. Together, Lan and IDMN encompass the cortical language system (Friederici, 2017; Skeide & Friederici, 2016). However, temporal regions of these two networks are involved in different functions. In fact, the superior temporal gyrus (Lan) is part of the semantic stream (Lopopolo, Frank, Van Den Bosch, & Willems, 2017) and is primarily implicated in passive listening but not reading (Hagoort & Indefrey, 2014). In contrast, the middle temporal gyrus (IDMN) is recruited during passive reading as well as in listening (Hagoort & Indefrey, 2014), and is associated with the syntactic stream (Lopopolo et al., 2017). Furthermore, regions of the IDMN are involved in tasks with higher semantic demands (Hagoort & Indefrey, 2014), and in the initial stages of learning new languages (Weber, Christiansen, Petersson, Indefrey, & Hagoort, 2016).

Considering this evidence, we suggest that BNP identified two networks with distinctive linguistic functions. Further studies are necessary to characterize the differential role of Lan and IDMN in language processing. Given the importance of IDMN regions in understanding observed actions (Nicholson et al., 2017; Wheatley et al., 2007) and in syndromes associated with social impairment (Besnard, Allain, Lerma, et al., 2016; Conchiglia, Della Rocca, & Grossi, 2007), this network may constitute a link between internal thoughts and semantic knowledge stored in the temporal lobe, articulating internally generated information in socially meaningful elements (gestures or sounds).

4.4 | Visual networks within a comprehensive visual system

The primary visual network (Vis1) encompassed primary visual cortex and early regions of the dorsal and ventral streams. A second visual network (Vis2) overlapped with the RN8 described in Doucet et al. (2011), including lateral and ventral occipital regions. Vis1 and Vis2 were activated during the visual tasks and deactivated during the motor and linguistic tasks. Vis2 generally showed higher levels of activations in most tasks. The third visual network (Vis3), composed of the MT complex and more anterior and dorsal cortical regions, was not deactivated during motor tasks and was particularly recruited during social tasks (i.e., the only visual task involving moving objects).

Compared to Vis2 and Vis3, Vis1 was significantly more connected with other sensory networks (Aud, SM2). Vis3 was more connected with pDAN than Vis2. Interestingly, the spatial extent of the composite visual system defined by BNP (Vis1 + Vis2 + Vis3) is coherent with cortical regions showing a consistent retinotopic organization (Serenio et al., 2013; Wang, Mruczek, Arcaro, & Kastner, 2015).

This evidence suggests that BNP detected a cortical visual system related to the topographic representation of visual input from the retina. Within this system, Vis1 is associated with the first stages of visual processing, Vis2 encompasses mainly areas of the ventral stream, and Vis3 includes areas related to the dorsal stream and to the analysis of moving objects in the visual field. Including retinotopic data may allow more accurate profiling of visual subsystems.

4.5 | Sensory and higher-order networks in the insular lobe

Among studies that focused on functional specializations within the insular lobe, many agreed on a tripartite model where the anterior-dorsal, anterior-ventral, and posterior insula are related to cognitive, affective, and sensorial functions, respectively (Deen, Pitskel, & Pelphrey, 2011; Uddin et al., 2014). We identified five networks in the insular lobe: CON encompassed dorsal anterior insular parcels; FPN comprised the anterior area AVI; Limb included the ventral anterior insula; SM2 enclosed the intermediate and posterior insula; Aud comprised posterior ventral insular parcels.

Among these networks: CON was significantly activated during visual and motor tasks; FPN was activated during visual tasks and showed a modulation due to the cognitive load (2-back > 0-back); SM2 was recruited only in motor and social tasks; Limb showed significant activity in the *place* conditions of the two working memory tasks and in the *ToM* condition of the social task. In addition, from anterior-ventral to posterior-dorsal insular networks, an increase in connectivity with higher order and sensory networks can be noticed, together with a decrease in connectivity with default networks.

Overall, our partition obtained with BNP supports the tripartite functional model of the insular lobe. The ventral anterior insula was part of Limb. The posterior insula was included in sensory networks associated with somatomotor and auditory modalities. Finally, the dorsal anterior insula was associated with CON and FPN.

Some issues about the insular organization remain unanswered. For example, the mid-insular cortex (included in SM2) is known to be involved in interoception as well as in the analysis of gustatory and olfactory stimuli (Avery et al., 2015; Gasquoine, 2014), whereas tasks involving these modalities are lacking in our study. Furthermore, some nodes (e.g., right anterior insula) show strong lateralization during task execution (Uddin et al., 2014), but the present approach did not highlight any extensive network lateralization.

4.6 | Control networks

There is evidence for FPN to be particularly related to adaptive flexible control (Dosenbach et al., 2008; Zanto & Gazzaley, 2013) exerted through variable connectivity with other brain networks (Cole et al., 2013). By contrast, CON seems involved in stable-set maintenance

and tonic alertness (Coste & Kleinschmidt, 2016; Sadaghiani & Espósito, 2015). Two main differences in the task profile were observed between FPN and CON: first, task-related activity in the FPN was higher in all the conditions of the working memory 2-back task, but not in the 0-back task; second, activity in the CON was higher in all the conditions of the motor task.

Our findings support the involvement of CON and FPN in maintaining task-relevant information (Dosenbach et al., 2007). We also confirm a differential association of FPN and CON with default and executive/sensory networks, respectively. CON likely integrates task-specific and task-unspecific cognitive control during goal-directed behavior through its functional interactions with other networks, including sensory networks (Ebisch, Mantini, Romanelli, et al., 2013). It remains an open issue why the human brain needs two systems which share a similar task-driven engagement, but at the same time express strikingly different patterns of functional connectivity. Considering our findings, tasks with increasing cognitive demands and motor tasks may be a good starting point for this investigation.

4.7 | Network profiles along principal components

Our results extend the observations by Margulies et al. (2016) concerning principal gradients of functional connectivity. We confirm the existence of such gradients also in principal components estimated along brain parcels. The *internal-external* component discriminated between sensory networks on the one end, and Limbic, FPN, and default networks on the other end. Among negative scorers in the *internal-external* component, there was a slight differentiation in the *visual-audiosomatic* component: the score for DMN1 and DMN2 was closer to zero, whereas FPN showed a slightly more positive score (closer to visual) and the score of IDMN and LAN was negative (closer to audiosomatic). Considering these findings as well as task activity profiles of these three networks, it can be speculated that FPN and IDMN constitute links between self-related processing, generally associated with core default regions (Northoff, Qin, & Nakao, 2010; Northoff & Sibille, 2014) and different sensorial modalities. Interestingly, the two DANs were differentiated by the *visual-audiosomatic* component consistently with their functional profiles: while dDAN was adjacent to visual networks, pDAN was closer to somatic/auditory networks. We also distinguished a *high-low* component, which discriminated CON and FPN at one extreme, while sensory and default networks (DMN1 and IDMN) were at the opposite extreme.

Among the task-related PCs, the *activations-deactivations* and *visual-linguistic* components essentially described the recruitment of brain networks in visual (first PC) and linguistic (second PC) tasks. Since ours is one of the first studies that investigate the PCs of the functional connectivity in cortical networks, the description of the link between the two remains preliminary.

4.8 | Methodological considerations and limitations

To define the network architecture, we used clustering algorithms aimed at identifying nonoverlapping networks, but functional networks may also be overlapping (Nomi et al., 2016). Fuzzy clustering methods may overcome this limit, with the possible disadvantage of

producing less distinct clusters (Panda, Sahu, Jena, & Chattopadhyay, 2012). Moreover, whereas our results show that GMM clustering better fits our starting data, this is not always necessarily true. Our findings imply that clustering algorithms should generally be compared when dealing with data structures for which a priori assumptions cannot be made.

The selection of the input data structure for the PCAs as well as a method for retaining PCs is a critical point to be considered. The implementation of the parallel analysis to select the ideal number of PCs allowed to define a high-resolution brain architecture consisting of functionally specialized networks. Conversely, a low-resolution architecture made up of heterogeneous networks was defined without data reduction (for a description of the low-resolution architecture, see Supporting Information). Through a Monte Carlo simulation which starts from a data structure with the same characteristics of the real data and estimates the ideal number of PCs to retain, the parallel analysis allowed to preserve the most appropriate information to define brain subsystems. Instead, including additional PCs blurred the boundaries of such subsystems. The diversity within low-resolution networks corroborates the usefulness of the data reduction to catch subtle differences between brain subsystems.

Selecting the most relevant PCs ensures that we are using the most distinctive intrinsic (rest) and extrinsic (task) features for clustering. Instead, PCs with a low eigenvalue are probably representing subtle differences among highly related parcels. For example, regarding the PCA on resting-state data, while PCs related to large eigenvalues (i.e., the first 10 PCs) are capturing distinctive features of functional connectivity, most PCs with low eigenvalues are conditioned by the existence of very high correlations among highly related parcels. Therefore, many of the latter PCs likely represent the difference in functional connectivity patterns among highly related parcels, which may not be useful to estimate high-resolution networks. The parallel analysis is adopted in many fields of research as it outperforms other methods, like scree tests, chi-square tests, "eigenvalue greater than X" rules, and maximum likelihood methods (Humphreys & Montanelli, 1975; Patil et al., 2010; Silverstein, 1990; Zwick & Velicer, 1986). Importantly, this statistical-simulation approach to the selection of the number of components to retain increases the reproducibility of the study itself and allows to use the same criterion to determine the number of PCs to retain for both rest and task PCAs.

A major disadvantage of the present study is the relatively small number of tasks included. Adding more tasks involving various cognitive demands would improve the accuracy of the resolution of brain networks and their functional characterization (i.e., autobiographical and episodic memory tasks; language production and auditory listening blocks; tasks involving different sensory modalities; tasks with distractors).

Second, BNP did not replicate some previously identified networks topographies. For example, the primary somatomotor network SM1 fails to identify the division between hands and face representations, because this division was intentionally omitted in the characterization of the parcellation used (Glasser et al., 2016). We recognize that the implementation of our method (or upgraded versions of it) to other parcellations and data sets would provide future topics for the neuroscientific research. For example, the application of the BNP to

the Schaefer et al. (2017) progressive parcellations may be useful to study subnetworks and clustering performances using task and rest data by gradually increasing the resolution of the parcellation. However, we recognize that the parcellation used in our study is the only multimodal parcellation available so that parcels are likely to represent biological sub-units of the human cortex (Glasser et al., 2016).

As already pointed out by Glasser et al. (2017), some aspects of the preprocessing steps of fMRI data used in the present work are currently under consideration. For example, the present preprocessing pipeline does not remove spatially specific structured noise (Griffanti et al., 2014; Salimi-Khorshidi et al., 2014). These aspects remain a fundamental purpose of the HCP and are under investigation by the scientific community.

Finally, our approach did not consider cortical hubs (De Pasquale, Della Penna, Snyder, et al., 2012; Power, Schlaggar, Lessov-Schlaggar, & Petersen, 2013) that likely constitute a relevant dimension to consider when characterizing networks (Bullmore & Sporns, 2012; De Pasquale, Della Penna, Sabatini, Caravasso Falletta, & Peran, 2017). Hopefully, graph theory parameters (e.g., cortical hubs) can be integrated soon in further BNP developments.

5 | CONCLUSIONS

BNP allowed the characterization and the description of the functional properties of brain networks, starting from both task-induced activity and resting-state functional connectivity data. The high-resolution functional architecture obtained by BNP provides useful insights into the understanding of the function signatures of brain networks. Although the brain architecture here presented should not be considered *the ultimate network configuration*, our findings open a new approach with enhanced sensitivity and reliability toward the study and the comprehension of the functional architecture of the brain with increasing complexity.

ACKNOWLEDGMENTS

We thank Cosimo Del Gratta for his comments and the reviewers for their critical and constructive feedback on previous versions of the manuscript. This work was supported by Fundação Bial grant 195/16 to SE. Data were provided by the Human Connectome Project (HCP), the Washington University, University of Minnesota, and University of Oxford Consortium (Principal Investigators David Van Essen and Kamil Ugurbil; Grant 1U54MH091657) funded by 16 NIH Institutes and Centers that support the NIH Blueprint for Neuroscience Research, and the McDonnell Center for Systems Neuroscience at Washington University.

CONFLICT OF INTEREST

The authors declare no competing financial interests.

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How to cite this article: Di Plinio S, Ebisch SJH. Brain network profiling defines functionally specialized cortical networks. *Hum Brain Mapp*. 2018;39:4689–4706. <https://doi.org/10.1002/hbm.24315>