Persistency and Flexibility of Complex Brain Networks Underlie Dual-Task Interference

Mohsen Alavash,^{1,*} Claus C. Hilgetag,^{2,3} Christiane M. Thiel,^{1,4} and Carsten Gießing^{1,4}

¹Department of Psychology, Biological Psychology Lab, European Medical School, Carl von Ossietzky Universität Oldenburg, 26111 Oldenburg, Germany

²Department of Computational Neuroscience, University Medical Center Hamburg-Eppendorf, 20246 Hamburg, Germany

³Department of Health Sciences, Boston University, Boston, Massachusetts 02215

⁴Research Center Neurosensory Science, Carl von Ossietzky Universität Oldenburg, 26111 Oldenburg, Germany

Abstract: Previous studies on multitasking suggest that performance decline during concurrent task processing arises from interfering brain modules. Here, we used graph-theoretical network analysis to define functional brain modules and relate the modular organization of complex brain networks to behavioral dual-task costs. Based on resting-state and task fMRI we explored two organizational aspects potentially associated with behavioral interference when human subjects performed a visuospatial and speech task simultaneously: the topological overlap between persistent single-task modules, and the flexibility of single-task modules in adaptation to the dual-task condition. Participants showed a significant decline in visuospatial accuracy in the dual-task compared with single visuospatial task. Global analysis of topological similarity between modules revealed that the overlap between single-task modules significantly correlated with the decline in visuospatial accuracy. Subjects with larger overlap between single-task modules showed higher behavioral interference. Furthermore, lower flexible reconfiguration of single-task modules in adaptation to the dual-task condition significantly correlated with larger decline in visuospatial accuracy. Subjects with lower modular flexibility showed higher behavioral interference. At the regional level, higher overlap between single-task modules and less modular flexibility in the somatomotor cortex positively correlated with the decline in visuospatial accuracy. Additionally, higher modular flexibility in cingulate and frontal control areas and lower flexibility in right-lateralized nodes comprising the middle occipital and superior temporal gyri supported dual-tasking. Our results suggest that persistency and flexibility of brain modules are important determinants of dual-task costs. We conclude that efficient dual-tasking benefits from a specific balance between flexibility and rigidity of functional brain modules. *Hum Brain Mapp* 36:3542–3562, 2015. © 2015 Wiley Periodicals, Inc.

Key words: multitasking; interference; modularity; flexibility; fMRI; complex networks

Additional Supporting Information may be found in the online version of this article.

Contract grant sponsor: Hanse-Wissenschaftskolleg (M.A. and C.G.); Contract grant number: DFG (TH766-6/1) (C.M.T.); Contract grant sponsor: Cluster of Excellence Hearing4all (C.M.T.); Contract grant number: SFB 936/A1 (C.C.H.)

This study was performed at the Department of Psychology, Carl von Ossietzky Universität Oldenburg, and Pius Hospital, Oldenburg, Germany.

Conflict of interest: The authors declare no competing financial interests.

*Correspondence to: Mohsen Alavash; Department of Psychology, Carl von Ossietzky Universität Oldenburg, Ammerländer Heer St. 114-118, 26111 Oldenburg, Germany. E-mail: mohsen.alavash@uni-oldenburg.de

Received for publication 5 February 2015; Revised 27 April 2015; Accepted 19 May 2015.

DOI: 10.1002/hbm.22861

Published online 12 June 2015 in Wiley Online Library (wileyonlinelibrary.com).

INTRODUCTION

When subjects perform two tasks concurrently, their performance often declines compared with the single-task conditions. The cognitive architecture underlying these dual-task costs has been investigated by several behavioral and neuroimaging experiments [Huestegge et al., 2014; Klingberg, 1998; Lien et al., 2006; Marois and Ivanoff, 2005; Pashler, 1994]. In brief, it has been argued that dual-task interference can occur at different processing stages, including sensory processing, central processing, or response selection (see Schweickert et al. [2012], chapters 5, 6, and Franconeri et al. [2013], for a summary). Recent studies suggest that the brain's capacity limit in dual-tasking results from interference between neural processes [Cohen et al., 2014; Nijboer et al., 2014; Remy et al., 2010]. Nevertheless, the limiting organizational factors which impose constraints on the brain's capacity in dual-tasking are unclear.

Series of behavioral experiments conducted by Magen and Cohen [2007, 2010] suggest that dual-task interference results from overlapping cognitive modules involved in both tasks. However, most cognitive theories define modules as abstract computational entities without relating them to the concrete brain network organization. In this study, we use complex network and graph-theoretical analysis to investigate how the modular organization of functional brain networks relates to behavioral dual-task costs.

Graph-theoretical studies have demonstrated that the brain exhibits complex interactions between its interconnected processing nodes which are organized into modules [Bassett et al., 2010a; Bassett and Gazzaniga, 2011; Meunier et al., 2010]. Modules characterize specialized functional units whose interplay regulates the behavior of a complex system such as the brain [Gaspar and Csermely, 2012]. How this modular organization relates to behavior in dual-task conditions is unknown. Considering training effects in dual-tasking [Dux et al., 2009], one can associate dual-task costs not only with the interference between overlapping modules, but also the inability of brain networks to adapt to a challenging dual-task condition.

In the present study, we conducted an fMRI experiment in which subjects first performed two tasks one after the other, followed by performing both tasks in parallel (Fig. 1A). We used complex network analysis to relate dual-task interference to the persistency and flexibility of functionally defined brain network modules. We asked whether topological overlap between single-task modules (persistency of modules) predicted dual-task interference. Furthermore, we asked whether, as a consequence of the adaptation to the dual-task condition, the reconfiguration of single-task modules (flexibility of modules) predicted better performance in the dual-task condition (Fig. 1C, see Bassett et al. [2010b], for a similar facilitatory effect of network flexibility in the context of motor learning). To answer both questions, we employed a unified graph-

theoretical approach to quantify topological similarity between task-related network modules (Fig. 1D). It was hypothesized that the topological similarity between single-task network modules is associated with higher dual-task interference, as higher similarity suggests larger overlap between component task modules in the dual-task condition, thereby increasing interference. We also expected that topological similarity between each single-task and the dual-task network modules is associated with higher dual-task interference, as in this case higher similarity suggests lower flexibility in the adaptive reconfiguration of component task modules.

MATERIALS AND METHODS

Subjects

Twenty-four healthy, right-handed subjects (12 females, 12 males, all native German speakers) whose age was in the range of 19–32 years (mean = 24.22 years, standard error of mean [SEM] = 0.74 years) participated in the experiment. Two male subjects showed large head movements during scanning (more than 4 mm of translation or degrees of rotation) and were excluded from further analyses. Ethical approval was obtained from the ethics committee of the University of Oldenburg. All procedures were carried out with written informed consent of all subjects and in accordance with the principles of the Declaration of Helsinki. Subjects received a monetary compensation for their participation.

Experimental Design and Tasks

Each scanning session was divided into four runs (Fig. 1A): resting-state, single-task 1, single-task 2, and dual-task. The order of the single-tasks was randomized across subjects.

Resting-state

During the resting-state scan subjects were instructed to lie still inside the scanner, close their eyes and not to think about something specific for around 13 min (512 functional volumes).

Single visuospatial task

During the single visuospatial task [adapted from Hilgetag et al., 2001] subjects were asked to report the location of small Gabor patches briefly presented either in the left or right visual periphery on a grey background using the left middle or index finger, respectively (Fig. 1A). Each trial started by presenting a fixation cross for 1,000 ms. Following the fixation cross a peripheral target appeared for 40 ms at ~20 degrees of visual angle. There were also trials on which no target was presented (catch trials). Each trial ended by changing the fixation cross into a question

Figure 1.

mark, asking the subject to report the target location by pressing one of two response buttons as quickly and accurately as possible. The contrast of Gabor patches was fixed at two different levels, one easy (standard deviation of pixel intensities = 0.026) and one difficult (standard deviation of pixel intensities = 0.012), to avoid ceiling or floor effects. There were 40 trials for each left and right condition and 60 catch trials. The order of conditions was randomized across trials.

Single speech task

During the single speech task subjects were asked to discriminate two target consonant-vowels (CVs) as either /da/ or /ga/ (recorded from a male German native speaker) presented together with a band-limited Gaussian white-noise (cut-off frequency = 4 kHz) (Fig. 1A). In addition to the target CVs, a third speech sound /ba/ was presented in synchrony with the target CVs, but at a lower intensity, to make the task sufficiently challenging. The difference between the intensity of the target CVs (I_t) and /ba/ (I_b) was fixed at two different levels, one easy ($\frac{20 \log I_t}{I_b} = 12 \text{ dB}$) and one difficult ($\frac{20 \log I_t}{I_b} = 4 \text{ dB}$), to avoid ceiling or floor effects. Subjects were instructed to discriminate the compound speech sounds presented in the back-

ground noise as either /da/ or /ga/. Subjects reported their discrimination using the right middle or index finger (complementary to the use of the left hand in the visuospatial task). Correspondence between the target CVs and fingers was randomized across subjects. Each trial started by presenting a fixation cross for 1,000 ms. Following the fixation cross a compound speech sound was presented together with the background noise. After 40 ms the fixation cross turned into a question mark, asking the subject to report the target CV by pressing one of two response buttons as quickly and accurately as possible. There were also trials on which no speech sound was presented (catch trials). There were 40 trials for each /da/ and /ga/ condition and 60 catch trials. The order of conditions was randomized across trials.

Dual-task

During the dual-task subjects performed the visuospatial and speech tasks in parallel (Fig. 1A). There was no delay between the onsets of the visuospatial and speech stimuli to ensure strong interference between both component tasks. Subjects kept using the same hand and fingers to report their responses. Each trial started by presenting a fixation cross for 1,000 ms. Following the fixation cross a

Figure 1.

Illustration of the paradigm, behavioral results and methodological framework of the study. **(A)** Experimental Design: Each subject was measured in four different conditions: (1) Resting-state scan: Subjects were instructed to rest inside the fMRI scanner and close their eyes. (2) Visuospatial task: Subjects were asked to report the location of small Gabor patches briefly presented either in the left or right visual periphery using their left middle or index finger, respectively. The contrast of the Gabor patches was adjusted at two difficulty levels: one easy and one difficult (see Materials and Methods). Here, Gabor patches are magnified and the scene size is shrunk for clear illustration. (3) Speech task: Subjects were instructed to discriminate two compound CVs as either /da/ or /ga/ using their right middle or index finger. The speech sounds were presented in synchrony with a band-limited Gaussian white-noise, and were mixed with a third speech sound /ba/ to make the task challenging. Correspondence between the target CVs and fingers was randomized across subjects. (4) Dual-task: Subjects performed the visuospatial and speech tasks in parallel. Subjects kept using the same hand and fingers to report their responses. The order of the single tasks was randomized across subjects. **(B)** Accuracy and Reaction Times During Single-Task and Dual-Task Conditions. Bars illustrate mean accuracy and mean of median reaction times. Error bars represent standard error of means. **(C)** Methodological Framework: Visualization of brain modules derived from a representative subject. Arrows illustrate the hypothesized associations between the brain network modules and dual-task interference. High topological overlap between single-task

network modules (persistence of modules) can lead to interference effects during dual-task processing. In contrast, higher topological reconfiguration of single-task network modules in adaptation to the dual-task condition (flexibility of modules) possibly leads to less behavioral dual-task interference. Both hypotheses were tested based on the topological similarity between network modules across different task conditions. **(D)** Quantification of Topological Similarity Between Task-Related Network Modules: To estimate the topological similarity between brain network modules, the nodal composition of a pair of modules (m, n) was compared across task-related networks g_1 and g_2 and similarity weights $\omega_{m,n}$ were computed which reflect the percentage of common nodes between modules (m, n). For example, comparing the module $m = 1$ of the toy graph g_1 on the left side and the module $n = 1$ of the toy graph g_2 on the right side, the two modules share one common node (i.e., node 9) out of six nodes, resulting in the $\omega_{1,1} = \frac{1}{6}$. Similarity weight $\omega_{m,n}$ ranges between zero (nonoverlapping modules) and one (completely overlapping modules). The similarity weights derived from this procedure were then summed and the result was divided by the total number of module comparisons (in our example 9) to obtain a global measure of topological similarity between modules across two networks. To visualize the task-related brain networks in graph space, the Fruchterman-Reingold algorithm was used to find the optimal node placement for each network with respect to its modules, and the Kamada-Kawai algorithm was employed to place the nodes within each network module [Traud et al., 2009].

Gabor patch was briefly presented either in the left or right visual periphery. This was concurrent with the presentation of a compound speech sound together with the background noise. After 40 ms the fixation cross turned into a question mark, asking the subject to report the response to each component task as quickly and accurately as possible. To reduce the subjective expectancy due to successive dual presentation of visuospatial and speech targets, there were also trials on which no visuospatial stimulus, or no speech stimulus, or neither stimuli was presented (catch trials). Note that in the dual-task, all stimuli were presented at the easy levels. There were 20 trials for each combination of {visuospatial, speech} condition and 60 catch trials. The order of conditions was randomized across trials.

The duration of each task period (single visuospatial, single speech and dual-task) was approximately 9 min (327 functional volumes).

Scanning Parameters

T2*-weighted gradient echo planar imaging volumes with blood-oxygen-level-dependent contrast were recorded by means of a 3-Tesla MRI scanner (Siemens MAGNETOM Verio (Siemens AG, Erlangen, Germany): Repetition time (TR) = 1.5 s, echo time (TE) = 30 ms, flip angle (FA) = 80 degrees, voxel size = 3×3×3.5 mm, between-slice gap = 0.87 mm, number of slices = 27, image size = 64×64 pixels). Structural T1-weighted images (TR = 1.9 s, TE = 2.52 ms, FA = 9 degrees, voxel size = 0.9×0.9×1 mm, number of slices = 176, image size = 256×256) were acquired after completion of functional scans.

Analysis of Behavioral Data

Performance of the subjects during single-tasks was measured by means of average accuracy (%) and median reaction time [ms; Baayen and Milin, 2010]. To capture the decline in performance in the dual-task condition, we focused on the accuracy and median reaction times for detecting easy visuospatial (vs) and easy speech (sp) targets under single (visuospatial_{easy} and speech_{easy}) and dual-task (dual_{vs} and dual_{sp}) conditions. A measure of decline in accuracy, namely *interference score*, was assigned to each subject with respect to each single visuospatial (interference_{vs}) and speech (interference_{sp}) task:

$$\text{interference}_{\text{vs}} = \text{visuospatial}_{\text{easy}} - \text{dual}_{\text{vs}} \quad (1)$$

$$\text{interference}_{\text{sp}} = \text{speech}_{\text{easy}} - \text{dual}_{\text{sp}} \quad (2)$$

A positive interference score indicates a decline in accuracy in adaptation to the dual-task condition. To make estimates of interference in terms of reaction time (RT) consistent with those of accuracy, the order of the terms in the right-hand side of the Eqs. (1) and (2) for reaction times was reversed (e.g., interference_{vs} = dual_{vs} - visuospatial_{easy}). Thus, for both accuracy and RT, a positive interference score

indicates decline in performance in the dual-task compared with the single-task condition. A median split applied to each type of interference scores divided the subjects into two groups, namely high-interference and low-interference, with respect to visuospatial or speech performance.

Preprocessing of Functional Data

After removing the first nine images to account for possible T1 saturation effects, the functional images were corrected for head motion by spatially realigning them to the first volume using SPM8 [Wellcome Trust Centre for Neuroimaging, University College London; Frackowiak et al., 2004]. The functional images were spatially normalized to standard stereotaxic MNI space [Montreal Neurological Institute; <http://www.mni.mcgill.ca/>]. No spatial smoothing was applied on the images in order not to induce artificial correlations between the time series which subsequently constitute the input data for functional connectivity analysis.

Removing the Effects of External Stimulation from Task Data

One issue in functional connectivity analyses of task data is indirect correlations between processing nodes, which are induced by a common input to the nodes as a result of the external presentation of stimuli [McIntosh and Korostil, 2008; Smith et al., 2011]. External stimulation of one or different modalities evokes temporally correlated activities between brain nodes; however, this coactivation does not necessarily imply direct information flow between these regions. To diminish the effect of external stimulation in task-related data and exclude functional connections that only reflect indirect correlations, a general linear model (GLM) with finite impulse response basis functions was used, so that fMRI data were predicted in different task conditions. Subsequently the residual data obtained from the GLM (referred to as Task_{res} data from now on) was used for connectivity analysis [Cole et al., 2014; Zhang and Li, 2010].

Connectivity Analysis and Network Construction

For resting-state (RS) as well as Task_{res} (see above) data a parcellated AAL template [Tzourio-Mazoyer et al., 2002] covering 506 cortical regions was used to estimate the mean fMRI time series for each cortical region per subject [Fornito et al., 2010; Zalesky et al., 2010]. In addition to this anatomical template, a functional template [Craddock et al., 2012] comprising 518 cortical nodes was used to test whether the effects were present when networks were constructed based on a functional parcellation (results are presented in Supporting Information Fig. S1). To minimize the effects of spurious temporal correlations induced by physiological and movement artifacts, a GLM was used to regress out the six rigid-body movement parameters, and the white-matter as well as cerebrospinal fluid mean time series [Jo et al., 2013]. It has been

previously shown that behavioral correlates of brain network topology are best observed in the low-frequency functional networks [Achard et al., 2006; Alavash et al., 2014; Bassett et al., 2010b; Giessing et al., 2013]. Therefore, regional time series were band-pass filtered by means of maximum overlap discrete wavelet transform (Daubechies wavelet of length 8; Percival and Walden [2000]), and the results within the range of 0.08–0.17 Hz (wavelet scale 2) were used for further analyses. The use of scale 2 was motivated by prior findings showing that experimentally induced changes in attentional performance [Giessing et al., 2013], or behavioral scores in a numerical working memory task [Alavash et al., 2014] predominately correlated with changes in functional connectivity in the same frequency range.

To obtain a measure of association between each pair of cortical regions, Pearson correlations between wavelet coefficients were computed which in turn gave 506 by 506 correlation matrices for each resting-state (RS) and Task_{res} data per subject. A recent study by Cole et al. [2014] suggests a new framework for functional connectivity analysis based on the intrinsic versus evoked network architectures, where the authors documented that the brain's functional network architecture during task performance is shaped primarily by an intrinsic network architecture that is also present during rest, and secondarily task-evoked network changes. In this study, context-dependent changes in functional connectivity during task execution, as compared to resting-state, were captured by subtracting RS correlation matrices from correlation matrices generated from Task_{res} data. This subtraction was applied on the signed weighted correlation matrices, and the resulting functional connectivity matrices were thresholded based on the absolute difference in correlation values. If the strength of the absolute difference in correlations survived a connectivity threshold, the corresponding signed connection weights were kept in the matrix. This procedure can be viewed as contrasting connectivity patterns during task performance with those of resting-state to capture task-induced changes in functional connectivity [Cole et al., 2014]. Note that while lower values obtained from this subtraction represent a functional shift toward the resting-state, higher values capture functional connections engaged more in task processing. In summary, prior to graph construction and network analysis we (1) diminished artificially induced indirect correlations and (2) focused our analysis on those functional connections which showed an increase in connectivity during task processing in comparison to resting-state.

Different approaches have been used to construct brain graphs from functional connectivity matrices and statistically analyze network diagnostics [Fornito et al., 2013; Van Wijk et al., 2010]. One approach is to investigate brain graphs across different network densities by including edges in the graph according to the rank of their correlation values [Alexander-Bloch et al., 2010; Ginestet et al., 2011]. Other studies have used specific significance or p -value thresholds instead of rank values to remove spurious correlations [Achard et al., 2006; Bassett et al., 2010b]. Note that, given a fixed sample size, a significance (or p -value) threshold can be directly transferred into a correlation threshold. In our analysis, we combined both

approaches using different correlation values to threshold the absolute correlation matrices on different levels of significance. This approach did not artificially force different (i.e., visuospatial, speech or dual) task networks to have the same number of edges, and allowed us to document that the effects did not depend on a specific significance threshold. In summary, 50 equally distributed connectivity thresholds in the range of 0.01–0.50 were applied to the “Task_{res} minus RS” (see above) connectivity matrices to obtain adjacency matrices, based on which signed weighted undirected graphs were constructed. The results obtained from thresholding the graphs at fixed network densities are also presented and discussed in Supporting Information Figure S2.

Detection of Functional Network Modules

Unlike most other network measures, the optimal modular structure for a given network is typically estimated with optimization algorithms, rather than computed exactly [Steinhaeuser and Chawla, 2010]. The quality of the partitions resulting from a given method is often measured by the so-called *modularity* (Q) index. Here we incorporated a widely-used modularity measure originally proposed by Newman [2006], and used its implementation in the Brain Connectivity Toolbox [Rubinov and Sporns, 2010] which generalizes the modularity maximization algorithm known as Louvain [Blondel et al., 2008] to signed weighted undirected graphs. Let us denote the presence of a positively weighted connection between nodes i and j by $a_{ij}^+ = 1$ and $a_{ij}^- = 0$, and its corresponding connection weight by $w_{ij}^+ \in (0, 1]$, $w_{ij}^- = 0$ (equivalently for a negatively weighted connection: $a_{ij}^- = 1$, $a_{ij}^+ = 0$, and $w_{ij}^- \in (0, 1]$, $w_{ij}^+ = 0$). The strength of node i is defined as the sum of connection weights of i for each of the positive or negative graph representations, i.e., $s_i^\pm = \sum_j w_{ij}^\pm$, and the total weight as the sum of all connection weights (counted twice for each connection), i.e., $v^\pm = \sum_{ij} w_{ij}^\pm$. To take the sign of connection weights into account, Rubinov and Sporns [2011] proposed the following quality index for decomposition of brain graphs into modules:

$$Q^* = Q^+ + \frac{v^-}{v^+ + v^-} Q^- \quad (3)$$

where

$$Q^+ = \frac{1}{v^+} \sum_{ij} \left(w_{ij}^+ - \gamma^+ e_{ij}^+ \right) \delta_{m_i m_j} \quad (4)$$

and

$$Q^- = -\frac{1}{v^-} \sum_{ij} \left(w_{ij}^- - \gamma^- e_{ij}^- \right) \delta_{m_i m_j} \quad (5)$$

Similar to the classical measure of network modularity [Newman, 2006], $e_{ij}^\pm = \frac{s_i^\pm s_j^\pm}{v^\pm}$ is the probability of a connection between i and j under the assumption of randomly

distributed edges, $\delta_{m_i, m_j} = 1$ when i and j are in the same module and $\delta_{m_i, m_j} = 0$ otherwise, and $\gamma^\pm$ are structural resolution parameters [Fortunato and Barthelemy, 2007; Lohse et al., 2014] which for simplicity are set to unity in our case [as in Bassett et al., 2010b]. For further details and a discussion on the contribution of Q^+ and Q^- to the modularity index Q^* the reader is referred to Rubinov and Sporns [2011].

Due to stochastic initialization of the greedy optimization, the module detection algorithm was applied 100 times for each network per connectivity threshold, and the partition which delivered the highest Q^* value was kept (see Bassett et al. [2013] and Lancichinetti and Fortunato [2012] for other approaches to construct representative high-modularity partitions).

Estimating Topological Similarity between Network Modules

The aim of our similarity analysis was to quantify (1) the topological overlap between brain network modules involved in both single-tasks and (2) the nodal flexibility of single-task modules in adaptation to the dual-task condition, thereby investigating the relation between persistency and flexibility of complex brain networks and dual-task interference effects. We hypothesized that the persistency of single-task network modules predicts interference effects during dual-task processing. Furthermore, we expected that the flexible reconfiguration of single-task network modules in adaptation to the dual-task condition predicts better dual-task performance. To quantify the topological persistency and flexibility of brain network modules we computed the so-called Jaccard index [Steen et al., 2011]. Here, the Jaccard index estimated the nodal similarity between two modules m and n , each obtained from a modular decomposition of a task-related graph. The Jaccard index was computed by dividing the number of brain nodes which belonged to both modules m and n (the intersection of both modules) by the number of brain nodes which belonged to brain modules m or n or both (the union of both modules). Accordingly, for a given module m of graph g_1 and module n of graph g_2 which consist of two sets of nodes $\{\text{nodes}\}_{g_1}^m$ and $\{\text{nodes}\}_{g_2}^n$ respectively, similarity weight $\omega_{m,n}$ is given by:

$$\omega_{m,n} \equiv \frac{|\{\text{nodes}\}_{g_1}^m \cap \{\text{nodes}\}_{g_2}^n|}{|\{\text{nodes}\}_{g_1}^m \cup \{\text{nodes}\}_{g_2}^n|} \quad (6)$$

This procedure gave us a similarity weight for each pair of brain modules across two task-related networks g_1 and g_2 (see Fig. 1D, similarity weights range between zero and one).

To estimate the topological similarity between single-task modules we compared each pair of modules across the networks obtained under single visuospatial (vs) and single speech (sp) task conditions (i.e., g_{vs} and g_{sp}). When

single-task modules are highly similar and persistent in their nodal composition, a high similarity weight is obtained, indicating larger topological overlap between modules, and potentially greater interference during dual-task processing. This way, we used the similarity weights obtained from comparing single-task network modules as an indication of the modular persistency in the context of dual-task processing.

To estimate the topological similarity between each single-task and the dual-task modules, we compared each pair of modules across the single visuospatial (or single speech) task network and the dual-task network (g_{dual}). In this case, a higher similarity weight would indicate lower nodal flexibility or less reconfiguration of a given task (visuospatial or speech) module in adaptation to the dual-task condition. Accordingly, we used the similarity weights obtained from comparing each single-task and the dual-task network modules as an inverse indication of the modular flexibility in the context of dual-task processing.

In summary, we used a unified approach based on the consistency in nodal composition of brain network modules to quantify network correlates of interference and flexibility in the context of dual-tasking. Similar approaches to the one undertaken here have been used to compare the consistency of community structures [Moussa et al., 2012; Steen et al., 2011], to estimate the accuracy of a predicted community structure in the context of network modularity [Ruan and Zhang, 2008] or to characterize dynamic modular evolution of brain networks in the course of learning [Bassett et al., 2010b].

To obtain a network diagnostic as a global measure of similarity between network modules per subject, similarity weights derived from comparing two task-related networks g_1 and g_2 were averaged:

$$\Omega_{g_1, g_2} \equiv \frac{\sum_m \sum_n \omega_{m,n}}{M \times N} \quad (7)$$

where Ω_{g_1, g_2} is the mean similarity between network modules, and M and N are the number of modules in networks g_1 and g_2 respectively (see Fig. 1D). Finally, the relation between mean similarity values and behavioral interference scores was statistically tested as described in the following section.

Statistical Analysis

Behavioral data

Median reaction times and average accuracies obtained from responses to target stimuli were compared between different task conditions (i.e. single vs. dual trials) and stimulus conditions (visuospatial stimuli: left or right Gabor patches; speech stimuli: the consonant-vowel /da/ or /ga/) by means of repeated measures analyses of variance (ANOVA). Prior to applying a median split to the interference scores [Eqs. (1) and (2)], the distributions of the

scores across subjects were statistically analyzed by means of the bootstrap Kolmogorov-Smirnov test with 10,000 repetitions to ensure that the data derive from a normally distributed population. The bootstrap Kolmogorov-Smirnov test, unlike the traditional Kolmogorov-Smirnov test, allows the presence of ties in the data [Sekhon, 2011]. The significance of the correlations between the four different types of behavioral interference scores (Eqs. (1) and (2) for accuracy and RT) was tested by means of rank-based nonparametric Spearman's ρ correlation [Spearman, 1904] and permutation tests with 10,000 permutations [Pesarin and Salmaso, 2010] applied to the correlation coefficients.

Global similarity between network modules

The relationship between global similarity of task-related modules and behavioral dual-task interference was investigated through three analyses. As described above, a median split applied to the behavioral interference scores divided the subjects into *high-interference* and *low-interference* groups with respect to visuospatial or speech performance.

First, to statistically test whether mean similarity between modules was significantly different between these two groups, mean similarities were averaged per subject over the whole range of connectivity thresholds (threshold-averaged mean similarity). The difference between the two groups in threshold-averaged mean similarities was then tested by means of a two-sample permutation test [Pesarin and Salmaso, 2010] with 10,000 repetitions (Fig. 2, first column, p -value). To visualize the difference between the two groups in terms of mean similarity between modules across a wide range of connectivity thresholds, mean similarities were averaged within each group per connectivity threshold (group mean similarity), which yielded group-specific mean similarities at each threshold (Fig. 2, first column, visualization).

Second, to ensure that the significant effect was not present only at a specific connectivity threshold, mean similarity for each subject was taken at each connectivity threshold, and the mean similarities were compared between high- and low-interference subjects by means of a two-sample permutation test with 10,000 repetitions (Fig. 2, second column).

Finally, the significance of the Spearman's ρ correlation between mean similarities and interference scores obtained for all subjects was tested by applying a permutation test on the correlation coefficients at each connectivity threshold with 10,000 repetitions (Fig. 2, third column). The Spearman's rank-order correlation [Spearman, 1904] provides a nonparametric statistic that can be used to detect monotonic trends in ordinal data that are not measured on an interval scale [Chen and Popovic, 2002]. The most significant correlation between mean similarities and interference scores was then visualized (Fig. 2, fourth column) where we plot the linear relationship between mean similarities and interference scores together with its parametric confidence interval for the confidence level of 0.95.

The first statistical analysis was conducted on the whole (integrated) range of the connectivity thresholds, whereas the second and the third analyses were applied at each discrete threshold.

Degeneracy of network modularity

Due to the presence of degenerate partitions of the network modularity function Q^* [Good et al., 2010], the module detection algorithm together with the global similarity analyses were repeated 100 times to ensure that the effects did not depend on a specific degenerate partition.

Nodal similarity between network modules

The goal of the nodal analysis was to identify brain regions where the mean similarity between brain network modules was significantly different between high- and low-interference subjects. To this end, first at each connectivity threshold the similarity weights $\omega_{m,n}$ [see Eq. (6)] were assigned to the set of brain nodes $\{i\}$ where module m of graph g_1 overlapped with module n of graph g_2 , i.e., $\{i\} \in \{\{\text{nodes}\}_{g_1}^m \cap \{\text{nodes}\}_{g_2}^n\}$. The similarity weights were then averaged over connectivity thresholds per brain node, which yielded a measure of node-specific mean similarity per subject. These node-specific mean similarities were compared between high- and low-interference groups by means of a two-sample permutation test with one million repetitions which adequately sampled the distribution of the p -values before and after the correction for multiple comparisons (see below). To statistically measure the difference between the two groups we used the Cliff's delta [Cliff, 1996] as a nonparametric measure of effect size. The Cliff's delta estimates the probability that a selected observation from one group is greater than a selected observation in another group minus the reversed probability, and thus represents the degree of overlap between two distributions. This statistic ranges from -1 (in our case when all mean similarity weights in the low-interference subjects are larger than all mean similarity weights in the high-interference group for a specific brain node) to $+1$ (if all mean similarity weights in the high-interference subjects are larger than all mean similarity weights in the low-interference group) and takes the value of zero if the two distributions are identical. Due to its ordinal structure, Cliff's delta is an appropriate effect size if data are not normally distributed (see Macbeth et al. [2011], page 547 for further details).

Significance thresholds

For statistical inference on behavioral and global network metrics we used $p < 0.05$ (two-sided) as the threshold of significance. In the context of the multiple comparisons entailed by the analysis of nodal similarities we used the Holm-Bonferroni method [Holm, 1979] to compute Family-wise Error Rates (FWE) and applied a significance threshold of $p < 0.01$ (two-sided). In contrast to the

Hochberg [1988] FWE correction, the method of Holm [1979] corrects for alpha-inflation without any further assumptions on the distribution of the test statistics.

RESULTS

Decline in Performance

Measures obtained from single-task and dual-task performance along with interference scores are summarized in Table I. Reaction times in response to visuospatial and speech targets were significantly delayed in the dual-task

compared with the single-task conditions (see Table II for details). Moreover, visuospatial accuracy was significantly impaired in the dual-task compared with the single visuospatial task condition, whereas speech accuracy was not significantly affected (Fig. 1B). In the case of the visuospatial task, reaction time data showed a significant task by target interaction (Table II); the increase in median reaction times in the dual-task condition was significantly larger for the right than left targets, but still significant for both, left and right targets (the p -values obtained from permutation tests for repeated measures were smaller than 0.0001 in both cases).

Figure 2.

TABLE I. Behavioral data obtained under the single task (separately for easy and difficult targets) and the dual-task conditions, and mean of the interference scores

		Easy targets	Difficult targets	Responses in the dual-task condition	Interference score ^a
Acc ^b	visuospatial	92.04 ± 1.8	68.86 ± 3.6	88.35 ± 2.2	3.57 ± 1.4
	speech	78.63 ± 3.0	75.79 ± 3.3	73.46 ± 3.5	4.94 ± 3.6
RT ^c	visuospatial	554 ± 19.0	613 ± 20.0	1026 ± 33.0	473 ± 36.0
	speech	846 ± 30.0	882 ± 37.0	1142 ± 33.0	296 ± 38.0

^aMean of interference scores ± SEM

^bMean accuracy (%) ± SEM

^cMean of median reaction times (ms) ± SEM

The results of the bootstrap Kolmogorov-Smirnov test suggest that the distributions of the interference scores [see Eqs. (1) and (2)] did not significantly deviate from a normal distribution (interference_{vs} in accuracy: $p = 0.17$; interference_{sp} in accuracy: $p = 0.18$; interference_{vs} in RT: $p = 0.57$; interference_{sp} in RT: $p = 0.34$).

There was a trend for a significant correlation between interference scores in visuospatial performance in terms of accuracy and reaction time ($\rho = 0.42$, $p = 0.055$). This means, in our sample, making more visuospatial errors in the dual-task condition compared to the single visuospatial task was concurrent with longer reaction time to the visuospatial targets, suggesting that the subjects were unlikely to adopt a strategic trade-off between accuracy and reaction time in their visuospatial performance. For speech performance the correlation was not significant

($\rho = -0.2$, $p = 0.346$). For accuracy the correlation between the interference scores in visuospatial and speech performance was $\rho = 0.08$, $p = 0.717$; and for RT the correlation was $\rho = 0.39$, $p = 0.074$. This means, in our sample, performance in the component tasks were not significantly anti-correlated across subjects, suggesting that the subjects were unlikely to have prioritized one component task over the other.

Persistency of Single-Task Network Modules: Global Interference

When single visuospatial and speech task modules were compared (persistency of modules), subjects with higher interference in visuospatial accuracy [i.e., higher

Figure 2.

Global similarities between task-related modules and their relations to the decline in visuospatial accuracy in the dual-task condition. While topological overlap between single-task modules correlated with the decline in visuospatial accuracy during dual-task processing, the flexible reconfiguration of single-task modules in adaptation to the dual-task condition predicted lower behavioral dual-task interference. Participants were grouped into a high-interference (first column, purple) and a low-interference (first column, green) group according to the decline in their visuospatial accuracy in the dual-task condition. Mean similarity between modules was quantified across single visuospatial and speech (**A**), single visuospatial and dual-task (**B**), and single speech and dual-task networks (**C**) to capture persistency (A) and flexibility (B and C) of functional brain network modules in the context of dual-tasking. First column: The mean similarities between task-related modules for high- versus low-interference subjects in visuospatial accuracy are illustrated. The mean similarity weights per subject were integrated across thresholds applied to the connectivity matrices and compared between the two groups by means of a two-sample permutation test with 10,000 repetitions and the resulting p -value (two-sided) was reported. Second column: Differences in mean similarity between both groups were computed (black points) and statistically compared at each connectivity threshold separately by means of permutation tests with

10,000 repetitions. Black points represent the arithmetic difference in means; red points visualize one side of the bias-corrected and accelerated (BCa) bootstrap confidence interval for a two-sided test at $p < 0.05$ [Efron, 1987], and solid points represent significant results obtained from the permutation tests at the significance level of $p < 0.05$ (two-sided). Third column: The Spearman's ρ correlation between mean similarities and interference scores in visuospatial accuracy across all subjects was tested at each connectivity threshold by means of permutation tests with 10,000 repetitions, and the resulting correlation coefficients were considered significant (solid points) if $p < 0.05$ (two-sided). Black points represent the Spearman's ρ correlation coefficients, red points visualize one side of the bias-corrected and accelerated (BCa) bootstrap confidence interval for a two-sided test at $p < 0.05$ [Efron, 1987], and solid points represent significant results obtained from the permutation tests at the significance level of $p < 0.05$ (two-sided). Black and red curves were estimated using local polynomial regression fitting by means of LOESS functions. Fourth column: Visualization of the linear relationship between mean similarity of brain modules and interference scores in visuospatial accuracy across all subjects at the connectivity threshold where the most significant Spearman's ρ correlation was obtained. Shaded area represents the two-sided parametric confidence interval at the significance level of $p < 0.05$.

TABLE II. The results obtained from ANOVA comparing accuracies and reaction times between different task (single vs. dual) and target (visuospatial: left or right, speech: /da/ or /ga/) conditions

		Effect of task ^a		Effect of target ^b		Task × target interaction	
		<i>F</i> (1,21)	<i>p</i> -value	<i>F</i> (1,21)	<i>p</i> -value	<i>F</i> (1,21)	<i>p</i> -value
Acc	visuospatial	9.06	0.007*	2.31	0.10	0.93	0.30
	speech	1.95	0.10	0.33	0.50	0.64	0.40
RT	visuospatial	169.90	1.56 e−11*	3.93	0.06	15.13	0.0008*
	speech	87.94	5.9 e−9*	1.68	0.20	0.04	0.80

* $p < 0.01$ ^aSingle-task versus dual-task^b“left” vs. “right” or “/da/ vs. /ga/”

interference_{vs} scores in accuracy; see Eq. (1)] showed significantly higher mean topological similarities between the single-task modules than low-interference subjects (Fig. 2, first row). The first statistical analysis, which was aimed at comparing the mean similarity weights between low- and high-interference subjects (see Materials and Methods), revealed that, when averaged over the whole range of connectivity thresholds, the two groups significantly differed

in the mean similarity between single-task modules. When mean similarity values were averaged across thresholds per subject, the threshold-averaged mean similarity was significantly higher in the high-interference than low-interference subjects ($p=0.007$, Fig. 2, first row, first column).

Second, when the mean similarity values were separately compared at each discrete connectivity threshold,

TABLE III. Brain regions where nodal similarity between task-related modules was associated with decline in visuospatial accuracy in the dual-task condition

Anatomical label ^a	MNI coordinate ^b			Cliff's delta	<i>p</i> -value ^c
	<i>x</i>	<i>y</i>	<i>z</i>		
(A) Nodal persistency of single-task modules					
Regions where the modular persistency was associated with higher visuospatial impairment					
R pre-/postcentral gyrus	36	−30	63	0.97	0.0045
R fusiform gyrus	28	−56	−13	0.97	0.0035
Regions where the modular persistency was associated with lower visuospatial impairment					
R inferior lingual gyrus	27	−45	−8	−0.97	0.0060
(B) Nodal flexibility of visuospatial task modules in adaptation to the dual-task condition					
Regions where the modular flexibility was associated with lower visuospatial impairment					
L/R posterior cingulate	1	−36	32	0.97	0.0040
L middle occipital gyrus	−33	−76	27	0.97	0.0070
L postcentral gyrus	−56	−25	41	1.00	0.0015
Regions where the modular flexibility was associated with higher visuospatial impairment					
R middle occipital gyrus	38	−70	26	−0.92	0.0066
(C) Nodal flexibility of speech task modules in adaptation to the dual-task condition					
Regions where the modular flexibility was associated with lower visuospatial impairment					
R superior frontal gyrus	8	28	56	0.97	0.0040
R middle frontal gyrus	22	58	−2	1.00	0.0015
L/R anterior cingulate	1	43	22	0.93	0.0070
L/R pre-/postcentral gyrus	−35	−14	46	1.00	0.0015
	36	−30	63	1.00	0.0015
L parahippocampal gyrus	−21	−24	−15	0.95	0.0060
Regions where the modular flexibility was associated with higher visuospatial impairment					
R middle occipital gyrus	38	−70	26	−0.93	0.0060
R superior temporal gyrus	60	−46	12	−1.00	0.0015
R rolandic operculum	50	6	12	−0.95	0.0045

^aL and R abbreviate the left and right hemispheres, respectively^bNode's center of gravity^cFWE corrected *p*-values at the significance level of $p < 0.01$ (two-sided)

high- and low-interference subjects in visuospatial accuracy showed significantly different mean similarity between single-task modules in the range 0.20–0.43 of connectivity thresholds ($p < 0.05$, Fig. 2, first row, second column, solid points).

The third analysis, which was aimed at testing the correlation between the mean similarity weights and the behavioral interference scores (see Materials and Methods), revealed significant positive correlations between mean modular overlap and interference_{vs} scores in accuracy across all subjects at connectivity thresholds in the range 0.24–0.46 ($p < 0.05$, Fig. 2, first row, third column, solid points). The most significant positive correlation was $\rho = 0.63$ ($p = 0.002$) observed at the connectivity threshold 0.35 (Fig. 2, first row, fourth column). To account for degenerate partitions of network modularity [Good et al., 2010] the module detection algorithm and global similarity analyses were repeated 100 times. At the connectivity threshold where the first iteration delivered the strongest correlation, the mean and SEM of the correlations between interference scores in visuospatial accuracy and overlap between single-task modules were $\bar{\rho} = 0.59 \pm 0.005$ (mean p -value = 0.006 ± 0.0005).

In summary, subjects with higher behavioral dual-task interference in accurate detection of visuospatial targets showed larger topological similarity or overlap between functional modules across single-task networks. Similar results were found when the functional parcellation template was used to construct the brain graphs (Supporting Information Fig. S1) or when networks were thresholded according to the rank of their connection weights and compared across different network densities (Supporting Information Fig. S2).

There was no significant correlation between the mean overlap of single-task modules and interference_{vs} scores in RT (result of the first analysis: $p = 0.65$), or interference_{sp} scores in accuracy (result of the first analysis: $p = 0.23$) or interference_{sp} scores in RT (result of the first analysis: $p = 0.21$).

From Single-Task to Dual-Task Condition: Global Flexibility

High-interference subjects in visuospatial accuracy [i.e., those with higher interference_{vs} scores in accuracy; see Eq. (1)] showed higher mean topological similarities between single visuospatial and dual-task modules compared with low-interference subjects (Fig. 2, second row).

The first analysis, which was aimed at comparing the mean similarity weights between low- and high-interference subjects (see Materials and Methods), revealed that the two groups significantly differed in the mean similarity between single visuospatial and dual-task modules. When data were averaged across thresholds per subject, the threshold-averaged mean similarity between single visuospatial and the dual-task modules was significantly higher

in the high-interference than low-interference subjects ($p = 0.007$, Fig. 2, second row, first column).

Second, when the mean similarity values were compared at each discrete connectivity threshold separately, high- and low-interference subjects in visuospatial accuracy showed significantly different mean similarity between visuospatial and dual-task modules in the range 0.23–0.44 of connectivity thresholds ($p < 0.05$, Fig. 2, second row, second column, solid points).

The third analysis, which was aimed at testing the correlation between the mean similarity weights and the behavioral interference scores (see Materials and Methods), revealed significant positive correlations between mean topological similarity of visuospatial with dual-task modules and interference_{vs} scores in accuracy across all subjects at connectivity thresholds in the range 0.23–0.46 ($p < 0.05$, Fig. 2, second row, third column, solid points). The most significant positive correlation was 0.69 ($p = 0.001$) observed at the connectivity threshold 0.28 (Fig. 2, second row, fourth column). For this threshold, the mean correlation obtained from 100 iterations of the analyses was $\bar{\rho} = 0.59 \pm 0.007$ (mean p -value = 0.009 ± 0.001).

There was no significant correlation between the mean overlap of the visuospatial and dual-task modules and interference_{vs} scores in RT (result of the first analysis: $p = 0.82$), or interference_{sp} scores in accuracy (result of the first analysis: $p = 0.42$) or interference_{sp} scores in RT (result of the first analysis: $p = 0.06$).

High- and low-interference subjects in visuospatial accuracy (i.e., interference_{vs} scores in accuracy, see Eq. (1)) also significantly differed in the topological similarity between single speech and dual-task modules (Fig. 2, third row). First, high-interference subjects showed significantly higher threshold-averaged topological similarity, hence less reconfiguration, of speech task modules than low-interference subjects ($p = 0.004$, Fig. 2, third row, first column).

Second, when the mean similarity values were compared at each discrete connectivity threshold, high-interference subjects showed significantly higher similarity over a wide range of connectivity thresholds ($p < 0.05$, Fig. 2, third row, second column, solid points).

The third analysis (see Materials and Methods) revealed significant positive correlations between mean nodal consistency of speech task modules and interference_{vs} scores in accuracy at connectivity thresholds in the range 0.24–0.46, the most significant one being 0.68 ($p = 0.0004$) observed at the connectivity threshold 0.43 (Fig. 2, third row, third and fourth column). For this threshold, the mean correlation obtained from 100 iterations of the analyses was $\bar{\rho} = 0.65 \pm 0.003$ (mean p -value = $0.001 \pm 8 \times 10^{-5}$).

There was no significant correlation between mean overlap of the speech and dual-task modules and interference_{vs} scores in RT (result of the first analysis: $p = 0.8$), or interference_{sp} scores in accuracy (result of the first analysis: $p = 0.1$) or interference_{sp} scores in RT (result of the first analysis: $p = 0.15$).

In summary, subjects with higher behavioral dual-task interference in accurate detection of visuospatial targets

showed higher topological similarity, hence less reconfiguration, of visuospatial and speech task modules in adaptation to the dual-task condition. Similar results were found when the functional parcellation template was used to construct the brain graphs (Supporting Information Fig. S1) or when networks were thresholded according to the rank of their connection weights and compared across different network densities (Supporting Information Fig. S2).

Network Modularity and Number of Modules

The mean and SEM of the modularity index Q^* [Eq. (3)] and the number of modules obtained from the task-related networks in our sample are presented in Supporting Information Figure S3. Note that as the size of a network decreases (in our case by increasing the connectivity threshold), modularity of the network increases, which implies higher number of modules. To investigate whether the between-subject variance in Q^* or the number of modules also explains the inter-individual variability in dual-tasking, we correlated the above-mentioned measures of network modularity with the interference scores in visuospatial accuracy (Fig. 3). There was a significant negative correlation with the modularity of the speech and the dual-task networks (Supporting Information Fig. S4). However, the correlation with the modularity of the visuospatial task network was not significant. Additionally, we found significant negative correlations between the behavioral interference scores and the number of modules in the visuospatial, speech, as well as dual-task networks (Supporting Information Fig. S5).

Maps of Topological Similarity Between Network Modules: Nodal Effects

Consistent with the effects obtained at the global level of the brain networks, we also found significant correlations between the decline in visuospatial accuracy in the dual-task condition and similarity between brain network modules at the nodal level. High-interference subjects showed higher mean topological overlap between modules across single-task networks at nodal level (Fig. 4A, red nodes; Table IIIA). Topological overlap between visuospatial and speech task modules was significantly greater in the high- compared with low-interference subjects in the right fusiform as well as pre- and postcentral gyri. Low-interference subjects, conversely, showed higher topological overlap between single-task modules in the right inferior lingual gyrus (Fig. 4A, blue node; Table IIIA).

Additionally, in adaptation to the dual-task condition, the nodal consistency of visuospatial task modules in brain regions including the posterior cingulate as well as the left middle occipital and postcentral gyri was significantly higher in the high-interference subjects compared with the low-interference subjects (Fig. 4B, red nodes; Table IIIB). The low-interference subjects, conversely, showed higher nodal consistency or less flexibility of visuospatial task

modules in adaptation to the dual-task condition in the right middle occipital gyrus (Fig. 4B, blue node). Finally, and in agreement with the global effects, in adaptation of speech task modules to the dual-task condition we found distributed brain regions where nodal consistency of speech task modules was significantly higher in the high-interference subjects in contrast to the low-interference subjects (Fig. 4C, red nodes; Table IIIC). These brain regions include the right superior and middle frontal gyri as well as the bilateral pre- and postcentral gyri and anterior cingulate. There was also a right-lateralized pattern of brain regions, including the right middle occipital and superior temporal gyri, where the consistency of speech task modules in adaptation to the dual-task condition was greater in the low-interference subjects (Fig. 4C, blue nodes; Table IIIC).

In summary, we were able to find brain regions where topological overlap between single-task modules was predictive for the decline in visuospatial accuracy in the dual-task condition. We also found widely distributed cortical regions whose lower flexibility in adaptation of each single-task to the dual-task condition was predictive for higher interference in dual-tasking. However, there were also brain nodes whose rigidity predicted better performance in the low-interference subjects.

Effects of Head Movements

It has been previously suggested that head movements during fMRI scans can introduce spurious correlations between brain nodes [Power et al., 2012]. To investigate possible confounds induced by head movements, we calculated the so-called *framewise displacement* [Power et al., 2012] based on the six rigid-body movement parameters estimated for each subject, and compared the results across the four runs of measurement (i.e. resting state, both single-tasks and the dual-task) by means of the nonparametric Friedman test [Friedman, 1937]. There was no significant difference between the means of framewise displacement values across runs ($\chi^2=0.8$, $df=3$, $p=0.84$) or the corresponding variances ($\chi^2=0.7$, $df=3$, $p=0.87$). We additionally used the means and variances of framewise displacement values to test their correlations with the behavioral interference scores in visuospatial accuracy [Eq. (1)] by means of nonparametric tests. We found no evidence that our results were affected by the subjects' head movements in the course of scans (see Supporting Information Table S1).

DISCUSSION

In this study, we measured resting-state and task fMRI in single-task and dual-task conditions and asked how the modular organization of task-induced complex brain networks relates to behavior when subjects performed two tasks simultaneously. The mean topological overlap between single-task modules positively correlated with

A Correlations with metrics of visuospatial (left) and speech (right) task networks

B Correlations with metrics of visuospatial (left) and dual-task (right) networks

C Correlations with metrics of speech (left) and dual-task (right) networks

Figure 3.

Correlations between different metrics of network modularity and the decline in visuospatial accuracy in the dual-task condition. Here, we illustrate the magnitude of the Spearman's ρ correlations between the interference scores in visuospatial accuracy and mean topological similarity between modules (red points), modularity Q^* (grey points), or number of modules (orange points) obtained from the task-related networks which were compared in the analysis of persistency (comparison across single task networks (A)) or flexibility (comparison

across a single task and the dual-task network (B/C)). The correlations were tested at each connectivity threshold by means of permutation tests with 10,000 repetitions, and the resulting correlation coefficients were considered significant (solid points) if $p < 0.05$ (two-sided). Differences between the values obtained for a specific metric across different comparisons are due to the stochastic initialization of the modularity detection algorithm. The smooth curves were estimated using local polynomial regression fitting by means of LOESS functions.

Figure 4.

behavioral dual-task costs; subjects with larger overlap between single-task modules showed higher decline in visuospatial accuracy in the dual-task condition. This finding suggests that the overlap between single-task modules is one organizational factor which constraints the brain's capacity in dual-tasking.

Furthermore, we showed that the mean topological similarity between each single-task and the dual-task modules positively correlated with the decline in visuospatial accuracy during dual-task processing. This finding suggests that consistency in the nodal composition of single-task modules in adaptation to the dual-task condition is disadvantageous for dual-tasking. To preserve successful performance under dual-task conditions, the topology of some component task modules needs to be flexibly reconfigured in a challenging dual-task condition. However, there were also brain regions where nodal consistency of modules was beneficial for dual-tasking (see below).

Brain Network Modularity as a Predictor of Task Performance

In recent years, graph-theoretical studies have discovered important organizational principles governing complex brain networks under task conditions, including workspace formation [Kitzbichler et al., 2011], network

flexibility and stability [Ekman et al., 2012; Wang et al., 2012], and rich-club organization [Grayson et al., 2014]. In particular, modularity of brain networks is an important measure which provides insights into the segregation and integration of information processing within the brain [Sporns, 2013]. Several studies have documented the importance of brain network modularity for cognitive performance and its advantage for fast adaptation, robustness of brain functions, and goal-directed behavior [Bassett et al., 2010a; Fornito et al., 2012]. Most of the studies to date have investigated the modularity of brain networks by means of the modularity index known as Q , and also the number of modules obtained from the modular decomposition [e.g., Di et al., 2013; Gamboa et al., 2013; Stevens et al., 2012]. In our sample, the negative correlations between the modularity Q^* and the number of modules with the behavioral interference scores in visuospatial accuracy suggest that, on the global level of the task-related brain networks, higher modularity reduces the behavioral interference in dual-tasking. This facilitation is better observed when one considers specifically the number of modules. Possibly, higher modularity and a larger number of modules lead to less topological overlap between the task-related network modules and reduce the behavioral dual-task interference (see below for a detailed discussion of the unique contribution of the similarity between modules).

Figure 4.

Brain regions where nodal similarity between task-related modules was significantly different between high- and low-interference groups in visuospatial accuracy. **(A)** Persistency of single-task modules. Red nodes: Subjects with larger decline in visuospatial accuracy in the dual-task condition showed significantly larger overlap between single-task modules within the right fusiform as well as pre- and postcentral gyri. Blue node: Low-interference subjects showed significantly higher nodal consistency of single-task network modules in the right inferior lingual gyrus. **(B)** Flexibility of visuospatial task modules in adaptation to the dual-task condition. Red nodes: Participants with larger decline in visuospatial accuracy in the dual-task condition showed significantly higher similarity between single visuospatial and dual-task network modules (that is, lower flexibility of visuospatial task modules) within the posterior cingulate as well as the left middle occipital and postcentral gyri. Blue nodes: Lower flexibility of visuospatial task modules in the right middle occipital gyrus was associated with lower decline in visuospatial accuracy during the dual-task condition. **(C)** Flexibility of speech task modules in adaptation to the dual-task condition. Red nodes: Subjects with larger decline in visuospatial accuracy in the dual-task condition showed higher similarity between speech task and dual-task network modules (that is, lower flexibility of speech task modules) within the right superior and middle frontal gyri, anterior cingulate as well as the bilateral pre- and postcentral gyri. Blue nodes: Lower flexibility of speech task

modules in the right middle occipital and superior temporal gyri and the right rolandic operculum was associated with lower decline in visuospatial accuracy during the dual-task condition. Node-specific mean similarities were compared between high- and low-interference groups by means of two-sample permutation tests with one million repetitions. To visualize the nodal effects, Cliff's delta was used as a nonparametric measure of effect size. Brain nodes are color-coded according to their Cliff's delta value. A positive delta value (red) indicates a significantly higher similarity between modules in high- compared with low-interference subjects. In contrast, a negative delta value (blue) indicates a significantly higher similarity between modules in low- compared with high-interference subjects. Therefore, while higher nodal similarity of modules at red nodes was associated with larger decline in visuospatial accuracy in the dual-task condition, higher similarity of modules at blue nodes predicted lower decline and more accurate visuospatial performance in the dual-task condition. Yellow circle: Within the right somato-motor cortex participants with higher dual-task costs in visuospatial accuracy showed larger modular overlap between single-task modules (A), and lower flexibility of speech task modules in adaptation to the dual-task condition (C). Brain slices: L and R indicate the left and right hemispheres, respectively. The brain volumetric slices represent the group-averaged T1 image and are ordered from the bottom to the top of the brain (left to right) according to their MNI z coordinate (mm).

Dual-task interference has been the focus of many behavioral and neuroimaging studies. Most previous neuroimaging studies have relied on the overlap between conventional activation maps to identify dual-task bottlenecks and to predict dual-task costs [Jiang, 2004; Just et al., 2001, 2008; Schubert and Szameitat, 2003; Szameitat et al., 2002; Watanabe and Funahashi, 2014]. For example, a recent study by Nijboer et al. [2014] compared activation maps obtained from single-task conditions and showed that dual-task accuracy decreased as the similarity between the activation maps increased. Note that we also applied the analysis approach of Nijboer et al. [2014] to our data, but found no significant correlation between interference scores and similarity between single-task activation maps (the highest correlation: $r(20)=0.19$, $p=0.39$). One possible reason for this null finding is that Nijboer et al. [2014] quantified the similarity between activation maps based on their Euclidean distance in a high-dimensional space (with the number of dimensions equal to the number of voxels) which has been documented to be relatively insensitive to discovering group differences [Aggarwal et al., 2001; Verleysen and François, 2005]. Furthermore, the results obtained from our analysis suggest that both modular overlap and flexibility are important to predict dual-task costs. In an additional analysis we calculated the partial correlation between the decline in visuospatial accuracy and the flexibility of visuospatial task modules and speech task modules in adaptation to the dual-task condition controlling for effects of modular overlap between single task modules. The purpose of this analysis was to test the unique correlations between the behavioral interference scores and the flexibility of single task network modules, while eliminating the variance explained by the modular overlap. The results revealed that both, the modular flexibility of visuospatial and speech task modules, still significantly contribute to the prediction of the behavioral dual-task costs after the effects of the modular overlap has been removed (partial correlations for the highest correlations in Fig. 2: with flexibility of visuospatial task modules $\rho(19)=0.36$, $p=0.047$; with flexibility of speech modules $\rho(19)=0.43$, $p=0.018$, one-sided).

Furthermore, we conducted partial correlation analyses to show the unique contribution of the persistency and flexibility of brain network modules in predicting the behavioral interference while eliminating the variance explained by the modularity Q^* and the number of modules. The correlation between the behavioral interference scores and the mean topological similarity of network modules remained significant after controlling for the effects of the modularity Q^* and the number of modules (Supporting Information Fig. S6, last column). Thus, the persistency and flexibility of brain network modules significantly explained unique parts of the residual variance in the behavioral interference scores which cannot be predicted by between-subject differences in the measures of network modularity, i.e., Q^* or the number of modules.

Overlap Between Single-Task Modules was Associated with Dual-Task Interference

Our results at the regional level revealed that dual-task costs can result from interference in different brain regions and processing stages. We found significant nodal effects for the relation between topological overlap across single-task modules and decrease of visuospatial accuracy in the dual-task condition in the right fusiform gyrus, a brain area which is modulated by object-based and spatial attention [Martínez et al., 1999; Noesselt et al., 2002].

Furthermore, decrease of visuospatial accuracy in the dual-task condition was associated with the overlap between single-task modules in the right pre- and postcentral gyri, previously associated brain regions with motor response generation [Porro et al., 1996; Yousry et al., 1997]. In our experiment, subjects responded to the visuospatial targets using their left hand, and to the speech targets using their right hand, whose corresponding somatomotoric representations are intrinsically correlated [Fox et al., 2007]. Possibly, subjects with higher dual-task costs showed larger modular overlap across single-task networks in the right pre- and postcentral gyri due to stronger interactions between the left and right somatomotor cortices. In summary, our data showed that the overlap between functional brain modules involved in visual, attentional, and motor processing correlates with behavioral dual-task interference.

Flexibility of Single-Task Modules was Associated with Dual-Task Interference

Topological reconfiguration of single-task modules in adaptation to the dual-task condition was a second important factor for predicting dual-task interference. When we quantified topological changes in the modular organization of single-task (speech or visuospatial) networks in adaptation to the dual-task condition, we found two sets of brain regions (Tables IIIB,C): while in some regions higher nodal consistency between single-task and dual-task modules predicted better dual-task performance, in other regions larger changes or higher flexibility in the modular organization supported dual-task performance.

In adaptation of visuospatial task modules to the dual-task condition, lower nodal flexibility of modules in brain regions including the posterior cingulate as well as the left middle occipital and postcentral gyri was predictive for higher visuospatial impairment in the dual-task condition. Higher decline in visuospatial performance was also associated with lower flexibility of speech task modules in adaptation to the dual-task condition in the anterior cingulate, right superior and middle frontal gyri as well as nodes within the left and right somatomotor cortices. Previous studies point to the anterior and posterior cingulate cortices as brain regions involved in control of attention, performance and conflict monitoring [Botvinick,

2007; Cohen et al., 2000; Leech and Sharp, 2014] and the middle and superior frontal gyri as prefrontal systems for attention [Nagahama et al., 1999; Yamasaki et al., 2002]. Several lines of evidence also support the involvement of the bilateral middle occipital gyri in visual perception and spatial attention [Imamoglu et al., 2014; Mangun et al., 1998; Martínez et al., 1999]. Taken together, our results suggest that lower flexibility of brain network modules in brain regions involved in visual processing, motor response generation and executive control is disadvantageous for the visuospatial task performance within the dual-task setting.

In adaptation of each single task modules to the dual-task condition, we also found a right-lateralized pattern of brain regions showing low modular flexibility in subjects whose visuospatial accuracy was impaired less in the dual-task condition. These regions include the right superior temporal gyrus, a previously reported hub within the right ventral frontoparietal attention network [Corbetta and Shulman, 2002; Geng and Vossel, 2013; Shulman et al., 2010]. In summary, our results show that a specific balance between nodal flexibility and rigidity of brain network modules promotes visuospatial performance in a dual-task setting.

Specifically, a brain node within the right somatomotor cortex showed the most consistent prediction (Fig. 4, yellow circle). First, subjects' visuospatial performance during the dual-task was worse if they showed large overlap between single-task modules in this region. Second, direct correlations between topological overlap and flexibility in this region revealed that subjects with larger overlap across single-task modules tend to show lower flexibility of single-task modules in adaptation to the dual-task condition (for flexibility of visuospatial task modules $\rho = -0.8$; for flexibility of speech task modules $\rho = -0.89$, $p < 0.0001$ in both cases). Third, in the same brain region, low flexibility of the speech task modules in adaptation to the dual-task condition was associated with higher behavioral dual-task interference. Thus, behavioral interference might result from brain modules which overlap in both single-tasks and stay rigid in adaptation from single-task to dual-task processing.

Correlations between flexibility of brain modular organization and behavioral performance were also documented by Bassett et al. [2010b] who investigated the reconfiguration of brain networks during a motor learning task. In their study, the authors used a network diagnostic based on the definition of module stationarity [Palla et al., 2007] to characterize dynamic modular evolution of brain networks (Eq. (2) in Bassett et al. [2010b]), and defined nodal flexibility as the number of times that each node changes module allegiance normalized by total possible number of changes. Our diagnostic is similar to that of Bassett et al. [2010b] in that the mean topological similarity between network modules across each single-task and the dual-task condition [Eq. (5)] characterizes nodal reconfiguration of brain networks in adaptation to

the dual-task condition, thereby providing a measure of nodal flexibility of brain network modules in the context of dual-tasking.

The importance of the rigidity of functional brain networks has also been stressed in recent network and graph-theoretical models. For example, it has been suggested that the performance in a memory task depends on a rigid "core" and a more flexible subsystem of the default mode network [Csrmely et al., 2013; Fornito et al., 2012]. Additionally, Bassett et al. [2013] showed that in the course of motor training, a set of primarily sensorimotor regions show relatively low flexibility, but there is also a set of multimodal regions showing high flexibility, which together suggest a "rigid core" and "flexible periphery" network organization subserving motor learning. In summary, our results are in agreement with previous findings suggesting that performance of cognitive tasks relates to both flexible and rigid functional network organization.

Methodological Considerations

Our results revealed significantly longer reaction times in speech trials during dual-task processing, but no significant effect of dual-tasking on speech accuracy and no significant correlations between topological similarity of modules and speech performance. Thereby, our results support previous findings which documented stronger cross-modal interference effects of auditory stimuli on visual processing, but weaker effects of visual processing on auditory performance [Bendixen et al., 2010; Bresciani et al., 2008]. Thus, stronger correlations between the topological attributes and visuospatial performance in contrast to speech performance might result from asymmetrical interference effects; during dual-task performance speech processing might displace visuospatial processing in overlapping brain modules and possibly induces larger decline in visuospatial performance.

The methodology undertaken in our study is unique in two major aspects. First, contrasting task fMRI connectivity matrices with those of resting-state allowed us to detect changes in functional connectivity patterns during task performance compared with resting-state. Second, our similarity analysis let us investigate both functional network interference and flexibility in the context of dual-tasking.

CONCLUSION

To conclude, the results of this study suggest that topological similarity between functional brain modules across task-related networks is closely related to individuals' efficiency in dual-tasking. Consistent with our hypotheses, we were able to link dual-task interference effects with the topological persistency and flexibility of functional brain network modules.

REFERENCES

- Achard S, Salvador R, Whitcher B, Suckling J, Bullmore E (2006): A resilient, low-frequency, small-world human brain functional network with highly connected association cortical hubs. *J Neurosci* 26:63–72.
- Aggarwal CC, Hinneburg A, Keim DA (2001): On the surprising behavior of distance metrics in high dimensional space. *Database Theory — ICDT 2001 Lecture Notes in Computer Science*, Vol. 1973. pp 420–434. Springer Berlin Heidelberg. DOI: 10.1007/3-540-44503-X_27.
- Alavash M, Doeblner P, Holing H, Thiel CM, Gießing C (2014): Is functional integration of resting state brain networks an unspecific biomarker for working memory performance? *Neuro-Image* 108:182–193.
- Alexander-Bloch AF, Gogtay N, Meunier D, Birn R, Clasen L, Lalonde F, Lenroot R, Giedd J, Bullmore ET (2010): Disrupted modularity and local connectivity of brain functional networks in childhood-onset schizophrenia. *Front Syst Neurosci* 4:147.
- Baayen RH, Milin P (2010): Analyzing reaction times. *Int J Psychol Res* 3:12–28.
- Bassett DS, Gazzaniga MS (2011): Understanding complexity in the human brain. *Trends Cogn Sci* 15:200–209.
- Bassett DS, Greenfield DL, Meyer-Lindenberg A, Weinberger DR, Moore SW, Bullmore ET (2010a): Efficient physical embedding of topologically complex information processing networks in brains and computer circuits. *PLoS Comput Biol* 6:e1000748.
- Bassett DS, Wymbs NF, Porter MA, Mucha PJ, Carlson JM, Grafton ST (2010b): Dynamic reconfiguration of human brain networks during learning. *Proc Natl Acad Sci USA* 108:7641–7646.
- Bassett DS, Porter MA, Wymbs NF, Grafton ST, Carlson JM, Mucha PJ (2013): Robust detection of dynamic community structure in networks. *Chaos* 23:013142.
- Bassett DS, Wymbs NF, Rombach MP, Porter MA, Mucha PJ, Grafton ST (2013): Task-based core-periphery organization of human brain dynamics. *PLoS Comput Biol* 9:e1003171.
- Bendixen A, Grimm S, Deouell LY, Wetzel N, Madebach A, Schroger E (2010): The time-course of auditory and visual distraction effects in a new crossmodal paradigm. *Neuropsychologia* 48:2130–2139.
- Blondel S, Guillaume J, Lambiotte R, Lefebvre E (2008): Fast unfolding of communities in large networks. *J Stat Mech* P10008.
- Botvinick MM (2007): Conflict monitoring and decision making: Reconciling two perspectives on anterior cingulate function. *Cogn Affect Behav Neurosci* 7:356–366.
- Bresciani JP, Dammeier F, Ernst MO (2008): Tri-modal integration of visual, tactile and auditory signals for the perception of sequences of events. *Brain Res Bull* 75:753–760.
- Chen PY, Popovic PM (2002) *Correlation: Parametric and Non-parametric Measures*. SAGE Publications.
- Cliff N (1996): *Ordinal Methods for Behavioral Data Analysis*. Routledge.
- Csermely P, London A, Wu LY, Uzzi B (2013): Structure and dynamics of core/periphery networks. *J Complex Netw* 1:93–123.
- Cohen JD, Botvinick M, Carter CS (2000): Anterior cingulate and prefrontal cortex: Who's in control? *Nature* 3:421–423.
- Cohen MA, Konkle T, Rhee JY, Nakayama K, Alvarez GA (2014): Processing multiple visual objects is limited by overlap in neural channels. *Proc Natl Acad Sci USA* 111:8955–8960.
- Cole MW, Bassett DS, Power JD, Braver TS, Petersen SE (2014): Intrinsic and task-evoked network architectures of the human brain. *Neuron* 83:238–251.
- Corbetta M, Shulman GL (2002): Control of goal-directed and stimulus-driven attention in the brain. *Nat Rev Neurosci* 3: 201–215.
- Craddock RC, James GA, Holtzheimer PE, Hu XPP, Mayberg HS (2012): A whole brain fMRI atlas generated via spatially constrained spectral clustering. *Hum Brain Mapp* 33:1914–1928.
- Di X, Gohel S, Kim EH, Biswal BB (2013): Task vs. rest-different network configurations between the coactivation and the resting-state brain networks. *Front Hum Neurosci* 7:493.
- Dux PE, Tombu MN, Harrison S, Rogers BP, Tong F, Marois R (2009): Training improves multitasking performance by increasing the speed of information processing in human pre-frontal cortex. *Neuron* 63:127–138.
- Efron B (1987): Better bootstrap confidence intervals. *JASA* 82:171–200.
- Ekman M, Derrfuss J, Tittgemeyer M, Fiebach CJ (2012): Predicting errors from reconfiguration patterns in human brain networks. *Proc Natl Acad Sci USA* 109:16714–16719.
- Fornito A, Zalesky A, Bullmore ET (2010): Network scaling effects in graph analytic studies of human resting-state FMRI data. *Front Syst Neurosci* 4:22.
- Fornito A, Harrison BJ, Zalesky A, Simons JS (2012): Competitive and cooperative dynamics of large-scale brain functional networks supporting recollection. *Proc Natl Acad Sci USA* 109: 12788–12793.
- Fornito A, Zalesky A, Breakspear M (2013): Graph analysis of the human connectome: promise, progress, and pitfalls. *Neuro-Image* 80:426–444.
- Fortunato S, Barthelemy M (2007): Resolution limit in community detection. *Proc Natl Acad Sci USA* 104:36–41.
- Fox MD, Snyder AZ, Vincent JL, Raichle ME (2007): Intrinsic fluctuations within cortical systems account for intertrial variability in human behavior. *Neuron* 56:171–184.
- Frackowiak RSJ, Ashburner JT, Penny WD, Zeki S, Friston KJ, Frith CD, Dolan RJ, Price CJ (2004): *Human Brain Function*, 2nd ed. Academic Press.
- Franconeri SL, Alvarez GA, Cavanagh P (2013): Flexible cognitive resources: Competitive content maps for attention and memory. *Trends Cogn Sci* 17:134–141.
- Friedman M (1937): The use of ranks to avoid the assumption of normality implicit in the analysis of variance. *JASA* 675–701.
- Gamboa OL, Tagliazucchi E, von Wegner F, Jurcoane A, Wahl M, Laufs H, Ziemann U (2013): Working memory performance of early MS patients correlates inversely with modularity increases in resting state functional connectivity networks. *NeuroImage* 94:385–395.
- Gaspar ME, Csermely P (2012): Rigidity and flexibility of biological networks. *Brief Funct Genomics* 11:443–456.
- Geng JJ, Vossel S (2013): Re-evaluating the role of TPJ in attentional control: contextual updating? *Neurosci Biobehav Rev* 37:2608–2620.
- Ginestet CE, Nichols TE, Bullmore ET, Simmons A (2011): Brain network analysis: separating cost from topology using cost-integration. *PLoS One* 6:e21570.
- Giessing C, Thiel CM, Alexander-Bloch AF, Patel AX, Bullmore ET (2013): Human brain functional network changes associated with enhanced and impaired attentional task performance. *J Neurosci* 33:5903–5914.

- Good BH, de Montjoye YA, Clauset A (2010): Performance of modularity maximization in practical contexts. *Phys Rev E* 81: 046106.
- Grayson DS, Ray S, Carpenter S, Iyer S, Dias TGC, Stevens C, Nigg JT, Fair DA (2014): Structural and functional rich club organization of the brain in children and adults. *PLoS One* 9: e88297.
- Hilgetag CC, Théoret H, Pascual-Leone A (2001): Enhanced visual spatial attention ipsilateral to rTMS-induced virtual lesions of human parietal cortex. *Nat Neurosci* 4:953–957.
- Hochberg Y (1988): A sharper Bonferroni procedure for multiple tests of significance. *Biometrika* 75:800–802.
- Holm S (1979): A simple sequentially rejective multiple test procedure. *Scand J Stat* 6:65–70.
- Huestegge L, Pieczykolan A, Koch I (2014): Talking while looking: On the encapsulation of output system representations. *Cogn Psychol* 73:72–91.
- Imamoglu F, Heinze J, Imfeld A, Haynes JD (2014): Activity in high-level brain regions reflects visibility of low-level stimuli. *NeuroImage* 102(Pt 2):688–694.
- Jiang Y (2004): Resolving dual-task interference: an fMRI study. *Neuroimage* 22:748–754.
- Jo HJ, Gotts SJ, Reynolds RC, Bandettini PA, Martin A, Cox RW, Saad ZS (2013): Effective preprocessing procedures virtually eliminate distance-dependent motion artifacts in resting state fMRI. *J Appl Math* 2013:935154. DOI: 10.1155/2013/935154.
- Just MA, Carpenter PA, Keller TA, Emery L, Zajac H, Thulborn KR (2001): Interdependence of nonoverlapping cortical systems in dual cognitive tasks. *Neuroimage* 14:417–426.
- Just MA, Keller TA, Cynkar J (2008): A decrease in brain activation associated with driving when listening to someone speak. *Brain Res* 1205:70–80.
- Klingberg T (1998): Concurrent performance of two working memory tasks: Potential mechanisms of interference. *Cereb Cortex* 8:593–601.
- Kitzbichler MG, Henson RN, Smith ML, Nathan PJ, Bullmore ET (2011): Cognitive effort drives workspace configuration of human brain functional networks. *J Neurosci* 31:8259–8270.
- Lancichinetti A, Fortunato S (2012): Consensus clustering in complex networks. *Sci Rep* 2:336.
- Leech R, Sharp DJ (2014): The role of the posterior cingulate cortex in cognition and disease. *Brain* 137:12–32.
- Lien MC, Ruthruff E, Johnston JC (2006): Attentional limitations in doing two tasks at once: The search for exceptions. *Curr Dir Psychol* 15:89–93.
- Lohse C, Bassett DS, Lim KO, Carlson JM (2014): Resolving anatomical and functional structure in human brain organization: Identifying mesoscale organization in weighted network representations. *PLoS Comput Biol* 10:e1003712.
- Macbeth G, Razumiejczyk E, Ledesma R (2011): Cliff's Delta Calculator: A non-parametric effect size program for two groups of observations. *Univ Psychol* 10:545–555.
- Magen H, Cohen A (2007): Modularity beyond perception: evidence from single task interference paradigms. *Cogn Psychol* 55:1–36.
- Magen H, Cohen A (2010): Modularity beyond perception: Evidence from the PRP paradigm. *J Exp Psychol Hum Percept Perform* 36:395–414.
- Mangun G, Buonocore M, Girelli M, Jha A (1998): ERP and fMRI measures of visual spatial selective attention. *Hum Brain Mapp* 6:383–389.
- Marois R, Ivanoff J (2005): Capacity limits of information processing in the brain. *Trends Cogn Sci* 9:296–305.
- Martínez A, Anllo-Vento L, Sereno MI, Frank LR, Buxton RB, Dubowitz DJ, Wong EC, Hinrichs H, Heinze HJ, Hillyard SA (1999): Involvement of striate and extrastriate visual cortical areas in spatial attention. *Nat Neurosci* 2:364–369.
- McIntosh AR, Korostil M (2008): Interpretation of neuroimaging data based on network concepts. *Brain Imaging Behav* 2:264–269.
- Meunier D, Lambiotte R, Bullmore ET (2010): Modular and hierarchically modular organization of brain networks. *Front Neurosci* 4:200.
- Moussa MN, Steen M, Laurienti PJ, Hayasaka S (2012): Consistency of network modules in resting-state fMRI connectome data. *PLoS One* 7:e44428.
- Nagahama Y, Okada T, Katsumi Y, Hayashi T, Yamauchi H, Sawamoto N, Toma K, Nakamura K, Hanakawa T, Konishi J, Fukuyama H, Shibasaki H (1999): Transient neural activity in the medial superior frontal gyrus and precuneus time locked with attention shift between object features. *NeuroImage* 10: 193–199.
- Newman ME (2006): Modularity and community structure in networks. *Proc Natl Acad Sci USA* 103:8577–8582.
- Nijboer M, Borst J, van Rijn H, Taatgen N (2014): Single-task fMRI overlap predicts concurrent multitasking interference. *NeuroImage* 100:60–74.
- Noesselt T, Woldorff MG, Hagner T, Hillyard SA, Schoenfeld A, Jancke L, Tempelmann C, Hinrichs H, Heinze HJ (2002): Delayed striate cortical activation during spatial attention. *Neuron* 35:575–587.
- Palla G, Barabási A, Vicsek T (2007): Quantifying social group evolution. *Nature* 446:664–667.
- Pashler H (1994): Dual-task interference in simple tasks: data and theory. *Psychol Bull* 116:220–244.
- Percival DB, Walden AT (2000) *Wavelet Methods for Time Series Analysis*. Cambridge University Press.
- Pesarin F, Salmaso L (2010): The permutation testing approach: A review. *Statistica* 70:481–509.
- Power JD, Barnes KA, Snyder AZ, Schlaggar BL, Petersen SE (2012): Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. *NeuroImage* 59:2142–2154.
- Porro CA, Francescato MP, Cettolo V, Diamond ME, Baraldi P, Zuiani C, Bazzocchi M, Prampero PE (1996): Primary motor and sensory cortex activation during motor performance and motor imagery: A functional magnetic resonance imaging study. *J Neurosci* 16:7688–7698.
- Remy F, Wenderoth N, Lipkens K, Swinnen SP (2010): Dual-task interference during initial learning of a new motor task results from competition for the same brain areas. *Neuropsychologia* 48:2517–2527.
- Ruan J, Zhang W (2008): Identifying network communities with a high resolution. *Phys Rev E* 77:016104.
- Rubinov M, Sporns O (2010): Complex network measures of brain connectivity: Uses and interpretations. *NeuroImage* 52:1059–1069.
- Rubinov M, Sporns O (2011): Weight-conserving characterization of complex functional brain networks. *Neuroimage* 56:2068–2079.
- Schubert T, Szameitat AJ (2003): Functional neuroanatomy of interference in overlapping dual tasks: An fMRI study. *Cogn Brain Res* 17:733–746.

- Shulman GL, Pope DL, Astafiev SV, McAvoy MP, Snyder AZ, Corbetta M (2010): Right hemisphere dominance during spatial selective attention and target detection occurs outside the dorsal frontoparietal network. *J Neurosci* 30:3640–3651.
- Schweickert R, Fisher DL, Sung K (2012): *Discovering Cognitive Architecture by Selectively Influencing Mental Processes*. World Scientific Publishing.
- Sekhon JS (2011): Multivariate and propensity score matching software with automated balance optimization: The matching package for R. *J Stat Softw* 42:1–52.
- Smith SM, Miller KL, Salimi-Khorshidi G, Webster M, Beckmann CF, Nichols TE, Ramsey JD, Woolrich MW (2011): Network modelling methods for fMRI. *NeuroImage* 54:875–891.
- Spearman C (1904): The proof and measurement of association between two things. *Am J Psychol* 15:72–101.
- Sporns O (2013): Network attributes for segregation and integration in the human brain. *Curr Opin Neurobiol* 23:162–171.
- Steen MS, Hayasaka S, Joyce K, Laurienti P (2011): Assessing the consistency of community structure in complex networks. *Phys Rev E* 84:016111.
- Steinhaeuser K, Chawla NV (2010): Identifying and evaluating community structure in complex networks. *Pattern Recogn Lett* 31:413–421.
- Stevens AA, Tappin SC, Garg A, Fair DA (2012): Functional brain network modularity captures inter- and intra-individual variation in working memory capacity. *PLoS One* 7:e30468.
- Szameitat AJ, Schubert T, Muller K, Cramon DY (2002): Localization of executive functions in dual-task performance with fMRI. *J Cogn Neurosci* 14:1184–1199.
- Traud AL, Frost C, Mucha PJ, Porter MA (2009): Visualization of communities in networks. *Chaos* 19:041104.
- Tzourio-Mazoyer N, Landeau B, Papathanassiou D, Crivello F, Etard O, Delcroix N, Mazoyer B, Joliot M (2002): Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. *NeuroImage* 15:273–289.
- Van Wijk BCM, Stam CJ, Daffertshofer A (2010): Comparing brain networks of different size and connectivity density using graph theory. *PLoS One* 5:e13701.
- Verleysen M, François D (2005): The curse of dimensionality in data mining and time series prediction. *Computational Intelligence and Bioinspired Systems—Lecture Notes in Computer Science*, Vol. 3512. pp 758–770. Springer Berlin Heidelberg DOI: 10.1007/11494669_93.
- Wang Z, Liu J, Zhong N, Qin Y, Zhou H, Li K (2012): Changes in the brain intrinsic organization in both on-task state and post-task resting state. *NeuroImage* 62:394–407.
- Watanabe K, Funahashi S (2014): Neural mechanisms of dual-task interference and cognitive capacity limitation in the prefrontal cortex. *Nat Neurosci* 17:601–611.
- Yousry TA, Schmid UD, Alkadhi H, Schmidt D, Peraud A, Buettner A, Winkler P (1997): Localization of the motor hand area to a knob on the precentral gyrus. *Brain* 120:141–157.
- Yamasaki H, LaBar KS, McCarthy G (2002): Dissociable prefrontal brain systems for attention and emotion. *Proc Natl Acad Sci USA* 99:11447–11451.
- Zalesky A, Fornito A, Harding IH, Cocchi L, Yucel M, Pantelis C, Bullmore ET (2010): Whole-brain anatomical networks: Does the choice of nodes matter? *Neuroimage* 50:970–983.
- Zhang S, Li CS (2010): A neural measure of behavioral engagement: Task-residual low-frequency blood oxygenation level-dependent activity in the precuneus. *NeuroImage* 49:1911–1918.