Anatomical and functional coupling between the dorsal and ventral attention networks

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ABSTRACT

Studies have indicated that the dorsal attention network (DAN) and the ventral attention network (VAN) functionally interact via several fronto-parietal connector hubs. However, the anatomical connectivity profiles of these connector hubs, and the coupling between the anatomical and functional connectivities of them, are still unknown. In the present study, we found that functional connector hubs anatomically bridged the DAN and VAN based on multimodal magnetic resonance imaging data from the Human Connectome Project (HCP) Consortium and an independent Chinese cohort. The three hubs had unique anatomical connectivity patterns with the attention sub-networks. For each connector hub, the pattern of anatomical connectivity resembled the functional one. Finally, the strength of the anatomical connectivity of these connector hubs was positively associated with the functional connectivity at the group- and individual-levels. Our findings help to better understand the anatomical mechanisms underlying the functional interactions between the DAN and the VAN.

1. Introduction

Attention is a behavioural and cognitive process that allows for selective concentration on behaviourally relevant information, while ignoring unimportant inputs. According to early neuroimaging studies, attention appears to be processed by two segregated functional sub-networks (Vossel et al., 2014). The dorsal attention network (DAN) is bilaterally distributed with core hubs that include the intra-parietal area (Tripathy et al., 2017) and frontal eye field (FEF) area (Astaie\textsuperscript{v} et al., 2003; Corbetta and Shulman, 2002; Corbetta et al., 2005; Fox et al., 2006; Giesbrecht et al., 2003; Hopfinger et al., 2000; Kastner et al., 1999; Shulman et al., 2003, 1999), which is responsible for endogenous goal-driven and exogenous orienting of attention (Corbetta et al., 2008; Corbetta and Shulman, 2002). The ventral attention network (VAN) chiefly consists of the right-lateralized temporo-parietal conjunction (TPJ) and the right fronto-insular cortex (Astaie\textsuperscript{v} et al., 2003, 2004; Corbetta et al., 2000, 2008; Fox et al., 2006; Kincade et al., 2005), which are involved in reorienting attention to salient stimuli (Corbetta et al., 2006). Knowledge about the functional organisation of attention sub-networks mainly comes from task-evoked functional magnetic resonance imaging (fMRI) that detects regional activation evoked by a specific task (Corbetta and Shulman, 2002). In contrast, resting-state fMRI (rsfMRI), which focuses on the synchronisation of spontaneous activity between brain regions, is frequently used to construct large-scale brain functional networks and their components (Bullmore and Sporns, 2009; Smith et al., 2009; Sporns, 2013). For example, the DAN and VAN have been successfully segregated based on resting-state functional connectivity (FC) analysis (Fox et al., 2006), indicating the existence of specialised functional connectivity modes between the two attention sub-networks.

Aside from the functional specialisations of the DAN and VAN, these two attention sub-networks also dynamically interact to control which information will be perceived in relation to top-down goals and bottom-up sensory stimulation (Bushman and Miller, 2007; McMain and Kastner, 2011). Early studies had demonstrated that the functional coupling between the DAN and VAN in normal subjects could predict attention performance (Wen et al., 2012), and disruption of the couplings between the DAN and VAN can induce attention deficits in multiple neuropsychiatric diseases (Chen et al., 2019). Task and resting-state fMRI also support the existence of functional overlap between the two-subnetworks, such as the right anterior middle frontal gyrus (aMFG), the TPJ, and the posterior inferior frontal gyrus (pIFG) (Corbetta et al., 2008; Fox et al.,

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These functional connector hubs are crucial for signal exchanges between the DAN and VAN, especially during reorienting (Arrington et al., 2000; Corbetta et al., 2008; Kincade et al., 2005; Macaluso et al., 2002).

The anatomical connectivity of the attention network had been explored by several studies using diffusion magnetic resonance imaging (dMRI) based fibre tracking techniques (Allan et al., 2019, 2020; Chica et al., 2018; Hattori et al., 2018; Sani et al., 2019; Schmahmann et al., 2007; Szczepanski et al., 2013; Thiebaut de Schotten et al., 2011; Umarova et al., 2010; Vossel et al., 2014). For example, the dorsal superior longitudinal fasciculus (SLF I) is indicated to mainly connect the core areas of the DAN (Allan et al., 2019; Schmahmann et al., 2007; Thiebaut de Schotten et al., 2011; Umarova et al., 2010), while the ventral SLF (SLF III) and inferior fronto-occipital fasciculus (IFOF) mainly connect the areas of VAN (Allan et al., 2020; Sani et al., 2019; Thiebaut de Schotten et al., 2011; Umarova et al., 2010). The middle SLF (SLF II), however, is reported to directly connect the DAN and the VAN, which may provide a crucial communication pathway for the two attention systems (Thiebaut de Schotten et al., 2011). These anatomical findings provided important supports on the structural basis of functional organization of the DAN and VAN, and functional interaction between them. However, knowledge about the anatomical underpinnings that bridge the DAN and VAN is still poor. Specifically, whether the functional connector hubs, which are identified via task-evoked activation and functional connectivity, are also the "anatomical" connector hubs bridging the DAN and VAN? Furthermore, earlier studies had demonstrated that the functional synchronization between brain areas is closely associated with direct or indirect anatomical connectivity (Duda et al., 2010; Honey et al., 2009; Koch et al., 2002), and whole-brain anatomical connectivity can predict the strength of functional connectivity (Honey et al., 2009). If the answer to the first question is yes, then it is worth knowing whether the strength of anatomical connectivity of these connectors can predict the strength of functional coupling between the DAN and VAN.

In the present study, we hypothesized that the functional connector hubs also anatomically bridge the DAN and VAN, and the anatomical connectivity profiles of these connectors are strongly coupled with the functional connectivity. To verify our hypothesis, we used the multimodal MRI data from the WU-Minn Human Connectome Project (HCP) Consortium and validation data from a Chinese cohort. First, we reconstructed the DAN, the VAN, and their connector hubs based on their functional connectivity profiles. This method has been stably established and replicated by several pioneer studies (Corbetta et al., 2008; Fox et al., 2006; He et al., 2007). Then, the anatomical and functional connectivity profiles between each connector hub and attention subnetwork were reconstructed and compared. Finally, we investigated potential associations between the strengths of the anatomical and functional connectivities.

2. Methods and materials

2.1. Participants

One hundred healthy young adults (age: 20–30 years; 50 females and 50 males) from the WU-Minn HCP Consortium and 50 healthy young adults (age: 18–30 years; 25 females and 25 males) from a local Chinese cohort were recruited for this study. Detailed subject recruitment information for the HCP cohort is provided at the website (http://www.humanconnectome.org). The inclusion criteria for the Chinese cohort included: being 18–30 years old, right-handedness, and Han nationality. Exclusion criteria included: 1) a history of alcohol abuse as identified by the Alcohol Use Disorders Identification Test (score > 7) (Saunders et al., 1993) or drug abuse; 2) non-right-handedness using the Chinese edition of the Edinburgh Handedness Inventory (Li, 1983; Oldfield, 1971); 3) a history or suspicion of a psychiatric disorder using the Mini-International Neuropsychiatric Interview (Sheehan et al., 1998); 4) neurological or severe somatic disorders; 5) MRI contraindications; 6) lifetime smoking habit > 20 cigarettes; 7) colour blindness or abnormal colour discrimination; 8) pregnancy; 9) family history psychiatric disorders; and 10) volunteers having relatives already included in the project. Recruitment from the Chinese cohort was approved by the Ethics Committee of Tianjin Medical University General Hospital, and written informed consent was obtained from each participant.

2.2. Data acquisition

2.2.1. HCP cohorts

The HCP dataset was obtained using a 3.0T WU-Minn-Ox HCP scanner with strong magnetic field gradients (100 mT/m) along with state-of-art dMRI pulse sequences (Glasser et al., 2016). The website (http://protocols.humanconnectome.org/HCP/3T/imaging-protocols.html) provides detailed parameters of these protocols. The main parameters for the present study are described here. The 3D T1-weighted structural MRI (sMRI) data were obtained using a magnetization prepared rapid acquisition gradient-echo (MP-RAGE) sequence with the following parameters: repetition time (TR) / echo time (TE) / inversion time (TI) = 2400/2.14/1000 ms, flip angle = 8°, field of view (FOV) = 224 mm × 224 mm, matrix = 320 × 320, slice thickness = 0.7 mm, resulting in a 0.7 mm isotropic voxel. The dMRI images were obtained using a multi-band, single-shot, spin-echo planar imaging (MB-SS-EPI) sequence with the following parameters: TR/TE = 5520/89.5 ms, flip angle = 78°, multi-band factor = 3, FOV = 210 mm × 180 mm, matrix = 168 × 144, slice thickness = 1.25 mm, 111 slices, resulting in a 1.25 mm isotropic voxel. The dMRI sequence included 6 runs, representing 3 different gradient tables, which corresponded to 3 shells of b = 1000, 2000, and 3000 s/mm²; and each table was acquired once with right-to-left and left-to-right phase encoding directions, respectively. Each gradient table included approximately 90 diffusion weighting directions plus 6 b0 acquisitions interspersed throughout each run. The resting-state fMRI images were obtained using the multi-band, single-shot, gradient-echo planar imaging (MB-SS-GRE-EPI) sequence: TR/TE = 720/33.1 ms, flip angle = 52°, multi-band factor = 8, FOV = 208 mm × 180 mm, matrix = 104 × 90, slice thickness = 2 mm, 72 slices, resulting in a 2 mm isotropic voxel. The resting-state fMRI data were acquired in 4 runs over 2 sessions, with a swapped phase encoding direction (2 runs using right-to-left and the other 2 going from left-to-right) and 1200 time points per run. During the fMRI scan, the individuals were kept motionless with their eyes open and fixed on a projection screen showing a bright cross-hair on dark background in a darkened scanning room.

2.2.2. Chinese cohorts

MRI data were acquired using a 3.0T Discovery MR750 scanner (GE Healthcare). High resolution 3D structural images were obtained using the brain volume sequence: TR/TE/TI = 8.14/3.17/450 ms, flip angle = 12°, FOV = 256 mm × 256 mm, matrix = 256 × 256, thickness = 1 mm, slices = 188, and 1 mm isotropic voxels. DMRI images were acquired using the SS-SE-EPI sequence with the following parameters: TR/TE = 7100/60.5 ms, flip angle = 90°, field of view = 256 mm × 256 mm, matrix = 128 × 128, thickness = 2 mm, gap = 0, slices = 70, 2 mm isotropic voxels, 5 b0 images and 64 diffusion images with different gradient directions and b = 1000s/mm². Resting-state fMRI data were obtained using the SS-GRE-EPI sequence: TR/TE = 2000/30 ms, flip angle = 90°, field of view = 220 mm × 220 mm, matrix = 64 × 64, thickness = 3 mm, gap = 1 mm, slices = 36. All subjects were instructed to close their eyes and keep motionless without falling asleep during the scanning.

The flow chart of the present study was present in Fig. 1.
2.3. fMRI data preprocessing

SPM12 (https://www.fil.ion.ucl.ac.uk/spm/software/spm12/) and FSL6.0 software (https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FslInstallation) were used for data preprocessing. The downloaded HCP rfMRI dataset underwent minimal preprocessing procedures, which included gradient distortion correction, motion correction, spatial normalisation to the Montreal Neurological Institute (MNI) space, high-pass filtering (Glasser et al., 2013; Van Essen et al., 2013), and denoising based on the ICA-fix algorithm (Griffanti et al., 2014). For details, please see (https://www.humanconnectome.org). To further remove noise, the minimally preprocessed data underwent covariates regression with the following nuisance regressors: 6 rigid motion parameters and their time derivatives, motion spikes (frames with framewise displacement higher than 0.5), average signals of white matter (WM), cerebrospinal fluid (CSF) and the whole brain. Bandpass filtering was then carried out with a frequency range of 0.01 to 0.08 Hz. Finally, the data were smoothed with a Gaussian kernel of $4 \times 4 \times 4 \text{mm}^3$ full widths at half maximum (FWHM) (SPM12).

The Chinese rMRI dataset was preprocessed using the following steps: slice timing (correcting for inter-slice time delay) (SPM12), motion correction (correcting for inter-volume head-motion induced displacement) (SPM12), spatial normalisation (the rMRI data were first affinely coregistered with the sMRI data using the FLIRT function, then the sMRI data were non-linearly coregistered into the MNI space using the FNIRT function. Finally, the deformation parameters of the linear and nonlinear co-registration were concatenated and were used to write the rMRI data into the MNI space with a voxel size of isotropic 2- mm) (FSL6.0), covariates regression(SPM12), bandpass filtering and smoothing(SPM12). The parameters of the preprocessing steps for the Chinese dataset were the same as those for the HCP dataset, with the exception of the minimal preprocessing procedures for HCP dataset.

2.4. Reconstruction of attention sub-networks and identification of connector hubs

The core areas of the attention network were extracted based on a meta-analysis of attention-evoked coactivation. BrainMap Sleuth 2.0.3 (http://www.brainmap.org) was used to search for the coordination of brain loci evoked by “attention” cognition experiments in “normal” “right-handedness” “adults”, and exclude conditions used to investigate the effects of handedness, diseases, gender, or drugs. All screened foci were transformed into the MNI space and checked to exclude those outside the brain. A total of 128 publications that included 360 experiments, 4793 subjects, and 3470 foci were finally incorporated into the final meta-analysis. A revised version of the Activation Likelihood Estimation (ALE) technique (Eickhoff et al., 2017; Turkeltaub et al., 2012) was applied for meta-analysis using GingerALE 2.3.6 (http://www.brainmap.org). This algorithm aims to identify regions showing convergent activation across experiments if the merged activation is higher than expected under random spatial associations. Multiple comparisons were corrected using a false discovery rate (FDR) method ($q < 0.01$ and cluster size $>1000 \text{mm}^3$) (Supplementary Figure 1A). Finally, 4 foci were identified as the core areas of the DAN, including the left superior parietal lobule (Asplund et al.), the right IPS, and the bilateral FEF (Asplund et al., 2010); 3 foci were identified as the core seeds of the VAN, including the right TPJ, the pIFG and the anterior insula (McMains and Kastner, 2011) (Supplementary Figure 1B).

A 6 mm-radius sphere was centred on the peak coordinate of each locus, and the overlapping voxels between the sphere and meta-analysis
loci were taken as the seeds for extracting the attention sub-networks (Supplementary Figure 1B and Supplementary Table 1). The building of attention sub-networks and their connectors are based on methods from previous studies (Corbetta et al., 2008; Fox et al., 2006). Specifically, Pearson correlation coefficients between the mean time series of each seed and each voxel of the whole brain were computed and transformed into z-values (namely, the FC) using Fisher’s r-to-z method. Then, conjunction analysis was applied to identify the DAN voxels exhibiting positive FC with all the DAN seeds, and to identify the VAN voxels showing positive FC with all the VAN seeds (q < 0.0001, FDR corrected; cluster size > 100 voxels). The connector hubs between the DAN and VAN were also identified using the conjunction analysis, which indicated that these connector hubs had positive FC with all the DAN and VAN seeds (Fig. 2) (SPM12). To verify the repeatability of the identified connectivity hubs, we separately performed the above analyses on each of the 4 HCP dMRI runs. Additionally, the Dice coefficient of the connector hubs (the number of overlapped voxels from all the hubs divided by the average number between each pair of runs) was calculated. The overlaps of the three connector hubs were relatively high across runs (Dice coefficient = 0.732 ± 0.034) (Supplementary Figure 2 and Supplementary Table 1). For fibre tracking, we chose the connector hubs from a single run that had the highest mean Dice coefficients compared with others runs. Finally, three functional connector hubs were extracted, including the right pIFG, the right aMFG, and the right superior marginal gyrus (SMG).

2.5. DMRI data preprocessing

The downloaded diffusion HCP data had been handled based on the minimal preprocessing pipelines, including intensity normalisation, distortion and motion correction, brain extraction, etc. (Glasser et al., 2013). In the present study, the b0 images were affinely coregistered to the sMRI space (b0-to-T1) using the FLIRT function. Then the sMRI were nonlinearly normalised into the MNI space (T1-to-MNI) using FNIRT function. Finally, the b0-to-MNI deformation parameters were calculated by concatenating the two preceding registration steps, i.e., b0-to-T1 and T1-to-MNI (applywarp function). The preprocessing steps for the dMRI data from the Chinese cohorts included eddy current and motion correction, brain extraction, and b0-to-MNI co-registration using the same parameters as the HCP data. Please note that the dMRI data were not warped into the MNI space using b0-to-MNI deformation parameters. Instead, we applied the deformation parameters on the attention connector hubs and parcellation hubs to inversely warp them into the subjects’ native diffusion space for fibre tracking and quantification, as shown in the following sections. FSL6.0 software was used for the above preprocessing.

2.6. Fibre tracking for attention connector hubs

The orientation distribution function of each voxel was fitted from the preprocessed dMRI data in the native space using a generalized q-sampling imaging algorithm (Yeh et al., 2010) with a diffusion sampling length ratio of 1.25 and ODF decomposition fraction of 0.05 (Yeh et al., 2013). The analysis was conducted using the DSI Studio 2017 build on the CentOS 6 platform (http://dsi-studio.labsolver.org).

Deterministic fibre tracking was carried out to construct the anatomical connectivity between the connector hubs and the whole attention networks using DSI Studio 2017 (Yeh et al., 2013) (http://dsi-studio.labsolver.org). Before fibre tracking, the three attention connector hubs were inversely transformed into the native diffusion space of each subject. The parameters used for fibre tracking were as follow: 1) the termination threshold for anisotropy (normalised quantitative anisotropy, nQA) was individually manually set to avoid fibres passing through (or terminating in) the CSF while keeping as many fibres as possible within the white matter (Yeh et al., 2013); 3) a maximum angular threshold of 60°; 4) a step size of 0.6 mm; 5) a fibre smoothing value of 0.2 (Fernandez-Miranda et al., 2015); and 6) a fibre length threshold between 30 and 300 mm. All of the fibre tracking steps were carried out in the individual diffusion space. To visualize the fibre distribution only, the fibre bundles of each connector hub for each subject were spatially normalised into the MNI space via the b0-to-MNI deformation parameters. The group-wise fibre probability map of each connector hub was generated by averaging the normalised individual fibres.

2.7. Anatomical connectivity parcellation and quantification

Based on the human Brainnetome atlas (http://atlas.brainnetome.org) (Fan et al., 2016), we further parcellated the attention network into 84 areas (excluding the 3 connector hubs), including 48 DAN nodes and 36 VAN nodes. Brainnetome atlas is a group-wise, cross-validated, and fine-grained (210 cortical and 36 subcortical brain regions) atlas parcellated based on the anatomical connectivity patterns between voxels, which is thus preferable for connectivity-based analysis (Fan et al., 2016). Then the 84 parcellated attention nodes were inversely transformed into the native diffusion space of each subject. The fibres that terminate in each connector hub and each of the parcellated attention node were separated, and the strength of each pair of anatomical connectivities was quantified by the following measures: 1) fibre number between each connector hub and each of the parcellated attention node; 2) fibre density: the fibre numbers divided by the average volume of the connected nodes; 3) length-corrected fibre number: the fibre number divided by the fibre length; and 4) length-corrected fibre density: the fibre density divided by the fibre length. Earlier studies have shown that measures of anatomical connectivity are not normally distributed (Hagmann et al., 2010; Honey et al., 2009), thus they were further resampled using the Gaussian redistribution method (Hagmann et al., 2010; Honey et al., 2009). To validate the reliability of the anatomical connectivity patterns of these connector hubs, we randomly separated the HCP cohorts into two independent subsets. Pearson correlations were then used to test the similarities in connectivity patterns between each pair of the three datasets; namely, HCP dataset 1, HCP dataset 2, and the Chinese dataset (q < 0.05, FDR corrected).
2.8. Anatomical and functional connectivity fingerprinting and their associations

Functional connectivity between each connector hub and each parcellated attention hub was calculated using Pearson correlations and Fisher r-to-z transformations based on the preprocessed fMRI data. The fingerprints of the anatomical and functional connectivities of the connector hubs were compared and validated for each dataset (HCP dataset 1, HCP dataset 2 and the Chinese dataset). Furthermore, the couplings between anatomical and functional connectivities were tested by calculating the Pearson correlation coefficient between the anatomical connectivity measures and FC at both the group and individual levels ($q < 0.05$, FDR corrected). Finally, the anatomical-functional couplings of the connector hubs were validated across different measures, different datasets, and different fMRI runs.

2.9. Data/code availability statement

The HCP dataset that supports the findings of this study is available by Human Connectome Project at https://www.humanconnectome.org/study/bcp-young-adult. In addition, the Chinese datasets that support the findings of this study would be available on the public data repository https://data.mendeley.com once upon acceptance.

3. Results

3.1. Anatomical connectivity profiles of the connector hubs

Based on the meta-analysis and conjunction analysis, we identified three connector hubs that were functionally coupled with both the DAN and VAN, including the right SMG, the pIFG and the aMFG (Fig. 2). An example of the anatomical fibres of these three connectors are shown in Fig. 3A.

Fibre tracking demonstrated that these three connectors were anatomically connected with both the DAN and VAN (Supplementary Figure 3–8). Besides, the anatomical connectivity patterns were unique across the three connector hubs (Fig. 3B, 3C). Specifically, in the DAN, the pIFG was primarily connected with dorsolateral area 6 of the right superior frontal gyrus (SFGR7_4), ventro-lateral area 6 of the right middle frontal gyrus (MFRG7_6), and ventro-lateral area 6 of the right caudal precentral gyrus (PrGR6_6). The aMFG was mainly connected with ventral area 9/46 of the left middle frontal gyrus (MFLG7_4), dorsal area 9/46 of the right middle frontal gyrus (MFGR7_1), and the right inferior frontal sulcus (IFGR6_2). SMG was mainly connected with the rostro-dorsal area 40 of the right inferior parietal lobule (IPLR6_3), intraparietal area 7 of the right superior parietal lobule (SPLR5_5), and lateral area 5 of the right superior parietal lobule (SPLR5_3). In the VAn, the pIFG was mainly connected with the ventral area 44 of the right inferior frontal gyrus (IFGR6_6) and the inferior frontal junction of the right middle frontal gyrus (MFRG7_2). The aMFG was mainly connected with ventral area 9/46 of the right middle frontal gyrus (MFGR7_4), and MFRG7_2. The SMG was mainly connected with the caudal area 40 of the right inferior parietal lobule (IPLR6_4), and rostroventral area 40 of the right inferior parietal lobule (IPLR6_6).

The anatomical connectivity profiles were similar across different datasets (Pearson correlation coefficient: $r[227] = 0.89$ between HCP dataset 1 and dataset 2; $r[144] = 0.74$ between HCP dataset 1 and the Chinese dataset; and $r[144] = 0.77$ between HCP dataset 2 and the Chinese dataset, $P < 0.001$, FDR corrected) (Fig. 3D, 3E).

3.2. Functional connectivity profiles of the connector hubs

The functional connectivity profiles of the three connector hubs were shown in Fig. 4. The functional connectivity patterns were also unique across the connector hubs (Fig. 4A). Specifically, in the DAN, the pIFG was strongly functionally coupled with PrGR6_6, IFGR6_2, and IPLR6_3; the aMFG was mainly functionally coupled with MFRG7_1, MFLG7_4,
Fig. 4. Functional connectivity profile of the DAN/VAN connectors. (A) The functional connectivity profile between the connectors and DAN/VAN areas in the HCP dataset. Bands with red, green, and blue represent connectivity of right pIFG, aMFG and SMG, respectively. Ring colour with light blue and pink represents areas in the DAN and VAN, respectively. (B) The functional connectivity profiles of the connectors in two subsets of HCP and the Chinese dataset. (C) Pearson correlation in functional connectivity profiles between each pair of the three datasets. Abbreviations: aMFG = anterior middle frontal gyrus, DAN = dorsal attention network, HCP = human connectome project, pIFG = posterior inferior frontal gyrus, SMG = superior marginal gyrus, VAN = ventral attention network. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Fig. 5. Fingerprints of the anatomical and functional connectivity of the DAN/VAN connectors. The fingerprints of the (A) pIFG, (B) aMFG and (C) SMG are drawn based on the fibre density (blue line) and functional connectivity (pink line), respectively. Ring colour with light blue and pink represents areas in the DAN and VAN, respectively. Abbreviations: aMFG = anterior middle frontal gyrus, DAN = dorsal attention network, FC = functional connectivity, HCP = human connectome project, pIFG = posterior inferior frontal gyrus, SMG = superior marginal gyrus, VAN = ventral attention network. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)
and SFG7.4; and the SMG was mainly functionally connected with IPL6.3 and PrGR6.6. In the VAN, the pIFG was mainly connected with IFGR6.6 and the dorsal dysgranular insula (INSR6.6); the aMFG was mainly connected with MFG7.4 and IPL6.4; and the SMG was mainly connected with IPL6.4, IPL6.4, and MFG7.4.

Pearson correlation demonstrated that the functional connectivity profiles were also similar across different datasets (r2277 = 0.98 between HCP dataset 1 and dataset 2, r1444 = 0.91 between HCP dataset 1 and the Chinese dataset; and r144 = 0.93 between HCP dataset 2 and the Chinese dataset, P < 0.001, FDR corrected) (Fig. 4B and 4C).

3.3. Anatomical and functional connectivity fingerprinting and coupling

As shown in Fig. 5, in each connector hub, the fingerprint of the anatomical connectivity was similar to the functional connectivity. In addition, the fingerprints of either the anatomical or functional connectivity were unique across different connector hubs. These patterns were also replicated in HCP dataset 1, HCP dataset 2, and the Chinese dataset.

We further evaluated quantitative coupling between the strengths of structural and functional connectivities of the attention connectors using Pearson’s correlation. For the HCP dataset, functional connectivity was strongly coupled with the structural connectivity indices of the attention connectors at the group level, including fibre number, fibre density, and their length-corrected fibre number and density (r [237] > 0.53, P < 0.05, corrected) (Fig. 6A). Anatomical-functional couplings also survived at the individual level (mean r[98] > 0.29, P < 0.05, corrected) (Fig. 6B). Moreover, we validated whether the anatomical-functional coupling was influenced by the dynamics of FC in different acquisition sessions. The coupling between the structural and functional connectivity of the attention connectors was also evident at either the group-level (r [237] > 0.52, P < 0.05, corrected) (Fig. 6C) or the individual level (r[98] > 0.29, P < 0.05, corrected) in each functional session (Fig. 6D). Finally, to test if the anatomical-functional coupling of the DAN-VAN connector is also reliably persistent across datasets, we repeated the same analysis in the Chinese dataset and found a strong anatomical-functional coupling (Fig. 7).

To explore if the anatomical-functional coupling is connektor-dependant, we also performed Pearson’s correlation between the strengths of each connector’s structural and functional connectivities. As shown in Fig. 8A, for the HCP dataset, each connector’s functional connectivity was strongly positively coupled with the length-corrected fibre density (pIFG: r[79] = 0.59, aMFG: r[80] = 0.57, SMG: r[74] = 0.42, P < 0.001, corrected). We conducted the same analysis in the Chinese dataset and also found strong anatomical-functional couplings in these three connectors (pIFG: r[50] = 0.54, aMFG: r[51] = 0.61, SMG: r[39] = 0.61, P < 0.001, corrected) (Fig. 8B). Furthermore, we carried...
We length-corrected connectivity using false discovery rate method ($q < 0.05$), respectively. The strength of anatomical connectivity was defined using different measures, including the fibre number, fibre density, length-corrected fibre number and density. Error bar represents 95% confidence interval.

The associations between the strength of anatomical connectivity and functional connectivity were calculated using the Pearson correlation coefficients at the group-level (A) and individual-level (B) for the Chinese dataset, corrected using false discovery rate method ($q < 0.05$), respectively. The strength of anatomical connectivity was defined using different measures, including the fibre number, fibre density, length-corrected fibre number and density. Error bar represents 95% confidence interval. Abbreviations: aMFG = anterior middle frontal gyrus, HCP = human connectome project, pIFG = posterior inferior frontal gyrus, SMG = superior marginal gyrus.

4. Discussion

The present study aimed to explore the anatomical connectivity profiles between the dorsal and ventral attention networks. Based on the multimodal magnetic resonance imaging data from the HCP Consortium and those from an independent Chinese cohort, we found that the functional connector hubs between the DAN and VAN anatomically bridged the two sub-networks. Moreover, each connector had unique anatomical connectivity profiles with the two attention sub-networks, indicating that these hubs play different roles in information exchange between the DAN and VAN. Finally, the anatomical connectivity profiles of these hubs closely resembled functional ones, and strong coupling was identified between the strength of anatomical and functional connectivities in these connector hubs. Our findings help to understand the anatomical basis underlying the functional interactions between the DAN and VAN. Although the DAN and VAN were considered to be two separate functional networks responsible for top-down and bottom-up functions, re-
spectively, a number of earlier studies have shown that these two attention sub-networks dynamically interact to control which information will be perceived (Buschman and Miller, 2007; McMains and Kastner, 2011; Vossel et al., 2014). For example, one study reported that Granger causal influences from the VAN to the DAN are positively associated with attention performance, while casual flow from the VAN to the DAN has a negative association with attention performance, indicating that DAN -> VAN signals filter out unimportant distractor information, whereas VAN -> DAN signals break the attention maintained by the DAN to enable attentional reorienting (Wen et al., 2012). A recent study based on concurrent transcranial magnetic stimulation (TMS) and fMRI studies demonstrated that TMS bursts over the IPS dramatically abolished sustained spatial attention response in the right TPJ of the VAN, indicating a causal influence of the IPS on the neural activity of the VAN (Leitao et al., 2015). Additionally, disruption of the couplings between the DAN and VAN has been found in a number of neuropsychiatric diseases with attention deficits (Fitzgerald et al., 2015; Jimenez et al., 2016). Task and resting-state fMRI also support the existence of a functional overlap between the two sub-networks, such as the right anterior middle frontal gyrus, the TPJ, and the posterior inferior frontal gyrus (Fox et al., 2006; He et al., 2007; Vossel et al., 2014). These functional connector hubs are crucial for signal interactions between the DAN and VAN, especially during attention reorienting (Asplund et al., 2010; Corbetta et al., 2008; Dugue et al., 2018; Japee et al., 2015). In this study, and based on the method proposed by Fox et al., we identified connectors that had strong intrinsic functional coupling with both the DAN and VAN, including the pIFG, AMFG, and SMG, which is consistent with previous reports (Fox et al., 2006; He et al., 2007). In addition, we independently extracted the connector hubs from the four sessions of the HCP fMRI dataset, and found that the results were highly consistent with each other, indicating that the connector hubs extracted from the resting-state data had high reliability.

One of the most important findings in the present study was that the functional connector hubs also anatomically bridged the DAN and VAN. In regards to the anatomical organisation of the attention network, several earlier studies had found that the attention network was interconnected by several long-association fronto-parietal pathways, including the superior longitudinal fasciculus, the arcuate fasciculus, and the inferior fronto-occipital fasciculus, et al. (Thiebaut de Schotten et al., 2011; Umarova et al., 2010). Moreover, recent studies have also reported that the microstructure variability of these attentional network connections can predict individual attention performance (Chechlacz et al., 2015; Chica et al., 2018; Wu et al., 2016). However, the anatomical connections between the DAN and VAN are relatively unknown. Based on the connector hubs extracted by functional connectivity, the present study identified the DAN and VAN were anatomically interconnected by these connectors. Moreover, the anatomical connectivity profiles of these connectors were highly stable across different sub-groups of the HCP dataset, and they can be replicated by another independent Chinese dataset. Our findings suggest that the functional interactions between the DAN and VAN may be carried by the anatomical pathways identified in the present study.

According to the location of the connectors of DAN and VAN, the anatomical interactions between the two networks can be mediated by three pathways: in the anterior pathway, the DAN and VAN are connected via the right anterior MFG (which primarily bridges the right FEF, the anterior and posterior MFG, and the left anterior MFG in the DAN), and the posterior and anterior MFG in the VAN; in the middle pathway, the right pIFG is the relay that primarily connects the right FEF and posterior MFG in the DAN, and the right posterior MFG and FIC in the VAN; in the posterior pathway, the right anterior SMG is the core relay that connects the right SPL and IPL in the DAN, and the right TPJ in the VAN. We speculate that the three anatomical pathways may be preferentially responsible for different aspects of attention functioning. The middle pathway directly connects the FEF of the DAN and the FIC of the VAN. The FEF is the source of top-down attention controling (Buschman and Miller, 2007), while the FIC has been implicated in detecting salient bottom-up stimuli (Menon and Uddin, 2010). Previous studies have also demonstrated that the right FIC is strongly coupled with the dACC, which participates in error monitoring and control (Shenav et al., 2016; Siegel et al., 2015). The FIC and dACC are also the core hubs of the salience network, which is mainly involved in detecting and filtering multimodal salient stimuli (Goulden et al., 2014; Seeley et al., 2007). Thus, we speculate that the middle pathway may act as a “judge” that participates in monitoring and filtering abundant stimuli to determine which source (bottom-up vs top-down) should be perceived. The anterior pathway has direct connections with the prefrontal cortex of both the DAN and VAN. The PFC is the higher-level cognitive cortex of humans, and previous studies have shown that it is the juncture of the dorsal and ventral visual pathways (Goodale and Milner, 1992). It is also the core hub for central cognitive networks (Chen et al., 2013), and it plays important roles in multiple cognitions, such as sustained attention, working memory, and executive controls (Ramnani and Owen, 2004; Wood and Grafman, 2003). Thus, the anterior pathway may preferentially act as a “commander” that receives filtered signals from the middle pathway, and exerts executive commands to the hubs of the posterior pathway. The posterior pathway has direct connections with the posterior parietal cortex (PPC) of the DAN and the TPJ of the VAN. Previous studies have shown that the PPC is closely associated with the formation of saliency maps during attention (Bisley and Mirpour, 2019; Buschman and Miller, 2007; Freedman and Ibs, 2018). The TPJ is the core hub in attention reorienting (Dugue et al., 2018; Natale et al., 2010). Therefore, the posterior pathway may be more important as an “executor” that handles the commands from the prefrontal cortex and then forms the saliency map for filtered stimuli.

Although both anatomical and functional connectivities reflect the relationship between the two brain regions, they have different definitions. Anatomical connectivity refers to the physical fibres between the two brain regions, while functional connectivity refers to the synchronisation in fluctuations of fMRI signals between them. In regards to the relationship between anatomical and functional connectivities, previous studies have demonstrated that functional synchronisation between brain areas are closely associated with direct or indirect anatomical connectivity (Honey et al., 2009; Teipel et al., 2010), and whole-brain anatomical connectivity can predict the strength of functional connectivities at both the group- and individual-level (Honey et al., 2009). Although the functional and anatomical connectivity profiles of the DAN and VAN have been reported (Fox et al., 2006; Thiebaut de Schotten et al., 2011; Umarova et al., 2010), little is known about the relationship between the two types of connectivities in the attention network. In the present study, several pieces of evidence support a close relationship between the functional and anatomical connectivities in the attention network: the functional connectors between the DAN and VAN defined by functional connectivity anatomically bridged the two attention sub-networks; the anatomical connectivity fingerprints of these connectors resembled the functional connectivity ones; the anatomical connectivity strengths of these connectors were significantly correlated with functional connectivities. Moreover, these findings were replicated between independent sub-sets of the HCP dataset, and between the HCP dataset and the Chinese dataset. The close coupling between the anatomical and functional connectivities of the connectors between the DAN and VAN indicates that the functional interactions between the two attention sub-network may have a structural basis. Our speculation is supported by an earlier study reporting that destruction of the fibre bundles between the dorsal and ventral attention nodes caused symptoms of spatial neglect and a disruption of the functional connectivity between them (He et al., 2007). It should be noted that not all of the identified anatomical connections of the connectors had strong functional connectivities (Fig. 4). As shown in Figs. 5, the strength of anatomical connections only explained a maximum of 29% of the individual variance in functional connectivity. The residual individual variance in functional connectivity may be explained by multiple complex factors.
including indirect synaptic connections, neuronal dynamics, neuromodulation, etc. (Harsay et al., 2012).

Several methodological considerations may strengthen the reliability of our findings. First, the main findings were based on a high-quality public dataset from the HCP project. The HCP project is engaged in obtaining and sharing high-quality brain MRI data based on custom-made, high-performance equipment and sophisticated imaging techniques (Van Essen et al., 2013). For example, the dMRI data used in the present study were acquired using a spatial resolution of 1.25 × mm³ and a high-angular multi-shell sampling scheme (diffusion directions = 288, b values = 1000, 2000, 3000 s/mm²). The rfMRI data were also collected with high spatial (2 × mm³) and temporal resolutions (720 ms per frame). In combination with sophisticated preprocessing and modelling methods, the HCP data can dramatically improve the accuracy of functional network construction and fibre tracking (Glasser et al., 2016). Second, the GQI-based fibre-tracking algorithm, as well as ODF decomposition, was introduced to construct anatomical connectivity between the DAN and VAN (Yeh and Tseng, 2013; Yeh et al., 2010). GQI estimates the spin distribution function (SDF) and can reliably reconstruct multiple cross fibres within a single voxel; thus, it is far better than traditional DTI-based fibre tracking methods in accurately estimating the anatomical connectivity profiles of the attention network. In the ISMRM 2015 Tractography challenge, the GQI-based fibre-tracking method achieved the highest valid connections (92%) with fewer invalid connections amongst 96 methods from 20 different research groups (Maier-Hein et al., 2017). Third, in order to validate the robustness of the results, a variety of comparative verification methods were used and the results were highly replicable; they include the following: a) the functional organisation of the DAN and VAN and their connector hubs were replicated across 4 sessions of the HCP rMRI dataset; b) the anatomical connectivity profiles of the connector hubs were strongly similar across HCP dataset1, the HCP dataset2, and the Chinese dataset; c) the functional connectivity profiles of the connector hubs were also strongly similar across the three datasets; d) the anatomical and functional connectivity fingerprints were similar and could be replicated across the three datasets; e) the different scalars we used to measure the strength of the anatomical connectivity of the connector hubs, including the fibre number, fibre density, length-corrected fibre number, and length-corrected fibre density. They all had strong coupling with the functional connectivity; f) the anatomical-functional couplings of these connectors were replicable at both the group- and individual-level; and g) the anatomical-functional couplings of these connectors were replicable in each HCP session. Taken together, high-quality dataset, advanced analytical methods and multi-level verifications ensured the reliability of the findings of this study.

There are some limitations in the present study. First, due to the lack of precise measurements of attentional performance in both the HCP and Chinese datasets, we could not establish a direct link between the connectivity profile of each anatomical pathway and their specific attentional functions. Second, the anatomical and functional connectivity involved in this study cannot characterize the direction of information communication between the DAN and the VAN, so it is unclear how these identified pathways convey attentional information. Third, it is not clear which molecular and biological pathways modulate individual variance in the anatomical connectivity profiles of these connector hubs. Clarifying these issues will help to fully understand the functional roles of the connector hubs and their anatomical circuits between the DAN and VAN.

Conclusions

In summary, the present study uncovered stable and reliable anatomical connections between the DAN and the VAN via functional connectors. These connector hubs had unique anatomical connectivity profiles with the DAN and VAN and resembled functional connectivity. The anatomical and functional connectivities are strongly coupled between the DAN and VAN. Our findings further the understanding of the anatomical mechanisms underlying the functional interactions between the DAN and the VAN.

Disclosure statement

The authors disclose no conflicts of interest.

CRediT author statement

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Data/code availability statement

The HCP dataset that support the findings of this study are available by Human Connectome Project at https://www.humanconnectome.org/study/hcp-young-adult. In addition, the Chinese datasets that support the findings of this study would be available on the public data repository https://data.mendeley.com once upon acceptance.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.neuroimage.2021.117868.

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