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More optimal but less regulated dorsal and ventral visual networks in patients with major depressive disorder

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ABSTRACT

Previous studies indicate that major depressive disorder (MDD) can profoundly modify the visual cortices as well as the visuo-attentional systems of brain. However, little is known on the specific pattern of the whole-network-level abnormalities. In this study, resting-state functional magnetic resonance imaging data were collected from 159 participants, including 86 medication-free MDD patients and 73 matched healthy controls. The dorsal/ventral visual networks were defined based on our previously published brain coordinates from activation likelihood estimation analyses. The static and dynamic network properties were respectively calculated and compared between MDD and control groups. Moreover, the inter-network connectivities quantified using the multivariate distance correlation between the dorsal attention network (DAN) and the two visual networks were also analyzed. Results indicated that both of the two visual networks in MDD were found with significantly increased clustering coefficient (dorsal: $p = 0.002$; ventral: $p = 0.004$) and higher small-worldness (dorsal: $p = 0.001$; ventral: $p = 0.002$) as compared with control group. A higher mean variability of dynamic functional connectivity was found in both two networks in MDDs (dorsal: $p < 0.001$; ventral: $p = 0.001$). Moreover, the two visual networks in MDD group showed decreased inter-network connectivities to DAN (dorsal: $p = 0.004$; ventral: $p = 0.013$). Taken together, these results may support that the ventral and dorsal visual systems under the pathological effect of depression are possibly characterized by a status of increased autonomy, i.e., a more optimal, economical, and efficient intra-network organization combining with increased independency and receiving less outside regulation from attention network, thus indicating the increased functional role of the brain visual systems in MDD.

1. Introduction

It has been recognized that the ability to identify and process the emotion-related visual information, such as facial expressions, is critical in communicating emotions and regulating interactions (Gosselin et al., 1995), and visual deficiency is considered as one of the important neuropathological underpinnings of major depressive disorder (MDD) (Eyre et al., 2016). Emerging evidences from both physiological and anatomical aspects indicated that abnormalities in visual function-related brain areas (e.g., occipital cortices) were involved in MDD. For example, there was evidence that deregulation of a series of neurotransmitters (e.g., reduced muscarinic Ach M2 receptor binding (Scarr,

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2009), reduced level of γ-Aminobutyric acid, GABA (Croarkin et al., 2011), etc.) was found in the occipital cortices in MDD, which may lie the pathophysiological basis for the visual-emotional deficiencies in depressed individuals. Anatomical evidence showed that the inferior fronto-occipital fasciculus (IFO) involved in the visual-emotional functionality (Catani et al., 2002) was found with reduced white matter integrity in MDDs. In addition, the superior parietal lobule (SPL), which is associated with the allocation of attention resources from dorsal attention network (DAN) to visual aspects, has been observed with reduced magnetization transfer ratios, thus may highlight the visuo-attentional dsyconnectivity in depression (Chen et al., 2016; Corbetta and Shulman, 2002; Kumar et al., 2004). Taken together with the reported visual perceptual dysfunctions at behavioral level, these evidences may lead to a focused investigation on the connectivities of visual network systems in MDD.

A number of previous findings may shed light on that visual system is characterized by a status of over recruitment in the brain of MDD patients. One theory posits that over excited visual perception for negative facial expressions is a stable cognitive vulnerability in MDD and is possibly associated with the occurrence or recurrence of depression (Dai and Feng, 2012). Moreover, decreased GABA content in the occipital cortex as indicated in previous studies was considered to contribute to a reduced spatial vision suppression, and subsequently resulted in an abnormally enhanced visual perception which was typically suppressed under attention stimuli (Chen et al., 2016; Golomb et al., 2009). Besides the internal change of visual networks per se, there is evidence supporting that the visual networks may be less controlled by the attention network in MDD, i.e., a visuo-attentional deficiency. Normally, the dorsal attention network (DAN), especially intraparietal sulcus (IPS), exert top-down regulation on visual areas in visuo-attentional task (Fox et al., 2006; Vossel et al., 2014), and reduce the visual cortical activities to suppress the peripheral task-irrelevant stimuli (Desseilles et al., 2009, 2011; Lavie, 2005). However, in depressed individuals, this attention-mediated suppression on visual regions is failed, thus indicating a deficiency in filtering of task-irrelevant visual stimuli. Specifically for example, Desseilles et al. found an increased functional connectivity (FC) between the IPS and V4 in normal control during visuo-attentional task but not in patients with MDD (Desseilles et al., 2009). These evidences of failed modulation of DAN to visual cortices perhaps underlie an inter-network dysconnectivities between the attentional and visual systems.

However, existing explorations on the visual network impairment in MDD were largely limited to scattered visual cortices or areas, thus has not been comprehensively characterized at a whole-network level. Similarly, the reported evidences of visuo-attentional dysregulation were also largely exploratory based on only scattered inter-regional dysconnectivities, while the inter-network connectivities between the two systems have not be directly evaluated, to date. To this end, the following study comprehensively analyzed the static and dynamic intra-network properties of the ventral and dorsal visual networks as well as their inter-network connectivities to DAN to shed light on the mechanisms of visual abnormalities in MDD.

2. Materials and methods

2.1. Subjects

This study was approved by the institutional ethics committee. Before the study, each participant was informed of all procedures of the study and signed the written informed consent. Magnetic resonance imaging (MRI) and clinical data were collected from 148 participants, including 86 patients (59 female and 27 male; median age, 30 years) diagnosed with MDD and 73 healthy controls (56 females and 17 males; median age, 29 years) recruited through advertisements. See Supplementary Appendix 1 for specific inclusion and exclusion criteria.

2.2. Image acquisition

All MR images were acquired on a clinical 3.0 T scanner (Achieva, Philips Medical Systems, Best, The Netherlands) equipped with an 8-channel SENSE head coil. To ensure the brain visual cortices were at resting state, all the subjects were instructed to keep awake with their eyes closed during MR scanning. For each subject, three-dimensional T1-weighted images (3D-T1WI) was acquired utilizing a turbo field echo (TFE) sequence with the following parameters: TR = 8.2 ms, TE = 3.8 ms, flip angle = 7°, Bandwidth = 191 Hz, FOV = 256 × 256 mm^2, voxel size = 1.0 × 1.0 × 1.0 mm^3. Resting-state functional MRI (rs-fMRI) scan was performed using a field-echo echo-planar imaging (FE-EPI) sequence with the following parameters: TR = 2000 ms, TE = 30 ms, flip angle = 90°, bandwidth = 4131 Hz, FOV = 240 × 240 mm^2, voxel size = 3.4 × 3.4 × 3.4 mm^3, 33 axial slices, and total volumes = 240. Moreover, a T2-weighted imaging were also acquired to detect and exclude for any clinical brain abnormalities.

2.3. Rs-fMRI data preprocessing

Preprocessing of the rs-fMRI data was performed using SPM12 (http://www.fil.ion.ucl.ac.uk/spm). For each participant, the first 10 time points were discarded from the fMRI time series to avoid initial signal instability. The resulting 230 vol were corrected for slice timing and for the head motion (a least squares approach and a six-parameter spatial transformation). Subjects with 1) head motion > 1.5 mm in any dimension, 2) angular rotation > 1.5°, or 3) a mean frame-wise displacement (FWD) > 0.25 were excluded for further analysis. Then, all the resultant functional images were coregistered to the individual 3D-T1WI and spatially normalized to the Montreal Neurological Institute (MNI) template (resampled with a voxel size of 3 × 3 × 3 mm^3) using the DARTEL (Diffeomorphic Anatomical Registration using Exponentiated Lie algebra) algorithm (Ashburner, 2007). Then, a spatial smoothing with an 8 mm full width at half maximum (FWHM) isotropic Gaussian kernel was performed to reduce the noise of the normalized functional images. Further processing respectively included voxel-wise detrending, filtering with a band pass filter of 0.01–0.08 Hz, and regression of the white matter signal, cerebrospinal fluid signal, and six motion parameters (Liu et al., 2018).

2.4. Construction of DAN and dorsal/ventral visual networks

The cortical locations of dorsal and ventral visual networks as well as the DAN were decided on the basis of previously published brain coordinates. For the ventral and dorsal visual networks, we adopted our previously established statistical maps of dorsal and ventral pathways, which were based on an ALE analysis (Turkeltaub et al., 2002) of 74 published fMRI studies concerning eight major categories of visual perceptual functions (Deng et al., 2016). Each peak coordinate in the resultant clusters of ALE was used as the center to create a spherical region of interest (ROI) with a radius of 5 mm (Figs. S1A and B). In addition, two ROIs of bilateral primary visual cortices were also established based on the previously published coordinates (Amunts et al., 2000), which were further converted from Talairach space to MNI space using Lancaster transform (Lancaster et al., 2007). The coordinates corresponding to DAN were defined based on the group-averaged cortical network seeds from 1000 brains in Yeo's study (Yeo et al., 2011). Similarly, the spherical ROIs of DAN were created by centering at each coordinate with a radius of 5 mm.

Totally, 31, 22, and 12 ROIs were created respectively for the dorsal visual network, ventral visual network, and DAN (See Table S1). Here, respectively for each of the three networks, the created ROIs were regarded as nodes, and the pair-wise resting-state functional connectivities (RSFCs) between each pair of ROIs calculated based on the rs-fMRI data were served as edges for constructing the corresponding

network. Accordingly, the pair-wise RSFC matrices were calculated respectively for ventral (22 × 22) and dorsal (31 × 31) visual networks for each individual.

2.5. The static and dynamic network properties

The static network measurements were established based on the RSFC of full-length rs-fMRI time series using previously described network quantification method (Watts and Strogatz, 1998). First, the weighted RSFC matrices were thresholded with a spectrum of network densities (5%–40% (Achard and Bullmore, 2007); interval, 1%) to ensure that the networks were comparable among different individuals. Then, for each matrix across the density range, the three network parameters of characteristic path length, clustering coefficient and small-worldness were calculated respectively to assess the abilities of integrated and segregated information processing of the visual networks. For a better evaluation of the network topology, a normalization was done for the three parameters by comparing to 1000 randomly generated networks (Milo et al., 2002), which respectively generated the λ, γ, and σ. Moreover, the mean connectivity strength was calculated by accumulating the RSFCs for each node, then averaging across all the nodes within a network. See *2. Calculation of static network properties* in Supplementary Appendix for the specific calculation method as well as the interpretation of the parameters.

Based on the segmented rs-fMRI time series with a series of successive non-overlapping time windows (Fig. S1C), the dynamic temporal variability of dorsal and ventral visual network connectivities (Deng et al., 2018) was calculated following the previously established method by Zhang et al. (2016). See *3. Calculation of dynamic network properties* in Supplementary Appendix for the specific methodologies. Then, the mean variability across all the ROIs of a network was calculated for each individual, and compared between groups.

2.6. Inter-network connectivities between DAN and dorsal/ventral visual network

The inter-network connectivities between DAN and ventral visual network as well as between DAN and dorsal visual network were measured using the multivariate distance correlation. The metric of multivariate distance correlation was originally proposed by Székely et al. (Székely, 2007) to quantify the multivariate dependence between high dimensional vectors, and its application in functional connectivity data has been validated and encouraged recently by other research (Lou et al., 2018; Geerligs et al., 2016). In the current study, we adopted the modified distance correlation statistic (also proposed by Székely et al. (Székely, 2013)), which was considered to be unbiased by the number of ROIs in each network. See *4. Calculation of inter-network connectivities* in Supplementary Appendix for the specific methodologies.

2.7. Statistical analysis

The demographic and clinical information of the subjects were evaluated using SPSS 23.0. Mann-Whitney *u*-test for non-normally distributed data was performed for the comparison of age, education level, HAMD, and HAMA scores between MDD and control groups. Between-group difference in gender was evaluated using the χ^2 test. A statistical significance level of $p < 0.05$ was adopted.

For the between-group comparisons of static properties of dorsal and ventral visual networks, two sample *t*-test was performed for the density-wise comparisons of network properties across 5%–40%, and a $p < 0.01$ with false discovery rate correction was used to correct for the 36 times of multiple comparisons. The area under the curve (AUC) value was additionally extracted over the whole density range for each individual and compared between two groups using the two sample *t*-test (or Mann-Whitney *u*-test for non-normally distributed data). For the comparisons of mean connectivity strength, dynamic variability, and the inter-network connectivity (i.e., distance correlation between DAN and the two visual networks), two sample *t*-test (or Mann-Whitney *u*-test for non-normally distributed data) was used. Here, for the network measurements of the same nature, a $p < 0.05$ with Bonferroni correction was adopted to correct for the number of tests (e.g., for static connectivity measurements, $p < 0.05/4$ static network metrics/2 visual networks = 0.00625). In addition, all the above comparisons were adjusted for age, gender, education level, and head motion (i.e., FWD) to control their confounding effects.

To evaluate the clinical significance of the network analyses, we assessed the correlation in MDD group between HAMD score and above network measurements using parital correlation with age, gender, education, head motion, and history of medication treatment added as covariates. Similarly, a $p < 0.05$ with Bonferroni correction was used to correct for the number of statistical tests for the network measurements of the same nature. To further clarify the possible confounding effect of several nuisance factors (e.g., anxiety) on the positive network findings, we additionally performed a regression analysis which included HAMA, age, gender, education, head motion, and history of medication treatment as independent factors. Here, $p < 0.05$ was used as an exclusive significance level.

3. Results

3.1. Demographics and neuropsychological test

Age ($p = 0.101$), gender ($p = 0.256$), education level ($p = 0.224$), and head motion during MR scan ($p = 0.225$) were matched between MDD and control groups. The median HAMD and HAMA scores of the patients were 28 and 17, and 56 out of 86 MDD patients had a HAMA score of ≥14. Detailed statistics of the demographic and clinical information were shown in Table 1.

3.2. Altered static network properties of dorsal/ventral visual network

For the dorsal visual network in the MDD group, γ was significantly increased over the density ranges of 0.13–0.30, λ has no significant change between MDD group and control group (Fig. 1), and σ was significantly increased over 0.13–0.32 compared with the control group (Fig. 1). AUC analyses across the whole density range revealed

Table 1
Demographic and clinical data of major depression disorder (MDD) and normal control (NC) groups.

	NC ($n = 73$)	MDD ($n = 86$)	statistics	*P*-value
Age (yr)	30(19–64)	29(18–64)	$Z = -1.642$	0.101
Gender (male/female)	17/56	27/59	$\chi^2 = 1.297$	0.256
Education level(yr)	14(0–24)	13(0–19)	$Z = -1.215$	0.224
HAMD	1(0–11)	28(17–52)	$Z = -10.894$	< 0.001[a]
HAMA	1(0–7)	17(6–40)	$Z = -10.851$	< 0.001[a]
Mean FWD	0.087(0.038–0.246)	0.081(0.037–0.239)	$Z = -1.213$	0.225

[a] Stands for statistically significant; Data are presented as "median (range)"; HAMD = Hamilton rating scale for depression; HAMA = Hamilton rating scale for anxiety; FWD = frame-wise displacement.

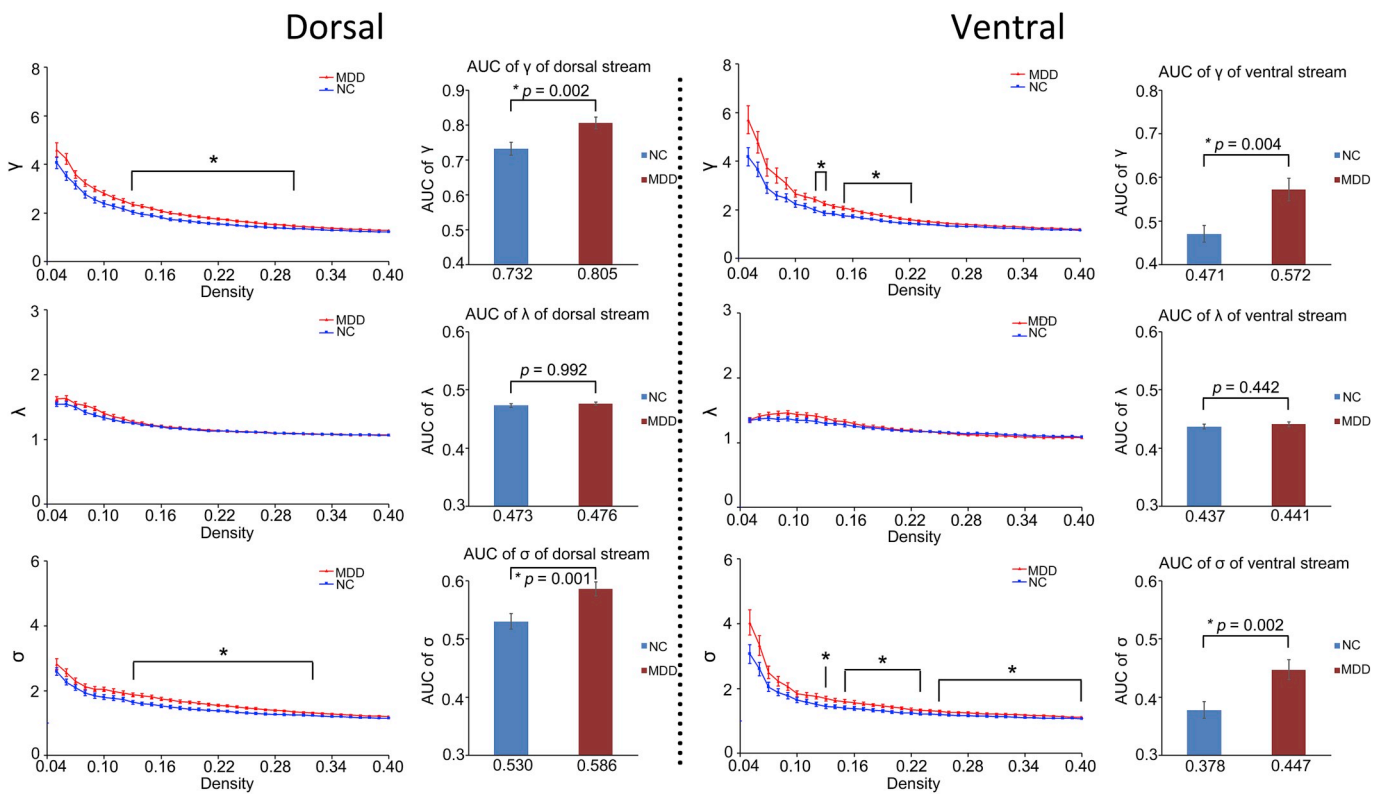

Fig. 1. Comparisons of the static network properties of dorsal (left panel) and ventral (right panel) visual networks between normal control (NC) group and major depressive disorder (MDD) group. For each panel, the first column shows the density-wise comparisons of γ, λ, and σ across the density range of 0.05–0.40 between NC and MDD groups. The second column shows the between-group comparison of area under the curve (AUC) value of the three network parameters extracted over the whole density range. All between-group differences with statistical significance is indicated with *.

Table 2
Comparisons of dorsal/ventral visual network parameters between major depression disorder (MDD) and normal control (NC) groups.

	NC (n = 73)	MDD (n = 86)	Group comparison results	
			Statistics	*P*-value
AUC of γ (dorsal stream)	0.600(0.370–1.083)	0.667(0.391–1.140)	$Z = -3.173$	0.002[a]
AUC of λ (dorssal stream)	0.415(0.362–0.496)	0.414(0.358–0.547)	$Z = -0.010$	0.992
AUC of σ (dorsal stream)	0.510(0.338–0.828)	0.558(0.336–0.856)	$Z = -3.180$	0.001[a]
AUC of γ (ventral stream)	0.536(0.359–1.239)	0.636(0.388–1.578)	$Z = -2.917$	0.004[a]
AUC of λ (ventral stream)	0.423 ± 0.034	0.428 ± 0.041	$T = -0.771$	0.442
AUC of σ (ventral stream)	0.438(0.317–0.993)	0.514(0.302–1.121)	$Z = -3.059$	0.002[a]
Strength (dorsal stream)	10.503(2.775–21.870)	7.893(2.154–20.395)	$Z = -3.871$	< 0.001[a]
Strength (ventral stream)	5.4401.461–13.399)	3.974(1.389–9.752)	$Z = -3.577$	< 0.001[a]
Mean FC variability (dorsal stream)	0.731(0.605–0.816)	0.755(0.625–0.820)	$Z = -3.591$	< 0.001[a]
Mean FC variability (ventral stream)	0.716(0.526–0.806)	0.728(0.548–0.784)	$Z = -3.190$	0.001[a]
Inter-network connectivity to DAN (dorsal stream)	0.730 ± 0.096	0.681 ± 0.097	$T = 2.950$	0.004[a]
Inter-network connectivity to DAN (ventral stream)	0.499 ± 0.150	0.430 ± 0.127	$T = 2.519$	0.013[a]

[a] Stands for statistically significant (with a threshold of $p < 0.05$); Statistics for *T*-test and Mann-Whitney *U* test are respectively indicated with *T* values and *Z* values, and the corresponding data sets were respectively described as "mean ± standard deviation" and "median (range)"; AUC = area under the curve; FC = functional connectivity; DAN = dorsal attention network.

significantly increased γ and σ in the MDD group compared with controls (p = 0.002 and 0.001, respectively). No significant between-group difference of λ was found (p = 0.992). Moreover, the mean connectivity strength of the dorsal visual network was significantly lower in MDD group compared with control group ($p < 0.001$) (Table 2, Fig. 1).

For the ventral visual network in MDD group, γ was significantly increased over the density ranges of 0.12–0.13 and 0.15–0.22, λ has no significant change, and σ was significantly increased at 0.13 and over 0.15–0.23 and 0.25–0.40 compared with the control group (Fig. 1). AUC analyses across the whole density range revealed significantly increased γ and σ (p = 0.004 and 0.002, respectively) compared with controls, and the between-group difference of λ was of no significance (p = 0.442). Moreover, the mean connectivity strength of the ventral visual network was significantly lower in MDD group compared with control group ($p < 0.001$) (Table 2, Fig. 1).

3.3. Changed temporal variability of dorsal/ventral visual network connectivity

Compared with healthy controls, both the dorsal and ventral visual networks were found significantly elevated mean temporal variability of FC in MDD group ($p < 0.001$ and p = 0.001, respectively) (Table 2, Fig. 2).

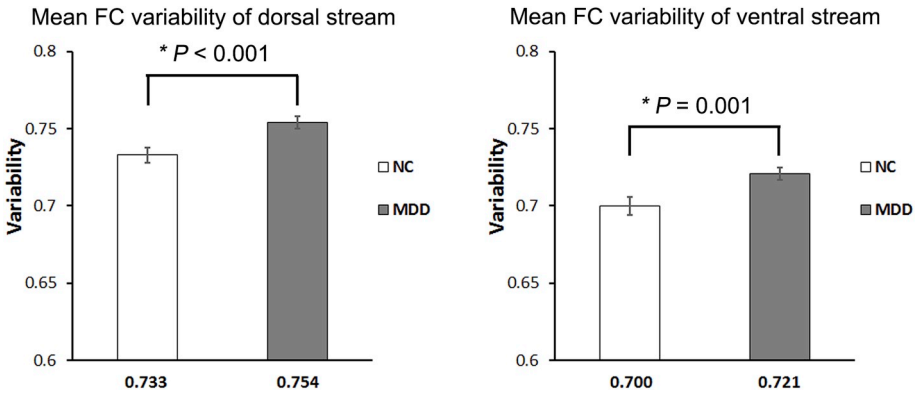

Fig. 2. Comparisons of temporal variabilities of ventral and dorsal network connectivity between major depressive disorder (MDD) and control (NC) groups. Mean functional connectivity variabilities of both the dorsal and ventral visual networks are significantly elevated in MDDs compared with NCs.

3.4. Inter-network connectivity between DAN and dorsal/ventral visual network

We used the multivariate distance correlation to quantify the inter-network connectivity between DAN and the two visual networks. We found that MDD patients showed significantly lower distance correlations of DAN seeds to both dorsal and ventral visual network ROIs (p = 0.004 and 0.013, respectively) (Table 2, Fig. 3).

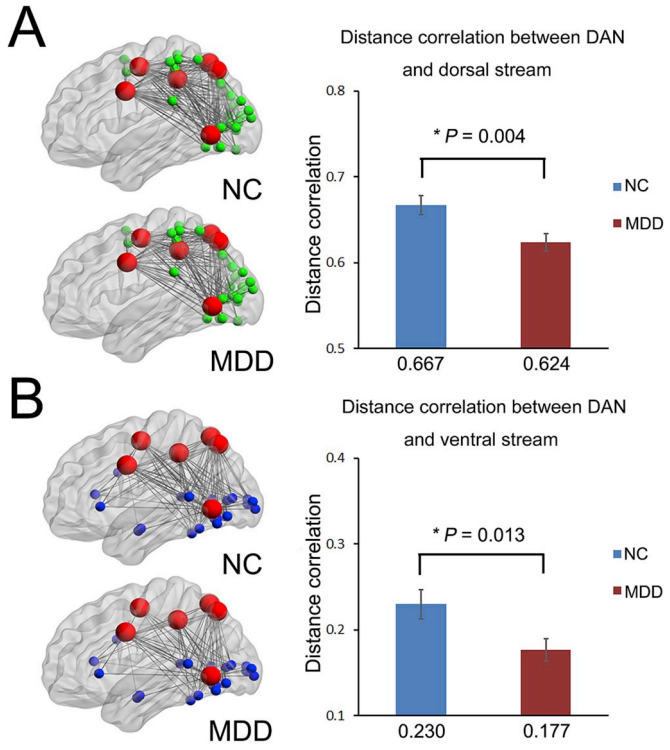

Fig. 3. Comparisons of distance correlations of dorsal and ventral visual networks to dorsal attention network (DAN) between major depressive disorder (MDD) and control (NC) groups. The network nodes of DAN, dorsal, and ventral networks are respectively shown as spheres in red, green, and blue, and the functional connectivities of > 0.2 are illustrated with grey lines. Distance correlation between DAN and both dorsal (A) and ventral (B) visual network are significantly decreased in MDDs compared with NCs. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

3.5. Relationship between network measurements and disease severity

We assessed the correlation between HAMD score and the network parameters. Results revealed that the inter-network connectivity between DAN and dorsal visual networks was negatively correlated to the HAMD score (r = −0.298, p = 0.007) (Fig. 4). Whereas, correlations of the rest network parameters to HAMD did not survived the Bonferroni correction.

3.6. Regression analyses of nuisance factors

Regression results showed that age had a significant contribution on σ of ventral stream (p = 0.042) and FC variability of ventral stream (p < 0.001). Both gender and HAMA had a significant contribution on dorsal-DAN inter-network connectivity (p = 0.047, and 0.035, respectively). For both of the dorsal and ventral streams, head motion showed a significant contribution to mean connectivity strength (both ps < 0.001) and to inter-network with DAN (dorsal: p = 0.004, ventral: p < 0.001) of the two networks. Whereas, education and history of medication treatment were found with no significant influence on any of the network parameters with between-group differences. Detailed results were summarized in Table S2.

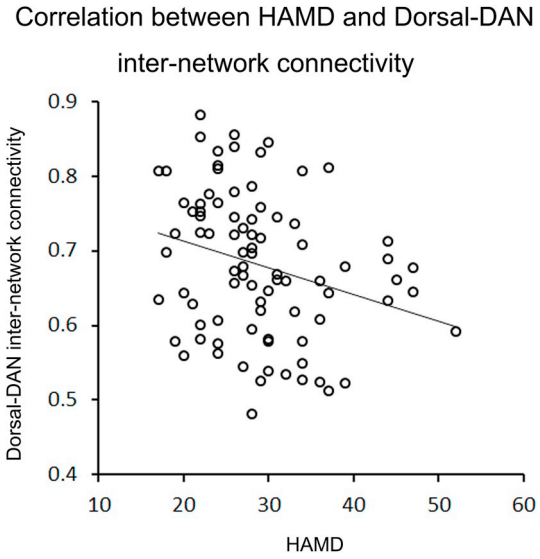

Fig. 4. Correlation of Hamilton rating scale for depression (HAMD) score to the inter-network connectivity between dorsal attention network (DAN) and dorsal visual network in the major depressive disorder (MDD) group. HAMD score is negatively correlated to the inter-network connectivity of the two networks (r = −0.298, p = 0.007).

4. Discussion

To data, this is the first attempt to characterize the whole-network-level abnormalities of ventral and dorsal visual pathways in MDD. Major findings include: 1) The two networks were characterized by a more optimized and economical intra-network architecture with an increased efficiency for localized information processing and with well preserved ability of network integration; 2) The temporal variability of the whole dorsal and visual network connectivities were increased in MDDs, which is more compatible with higher level functional activities; 3) A decreased inter-network connectivity of DAN to dorsal and to ventral visual networks was observed in MDD group. Overall, these findings taken together may indicate the higher independency as well as an increased functional role of the two visual networks in MDD patients.

For the static connectivity analyses, a significantly increased clustering coefficient along with a comparatively unchanged characteristic path length was observed in the dorsal and ventral visual networks in MDD patients. Clustering coefficient is considered as the ability of a network for localized information processing, i.e. the network segregation (Bullmore and Bassett, 2011). Specific to the visual system, this increased local interaction as currently observed is particularly consistent with the widely reported over recruitment of the visual cortices in MDD. Specifically, Golomb et al. identified an abnormally enhanced visual processing in MDDs in a visual motion perception task, i.e., motion perception for typically suppressed stimuli was enhanced (Golomb et al., 2009). This finding revealed an enhanced recruitment of visual cortices to perceive visual information in MDDs, and thus compatible with a hyper-efficient states of the visual brain system in the patients. In addition, more direct evidence from network topological analysis revealed a tendency that the functional hubs in depressed patients were shifted from classic centers (e.g., cingulate) towards occipital visual regions (Borchardt et al., 2015), emphasizing the increased role of the visual cortices for intrinsic information transfer. Therefore, taken together with our current results of increased clustering coefficient, we may consider that the ventral and dorsal visual networks are reorganized into a more efficient, while more economical (or well balanced) architecture in depressed individuals.

For the dynamic connectivity analyses, results revealed significantly increased temporal variabilities of both the ventral and dorsal networks in MDD patients. Previous study claimed that higher FC variability of a brain component could be compatible with its role in higher level functional activities (Zhang et al., 2016). For example, the multimodal association cortices that responsible for processing more complex cognitive activities usually receive and integrate information from multi-model primary cortices. Consequently, these cortices interact with multiple functional communities at different times with its BOLD series pattern switched frequently, thus yielding a high temporal variability. Therefore, being consistent with the static network findings of more optimized intra-network topology and increased hub density in visual cortices (Borchardt et al., 2015), the currently observed abnormal FC variability increase in dorsal and ventral visual networks might provide another evidence to support the increased functional role of the visual system in depression patients.

In the present study, we also interested in the visuo-attentional dysconnectivity in MDDs. Previously, the Load Theory of attention proposed a “top-down regulation” of parietal attention network on the visual cortices in healthy individuals (Lavie, 2005; Lavie et al., 2004): during visuo-attentional task, the increase of parietal activity driven by increasing attention load was associated with a negative modulation (or suppression) on visual cortex, indicating a better filtering of task-irrelevant visual stimuli. For example, in Desseilles' study of a visual attention task combined with task-irrelevant colored stimuli (Desseilles et al., 2009), healthy individuals showed decreased responses to the color stimuli in color-responsive area (i.e., V4) as the attention load of the task increases. By contrast, this Load Theory was failed in MDD patients by showing that the V4 activity remained low under both the low and high load tasks. This may imply that the visual and attentional systems were mutually independent in MDDs, to some extent. In addition, other evidence based on visual search task which was found with a slowed processing speed in depressed individuals (Potter et al., 2013), indicated that the slowed visual search was increasingly evident in MDDs when target detection was more attention-demanding (Hammar et al., 2003). Therefore, in line with these findings, the decreased inter-network connectivites between DAN and ventral&dorsal visual networks as currently observed may be reflective of the dysregulation from DAN to visual system in MDD.

Regarding the significance of the current network findings to the clinical outcome of MDD, an association was found between the disease severity and the dorsal-DAN internetwork connectivity decrease. In addition, regression analysis showed that the contribution of HAMA to the dorsal-DAN internetwork connectivity change cannot be excluded, further suggesting that the comorbidity between depression and anxiety was also related to dorsal-DAN internetwork dysconnectivity. Therefore, these findings further highlighted the close relationship between the visuo-attentional dysconnectivity and the genesis of symptoms in MDD. On the other hand, since no correlation was found between the intra-network measurements and the symptom, we may speculate that the intra-network reorganization of dorsal and ventral visual systems perhaps do not have a direct impact on the clinical outcome of depression, or is perhaps a compensation mechanism with limited extent.

Regarding how the current visual network changes are involved in or interact with the pathogenesis model of MDD, a series of speculations may be proposed as following. On one hand, from the perspective of top-down regulation, previous studies have demonstrated the reward stimuli could exert modulation effect on the visual processing during attentional control process (Hickey et al., 2010). Corresponding results have revealed that the reward-related activity initiates a serious of events and eventually leads to changes in attentional control and sensory representation. Besides, in rat model, the reward expectation is found represented in the activity of individual cells in primary visual cortex (Shuler and Bear, 2006). Thus, these findings confirmed the top-down regulation of reward system on the visual perceptual system. As a consequence, the high-level visual system responsible for the processing of visual perception may exhibit abnormalities. Therefore, our finding of the decreased internetwork connectivity between DAN and dorsal/ventral visual network may be indicative of the decreased top-down regulation from reward/attention system on visual system. On the other hand, evidence also revealed the altered down-top regulation from visual cortices to the emotional system in MDD patients. Sterzer's study showed a preferential access to awareness for mood-congruent stimuli in non-depressed individuals, i.e., depressive visual perception could induce a suppressed sensory information processing (Sterzer et al., 2011). Disruption of such a visual perceptual biases towards mood-congruent information may contribute to depressed mood and negative cognitive biases in MDD patients (Sterzer et al., 2011). This evidence may be in line with our finding of increased γ and σ of both ventral and dorsal visual networks in MDD patients. In another word, the excessively efficient, optimized dorsal/ventral network topology as currently observed may be compatible or reflective of the failed suppression of the processing of depressive visual perception in MDD patients. However, these speculations are largely hypothetical, and further studies are encouraged to clarify the specific relationship between visual perceptual abnormalities and depression.

5. Conclusion

In summary, this study revealed that the ventral and dorsal visual networks in MDD patients show a more efficient and optimized intra-network configuration (possibly to be compatible to its over recruitment status in MDD), while are more independent and isolated with

DAN (possibly indicative of receiving less outside regulation from DAN). Taken together, these results may support that the ventral and dorsal visual systems under the pathological effect of depression are characterized by a status of increased autonomy, indicating its increased functional role in brain. These findings may help comprehensively describe the abnormality pattern of brain visual systems in MDD at a whole-network-level, and also provide a new interpretation for the pathogenesis of MDD from the visual perspective.

Conflicts of interest

The authors declare no conflict of interest.

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Author contribution

All the listed authors have participated actively in the study: Kai Liu, Yanjia Deng designed the study; Bin Zhang, Yong Lin, Xiang Xue, Hui Chen, Jingyu Zhang, Kai Liu, and Danfeng Zou collected the data; Kai Liu, Hui Chen, and Youyong Kong analyzed the data; Hui Chen and Yanjia Deng wrote the manuscript; Kai Liu revised the manuscript; Ge Wen, Menglin Chen, and Jingdong Yan provided technical support; Yanjia Deng supervised the study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpsychires.2019.01.005.

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