




## RESEARCH ARTICLE

# Dynamic brain connectome and high risk of mental problem in clinical nurses

Ling Bai<sup>1,2</sup> | Gong-Jun Ji<sup>3,4</sup>  | Yongxia Song<sup>1</sup> | Jinmei Sun<sup>3,4</sup>  | Junjie Wei<sup>4</sup> | Fang Xue<sup>5</sup> | Lu Zhu<sup>6</sup> | Rui Li<sup>2</sup> | Yanfang Han<sup>2</sup> | Liu Zhang<sup>1</sup> | Jinying Yang<sup>7,8</sup> | Bensheng Qiu<sup>7,8</sup> | Guo-Rong Wu<sup>9</sup> | Jing Zhang<sup>5</sup> | Jingfang Hong<sup>1</sup> | Kai Wang<sup>3,4,10,11</sup>  | Chunyan Zhu<sup>3,4,10,11</sup>

<sup>1</sup>School of Nursing, Anhui Medical University, Hefei, China

<sup>2</sup>Department of Pneumology, The First Affiliated Hospital of Anhui Traditional Chinese Medicine University, Hefei, China

<sup>3</sup>Department of Neurology, The First Affiliated Hospital of Anhui Medical University, the School of Mental Health and Psychological Sciences, Anhui Medical University, Hefei, China

<sup>4</sup>Anhui Province Key Laboratory of Cognition and Neuropsychiatric Disorders, Hefei, China

<sup>5</sup>College of Nursing, Bengbu Medical University, Bengbu, China

<sup>6</sup>Institute of Literature in Chinese Medicine, Nanjing University of Chinese Medicine, Nanjing, China

<sup>7</sup>Laboratory Center for Information Science, University of Science and Technology of China, Hefei, China

<sup>8</sup>Hefei National Lab for Physical Sciences at the Microscale and the Centers for Biomedical Engineering, University of Science and Technology of China, Hefei, China

<sup>9</sup>Key Laboratory of Cognition and Personality, Southwest University, Chongqing, China

<sup>10</sup>Anhui Provincial Institute of Translational Medicine, Anhui Medical University, Hefei, China

<sup>11</sup>Institute of Artificial Intelligence, Hefei Comprehensive National Science Center, Hefei, China

## Correspondence

Jingfang Hong, College of Nursing, Anhui Medical University, Hefei, 230032, China.  
Email: hongjingfang@ahmu.edu.cn

Kai Wang and Chunyan Zhu, Department of Neurology, The First Affiliated Hospital of Anhui Medical University, the School of Mental Health and Psychological Sciences, Anhui Medical University, Hefei, 230032, China.  
Email: wangkai1964@126.com (K. W.) and aysallow@126.com (C. Z)

## Funding information

Youth Top-notch Talent Support Program of Anhui Medical University; National Key R&D Plan of China, Grant/Award Number: 2016YFC1300604; National Basic Research Program of China, Grant/Award Number: 2015CB856405; Doctoral Foundation of Anhui Medical University, Grant/Award Number: XJ201532; University Natural

## Abstract

With the growing population and rapid change in the social environment, nurses in China are suffering from high rates of stress; however, the neural mechanism underlying this occupation related stress is largely unknown. In this study, mental status was determined for 81 nurses and 61 controls using the Symptom Checklist 90 (SCL-90) scale. A subgroup ( $n = 57$ ) was further scanned by resting-state functional MRI with two sessions. Based on the SCL-90 scale, “somatic complaints” and “diet/sleeping” exhibited the most prominent difference between nurses and controls. This mental health change in nurses was further supported by the spatial independent component analysis on functional MRI data. First, dynamic functional connectome analysis identified two discrete connectivity configurations (States I and II). Controls had more time in the State I than II, while the nurses had more time in the State II than I. Second, nurses showed a similar static network topology as controls, but altered dynamic properties. Third, the symptom-imaging correlation analysis

Ling Bai, Gong-Jun Ji, and Yongxia Song contributed equally to this work.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2021 The Authors. *Human Brain Mapping* published by Wiley Periodicals LLC.

Science Research Project of Anhui Province, Grant/Award Number: KJ2020A0194; Foundation of the First Affiliated Hospital of Anhui Traditional Chinese Medicine University, Grant/Award Number: 2019rwyb12; National Natural Science Foundation of China, Grant/Award Numbers: 81771456, 81573017, 91232717, 31571149, 81971689, 31970979, 82090034

suggested the functional alterations in nurses as potential imaging biomarkers indicating a high risk for “diet/sleeping” problems. In summary, this study emphasized the high risk of mental deficits in nurses and explored the underlying neural mechanism using dynamic brain connectome, which provided valuable information for future psychological intervention.

#### KEYWORDS

dynamic, functional connectivity, mental health, nurse

## 1 | INTRODUCTION

Nurses play a pivotal role in today's health care environment. In contrast to the huge requirement, there is a shortage of 5.9 million nurses according to *The State of World Care Report 2020*. In China, with the growing population and rapid change in the social environment, nurses are suffering from high levels of stress. Particularly, during the outbreak of coronavirus disease (COVID-19), nurses were the clinical staff with the most physical contact with patients. With a high risk of infection, nurses worked under considerable psychological pressure (Liang, Chen, Zheng, & Liu, 2020), which not only threatened their productivity and well-being, but also appeared to cause mental health problems (Hilton, Scuffham, Sheridan, Cleary, & Whiteford, 2008; Milliken, Clements, & Tillman, 2007). Thus, estimating the mental health of nurses will provide valuable information for improving the medical and healthcare system, which may elevate the ability to fight the next outbreak.

Currently, the mental health of nurses is mainly estimated using neuropsychological tests. The Symptom Checklist 90 (SCL-90) scale is a classic self-report inventory, which is well developed and shown to have sound psychometric properties in a previous study (Bech, Bille, Moller, Hellstrom, & Ostergaard, 2014). SCL-90 has been widely used in investigating the mental status of Chinese nurses (Wang et al., 2018). A cross-temporal meta-analysis of 244 studies indicated that the SCL-90 scores of Chinese nurses increased steadily from 1998 to 2016 (Xin, Jiang, & Xin, 2019); however, most of the studies did not include a large sample of controls. The SCL-90 scores of nurses are usually compared to the Chinese norm obtained in 1986. With the rapid social development, the criteria of this old norm are inappropriate to assess people after 10 years have elapsed. Some studies selected hospital administrators or technical personnel as the control group, despite an educational background that is quite different from nurses. To control this point, nursing graduates who did not work in the clinic may be a better choice.

In addition to neuropsychological tests, neuroimaging has increasingly been adopted as an objective and important approach for psychological investigation. Using resting-state functional connectivity (RSFC), multiple biological features can be predicted, such as age (Dosenbach et al., 2010), intelligence (Li et al., 2020), personality (Kong et al., 2019), and diagnosis (Drysdale et al., 2017; Ji et al., 2019; Ji et al., 2019). It has also been used to estimate the neural underpinnings of realistic view adoption in nurses (Ogino, Kawamichi,

Kakeda, & Saito, 2019). Traditionally, most of these studies assumed that the participants were in a homogenous state during scanning, while ignoring the dynamic aspect over time. Current advances suggest that the dynamic psychological course can be captured using time-varying analyses and represented by different RSFC patterns (Allen et al., 2014; Gonzalez-Castillo et al., 2015). In the clinical application, several mental statuses (usually 2–7) and diagnosis-specific RSFC biomarkers could be identified by the dynamic analysis on resting-state functional MRI data (Rabany et al., 2019). However, few study investigated the static or dynamic RSFC network features in nurses.

In this study, we hypothesized that the mental health of nurses may be affected by years of clinical work. To test this hypothesis, a traditional neuropsychological test (i.e., SCL-90) was used to characterize the mental status of nurses, and RSFC with graph theory was adopted to show the functional architecture during the resting state. To exclude the effect of the educational background, nursing graduates who did not work in the clinic were included as the control group.

## 2 | MATERIALS AND METHODS

### 2.1 | Participants

To show the effect of clinical work on mental health, clinical nurses were recruited as the experimental group. To exclude the effect of the educational background, nursing graduates who did not work in the clinic were included as the control group. Of note, most of these people become postgraduate students. To match the three grades of postgraduates, the work experience of clinical nurses was limited to 3 years. The exclusion criteria were the same for both groups, as follows: (a) head injury, psychiatric or neurological disease, and alcohol or drug abuse; (b) psychiatric disease history in first-degree relatives; and (c) declined or unable to undergo MRI scanning. The study was approved by the Research Ethics Board for the Anhui University of Chinese Medicine. All participants were recruited from the local medical universities and the affiliated hospitals by advertisement.

### 2.2 | Neuropsychological testing and MRI

To estimate the mental health status, all participants completed the SCL-90 test with a 5-point rating scale for 90 items, ranging from “not

at all" to "extremely." The SCL-90 is a very commonly used neuropsychological test that includes the following 10 dimensions: somatic complaints; obsessive-compulsive; interpersonal sensitivity; depression; anxiety; hostility; phobic anxiety; paranoid ideation; psychoticism; and diet/sleeping (higher score implicating a lower level of mental health). Between-group comparisons were performed for the scores of the 10 factors, number of risk items, and total SCL-90 score with covariates including age, gender, and months after graduation. The significance of the multiple comparisons was corrected by the false discovery rate (FDR;  $q < .05$ ).

MRI data were obtained at the University of Science and Technology of China with a 3-T scanner (Discovery 750; GE Healthcare, Milwaukee, WI). High-resolution T1-weighted images were acquired in the sagittal orientation using a three-dimensional brain-volume sequence (repetition/echo time, 8.16/3.18 ms; flip angle, 12; field of view,  $256 \times 256 \text{ mm}^2$ ;  $256 \times 256$  matrix; section thickness, 1 mm; voxel size,  $1 \times 1 \times 1 \text{ mm}^3$ ). During resting-state functional MRI scanning, participants were instructed to rest with their eyes closed without falling asleep. To obtain a steady connectivity pattern, two sessions of functional images (434 volumes) were acquired using a single shot gradient-recalled echo planar imaging sequence (repetition/echo time, 2,400/30 ms; flip angle, 90; field of view,  $192 \times 192 \text{ mm}^2$ ;  $64 \times 64$  in-plane matrix; section thickness, 3 mm; voxel size,  $3 \times 3 \times 3 \text{ mm}^3$ ; 46 transverse sections).

## 2.3 | Image data preprocessing

The resting-state functional images were pre-processed using SPM12 software ([www.fil.ion.ucl.ac.uk/spm](http://www.fil.ion.ucl.ac.uk/spm)) and ANFI (<https://afni.nimh.nih.gov/afni/>). The processing steps were as follows: (1) delete the first five time points; (2) remove temporal spikes; (3) slice timing correction; (4) head motion correction; (5) co-registration to structural image; (6) regress out nuisance regressors (24 head motion parameters, and average signals in the cerebrospinal fluid, white matter, and whole brain); (7) spatial normalization to the Montreal Neurological Institute space using the matrix produced by structural image segmentation (Ashburner, 2007); and (8) spatial smooth with a 4-mm full width at half-maximum Gaussian kernel.

## 2.4 | Identification of intrinsic networks

To identify the intrinsic functional networks of our data, a group-level spatial independent component analysis (ICA) was performed using the GIFT software [v4.0b] (Calhoun, Adali, Pearlson, & Pekar, 2001). We used a relatively high model order (number of components, 100) to achieve a "functional parcellation" of refined components corresponding to known anatomic and functional segmentations (Allen et al., 2014). Two steps were performed for data reduction. First, subject-specific data reduction via principal components analysis retained 150 principal components. Then, the concatenated subject-reduced data were decomposed into 100 aggregate components

along directions of maximal group variability. To ensure the stability of estimation, the Infomax ICA algorithm was repeated 20 times in ICASSO, and aggregate spatial maps were estimated as the modes of component clusters (Damaraju et al., 2014; Himberg, Hyvarinen, & Esposito, 2004). Finally, the group components were back-projected to produce subject-specific spatial maps and time courses using the spatiotemporal regression approach (Calhoun et al., 2001; Erhardt et al., 2011).

Of the 100 independent components (ICs), 50 were identified as parts of intrinsic networks (Figure 1) and sorted according to the criteria of previous studies (Allen et al., 2014; Kim et al., 2017). Briefly, (a) the spatial distribution of component clusters mainly fell on gray matter, (b) showed less overlap with vascular, ventricular, or susceptibility artifacts; and (c) time course of the component was dominated by low-frequency signals ( $<0.1 \text{ Hz}$ ).

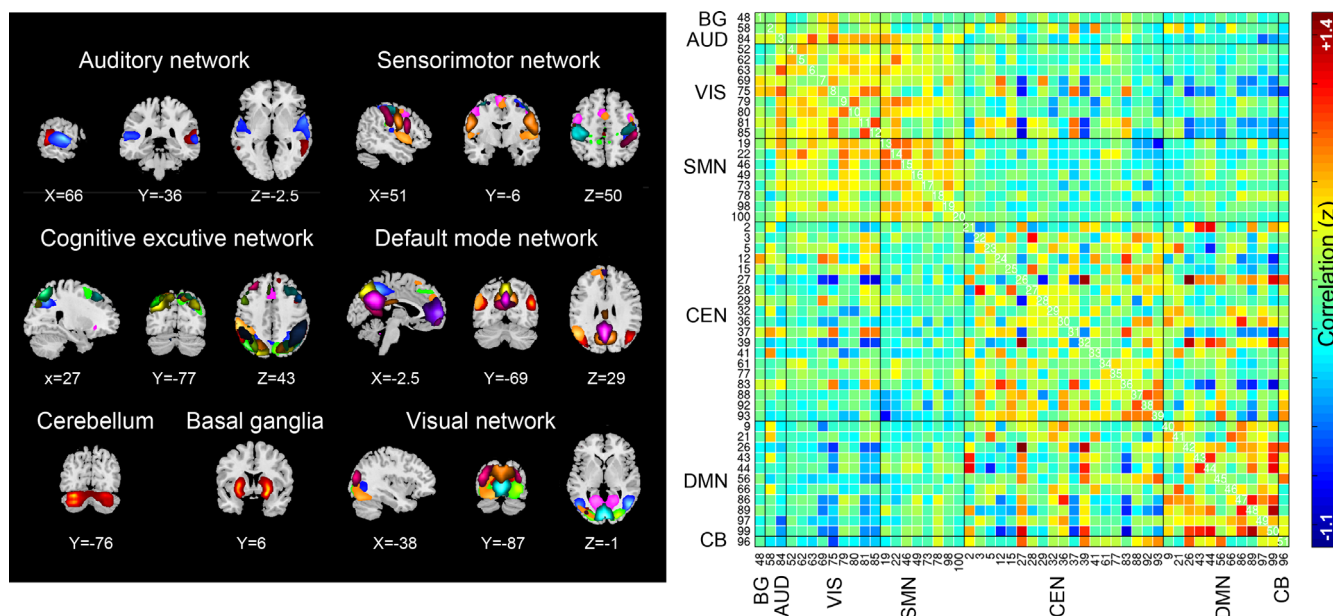
## 2.5 | Static functional network connectivity

To exclude physiologic noise, the time course of 50 ICs was low-pass filtered with a high-frequency cut-off of 0.15 Hz using a fifth order Butterworth filter. Then, pairwise Pearson's correlations were computed between ICs and converted using Fisher's z-transformation (Figure 1).

Network properties were computed for these matrices across a range of thresholds (i.e., sparsity). The lower range was defined as the average degree (i.e., the number of connections linked to the node) over all nodes under each threshold network, which was  $>2 \times \log(N)$  with  $N = 50$  denoting the number of components. The upper range corresponded to the lowest significant correlation coefficient ( $p < .05$ ) among all subjects. This generated the range from 0.18 to 0.48 (step = 0.04). Using the Brain Connectivity Toolbox (<http://www.brain-connectivity-toolbox.net/>), six global properties were computed as in our previous study (Ji, Ren, et al., 2019): network strength ( $S_p$ ); global efficiency ( $E_{\text{glob}}$ ); local efficiency ( $E_{\text{loc}}$ ); shortest path length relative to a random network ( $\Gamma$ ); clustering coefficient relative to a random network ( $\Lambda$ ); and small worldness ( $\Sigma$ ). The area under the global property curve that provided an overall estimation independent of the sparsity threshold was compared between groups by two-sample t-tests. Age, gender, and months after graduation were included as covariates in this analysis.

## 2.6 | Dynamic functional network connectivity (dFNC)

The dynamic functional connectivity between ICs was estimated using a sliding window approach. According to previous studies (Allen et al., 2014; Kim et al., 2017), each window contains 22 consecutive repetition time (52.8 s). The window was slid step-wise by one repetition time along the scanning time (212 volumes), resulting in 190 consecutive windows. Within each window, a  $50 \times 50$  matrix (Fisher's z transformed) was calculated using the regularized precision matrix



**FIGURE 1** Independent components and their static connectivity. The 50 independent components were sorted into seven functional networks: basal ganglia (BG); auditory (AUD); sensorimotor (SMN); visual (VIS); default mode (DMN); cognitive executive (CEN); and cerebellar (CB) networks. The correlation matrix between component pairs was computed using the entire resting-state data. Index numbers of independent components are written on the left and bottom sides of the matrix

(Smith et al., 2011) with L1 norm constraint to enforce sparsity (Friedman, Hastie, & Tibshirani, 2008). Then, the 190 matrices were clustered using a *k*-means algorithm. The optimal number of functional connectivity states (i.e., centroid) were estimated in a search window of *k* from 2–10. Among 18 clustering methods, 7 supported a *k* of 2 (mode) as the optimal number of states (see Figure S1). Three temporal properties of the dynamic states (fractional windows, mean dwelling time, and the number of transitions) were computed using the GIFT software (v4.0b) (Calhoun et al., 2001).

Network properties were computed for each window and sparsity (the same as the static network computation). Then, the property of each window was represented by the area under the global property curve. Finally, the coefficient of variation (CV) of the network property across the 190 windows was assessed to show the variability of topological metrics over time. The Student's *t* test or the Mann–Whitney *U* test was used to compare the between-group difference of the dFNC measures. Age, gender, months after graduation, and dynamic head motion were included as covariates in this analysis. The dynamic head motion was computed as the CV of frame-wise head motion (Jenkinson, Bannister, Brady, & Smith, 2002) across the 190 windows.

### 3 | RESULTS

#### 3.1 | Demographic and neuropsychological characteristics

There were 85 nurses and 61 controls included in this study. The two groups were well matched in age, gender, and months after graduation (Table 1). All 12 SCL-90 scores (10 factors, the number of risk

items, and total score) were significantly higher in nurses than controls (FDR corrected,  $q < .05$ ; Table 1). “Somatic complaints” and “diet/sleeping” showed the most prominent difference between groups.

Of the 146 participants, 36 nurses and 21 controls received multi-modality MRI scanning. No significant difference was demonstrated in age, gender, or months after graduation between the nurse and control groups (Table S1). Among the 12 SCL-90 scores, the “diet/sleeping” score was significantly higher in the nurse group than the control group (FDR corrected,  $q < .05$ ; Table S1).

#### 3.2 | Intrinsic network identification

Of the 100 ICs, 50 were grouped into one of the seven intrinsic brain networks (see the spatial maps and correlation matrix in Figure 1). These networks are as follows: basal ganglia (BG) network (IC 48); auditory (AUD) network (ICs 58 and 84); visual (VIS) network (ICs 19, 22, 46, 49, 78, 98, and 100); sensorimotor (SMN) network (ICs 52, 62, 63, 69, 75, 79, 80, 81, and 85); default mode (DMN) network (ICs 9, 21, 26, 43, 44, 56, 66, 86, 89, 97, and 99); cerebellar (CB) network (IC 96); and cognitive executive (CEN) network composed by dorsal attentional network (ICs 3, 5, 15, 28, 32, 36, 61, and 77), ventral attentional network (ICs 2, 12, 37, and 41), frontal–parietal network (ICs 27, 29, 39, 83, 88, 92, and 93).

#### 3.3 | Static network properties

No significant difference between groups existed for the six network properties (all  $p > .05$ ; Table S2).

**TABLE 1** Demographic and clinical characteristics of study participants

Measures	Nurse (n = 85)	Control (n = 61)	Statistics/ raw p value
<b>Demographics</b>			
Age (Y)	24.3 ± 1.26z	24.1 ± 1.47	0.60 <sup>b</sup> /.55
Gender (M/F)	3/82	2/59	<0.01 <sup>a</sup> /.94
Months after graduation	16.7 ± 7.75	17.1 ± 7.22	2507 <sup>c</sup> /.72
<b>SCL-90</b>			
Somatic complaints	1.5 ± 0.45	1.3 ± 0.23	1,520 <sup>c</sup> / $<.0001$
Obsessive-compulsive	1.8 ± 0.47	1.6 ± 0.42	2018 <sup>c</sup> /.02
Interpersonal sensitivity	1.6 ± 0.49	1.4 ± 0.42	2030 <sup>c</sup> /.03
Depression	1.6 ± 0.50	1.4 ± 0.42	1944 <sup>c</sup> /.01
Anxiety	1.6 ± 0.47	1.4 ± 0.37	1790 <sup>c</sup> /.001
Hostility	1.5 ± 0.45	1.3 ± 0.36	1994 <sup>c</sup> /.02
Phobic anxiety	1.4 ± 0.41	1.2 ± 0.26	1867 <sup>c</sup> /.004
Paranoid ideation	1.4 ± 0.42	1.2 ± 0.30	1893 <sup>c</sup> /.005
Psychoticism	1.4 ± 0.41	1.2 ± 0.41	1709 <sup>c</sup> /.0004
Diet/sleeping	1.6 ± 0.47	1.3 ± 0.37	1723 <sup>c</sup> /.0005
No. of risk items	38.8 ± 22.6	24.3 ± 17.3	1645 <sup>c</sup> /.0001
Total score	138.8 ± 36.9	121.3 ± 25.6	1819 <sup>c</sup> /.002

Note: Means ± SDs.

Abbreviations: F, female; M, male; NA, not available; Y, year.

<sup>a</sup>According to the chi-square test.

<sup>b</sup>According to the two-sample t-test.

<sup>c</sup>According to the Mann-Whitney U test.

### 3.4 | Dynamic network properties

Clustering analysis categorized the 190 dynamic connectivity patterns into two brain function states across all participants. The centroids of both clusters (Figure 2a; Figure S2) indicated strong functional connectivity within the network and relatively weak connectivity between networks. The highest correlations (top 5%) mainly consisted of connections within and between DMN, CEN, and VIS networks (Figure 2b). Compared to State II (58% frequency), State I (42% frequency) had a stronger RSFC strength both within (paired  $t = 5.3, p < .0001$ ) and between networks (paired  $t = 6.2, p < .0001$ ; Figure 2c).

A significant between-group difference existed in fractional windows (i.e., proportion of time spent in each state,  $t = 2.8, p = .007$ ; Figure 3a). Specifically, State I was observed less often in nurses (34.8 ± 24.2%) than controls (53.7 ± 24.4%), while State II occurred more frequently in nurses (65.2 ± 24.2%) than controls (46.3 ± 24.2%). The mean dwelling time in State I was shorter in nurses than controls ( $U = 201, p = .003, df = 55$ ), while State II was longer in nurses than controls ( $U = 188, p = .02, df = 50$ ; Figure 3b). Notably, five outliers (three nurses, two controls) were identified by nonlinear regression analyses (Motulsky & Brown, 2006), and excluded from the analysis for State II. Adding the outliers back did not change the significance. No differences were found with respect to the number of transitions between nurses (mean ± SD = 4.9 ± 2.23) and controls (mean ± SD = 5.0 ± 1.38,  $t = 0.55, p = .58, df = 55$ ).

Among the six global network properties, the variability of  $E_{loc}$  and  $E_{glob}$  were higher in nurses than controls (Figure 4; Table S2).

No significant difference was found for the variability of dynamic head motion,  $S_{net}$ , Gamma, Lambda, and Sigma ( $p > .05$ ).

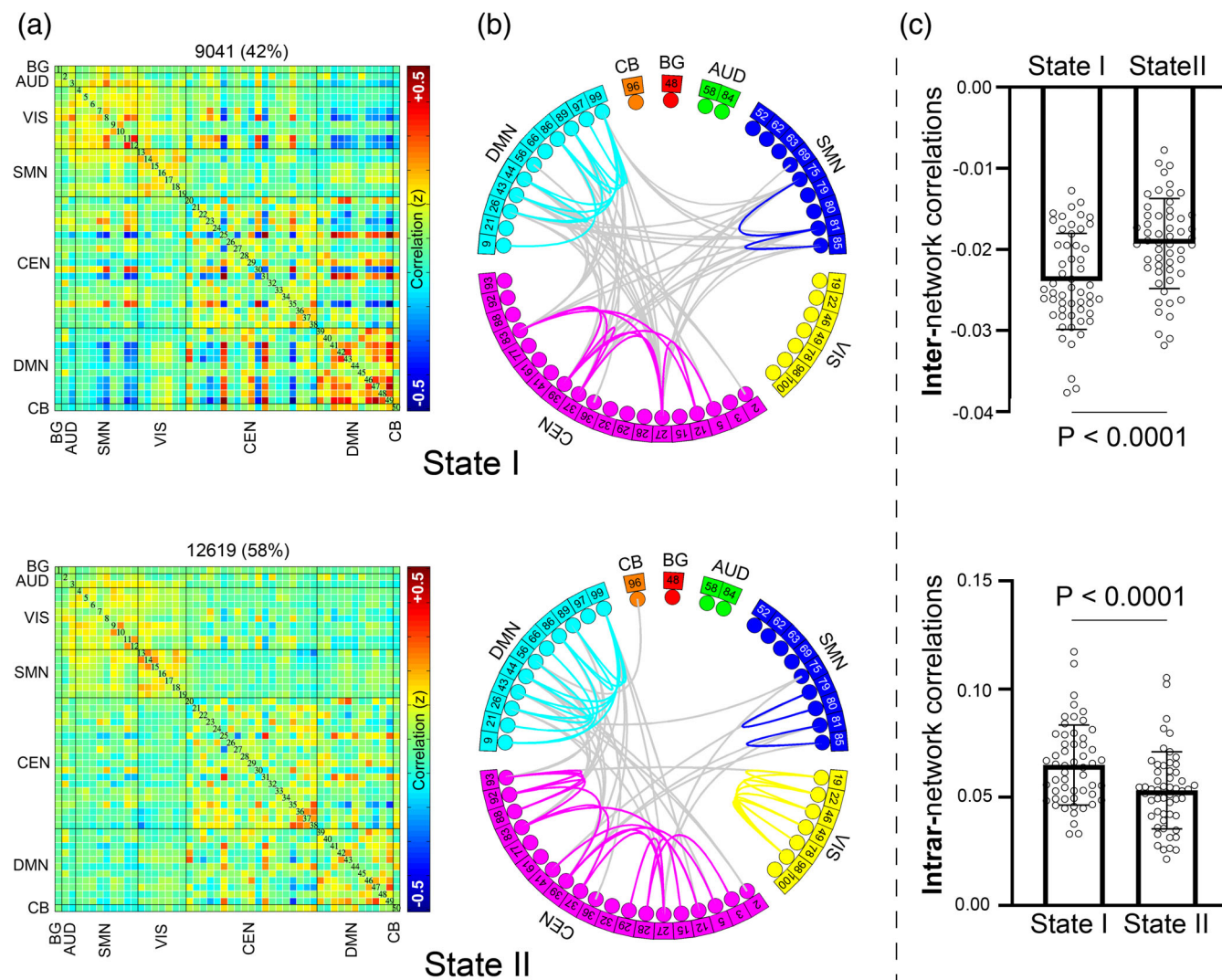
### 3.5 | Correlation analysis

The correlation between imaging and neuropsychological scores was performed across subjects participating in both experiments (36 nurses and 21 controls). Because only diet/sleeping score in SCL-90 was significantly different between these two subgroups, it was used to explain the neuropsychological meaning of imaging measures. Age, gender, months after graduation, and dynamic head motion were included as covariates in this analysis.

Since the dwelling time in States I and II were significantly negative correlated ( $\rho = -0.75, p < .001$ ), their difference (normalized by the total dwelling time) were computed to represent their relative duration in each subject. We did not use the ratio between states directly because some dwelling time was zero. This relative duration was positively correlated with the diet/sleeping score ( $\rho = 0.34, p = .014$ ; Figure 3(a)). The diet/sleeping score did not show significant correlation with either the variability of dynamic  $E_{loc}$  ( $\rho = 0.07, p = .60$ ) or  $E_{glob}$  ( $\rho = 0.06, p = .66$ ).

## 4 | DISCUSSION

This study investigated the mental health of clinical nurses using neuropsychological tests and dynamic brain functional connectome.



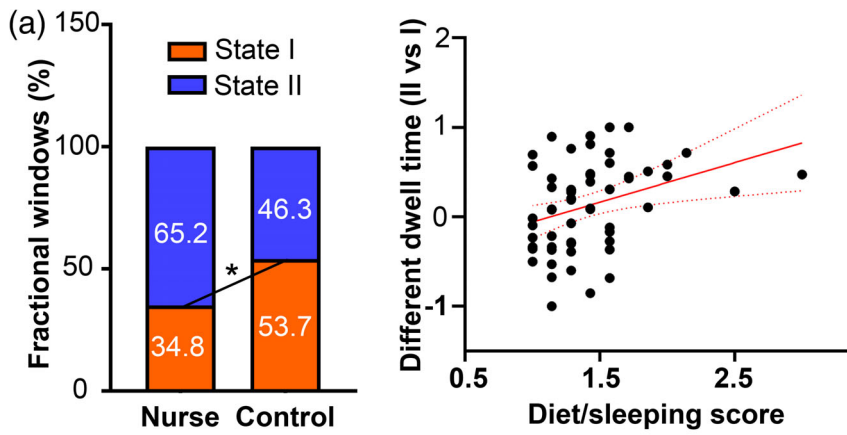
**FIGURE 2** Connectivity feature of two mental states. (a) Cluster centroids for each state. The total number of occurrences and percentage of total occurrences are listed above each matrix. (b) Top 5% connections (i.e., the largest absolute correlation coefficients) in the circular maps. Index numbers of independent components are written in squares. Color and gray lines represent intra- and inter-network connectivity, respectively. (c) The average intra-network connectivity strength is higher in State I than State II, while the inter-network connectivity was the inverse

As compared to controls, the nurses had higher risk of mental deficits in all SCL-90 dimensions. These neuropsychological findings were further supported by the subgroup functional MRI analysis. First, two frequently recurring connectivity patterns were identified (States I and II). Controls spent more time in State I than II, while the nurses spent more time in State II than I. Second, nurses showed a similar static network topology as controls, but higher variability of dynamic  $E_{loc}$  and  $E_{glob}$  than controls. Third, the symptom-imaging correlation suggested these functional alterations in nurses as potential imaging biomarkers of high risk for mental deficits.

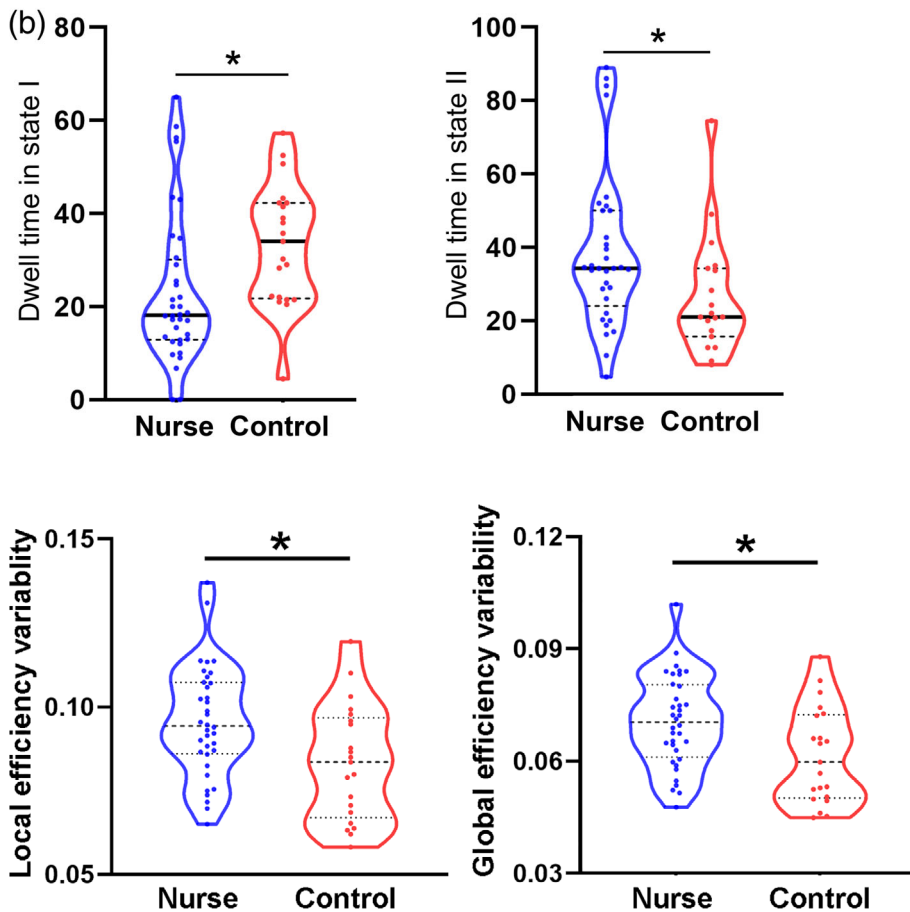
SCL-90 is a classic neuropsychological test that can efficiently evaluate potential symptoms in 10 dimensions; however, the norm in 1986 of this test in China is far behind the social change (Xin et al., 2019). In this study, we collected a large sample of SCL-90 tests from nurses. Compared to nursing graduates who did not work

in a hospital setting, the nurses were at higher risk for mental deficits than controls in all SCL-90 factors. When facing large-scale public health events, this psychological problem may be more severe. At the beginning of the 2019 coronavirus outbreak, the Chinese Medical Rescue Association developed a detailed psychological intervention plan for the medical staff (Chen et al., 2020); however, although some nurses showed excitability, irritability, and signs of psychological distress, the nurses declined psychological help and stated that they did not have any problems. For this reason, some nurses mentioned that they did not need a psychologist, but needed more rest without interruption (Chen et al., 2020). Thus, it is more practical to decrease the risk of mental deficits at ordinary time, which may eventually elevate the resistance of the medical system to a public health event.

In addition to traditional neuropsychological tests, the dynamic brain functional connectome is recognized as a novel approach to



**FIGURE 3** Temporal properties of the dynamic states. (a) The mean fractional windows spent in each state as measured by percentage (i.e., total time spent in State I vs. State II) is different between groups. The diet/sleeping score is positively correlated to the different dwelling time between States II and I. (b) The mean dwelling time (i.e., number of consecutive windows spent in each state before switching) in State I is shorter in nurses than controls, while that in State II is the inverse. \* FDR corrected  $p < .05$



**FIGURE 4** The temporal variance of brain network topology. The coefficient of variation of local and global efficiency is smaller in nurses than controls. \* FDR corrected  $p < .05$

track the dynamic mental state (Gonzalez-Castillo et al., 2015), and an objective biomarker for neuropsychiatric disease (Damaraju et al., 2014; Kim et al., 2017; Liao et al., 2013). In a subgroup of the participants, we additionally compared the mental state of nurses to controls using a functional connectome. Two recurring states (I and II) were identified in the  $\sim 16$  min functional scanning. Both the positive connectivity within networks and negative connectivity between networks were significantly stronger in the State I than State II. Thus, it appeared that some connections were more active than others in the State I, while the connectivity strength was more similar across connections in State II. Correlation analysis further indicated that the relative longer dwelling time in State II than I was associated with a

higher risk of diet/sleeping problems. Nurses had higher diet/sleeping scores than controls, and stayed a longer time in the State II than controls. The diet/sleeping problem is likely related to the frequent night shift, which disrupted the normal biological rhythms.

The human brain is efficiently organized in a small-world pattern that manifests as high efficiency and low path length in graph theory (Bullmore & Sporns, 2012). The small-world related network properties were similar between nurses and controls, suggesting that years of clinical work did not disrupt the efficient organization of brain function, although the nurses were at higher risk of mental deficits than controls. On the contrary, the dynamic variance of local and global efficiency was higher in nurses than in controls. These increased variances

may reflect higher functional flexibility to the change in environment. But this improvement may be achieved at a high cost of energy consumption, which exhausted the nurses.

Some limitations in this study should be mentioned. First, the findings of this study were from nurses working <3 years. With time, mental health status may decrease when nurses adapt to the hospital environment and work. Longitudinal studies may indicate to what extent our conclusions can be generalized to nurses with longer work experience. Second, only one neuropsychological scale was used in this study. SCL-90 is a classic test containing factors in multi-dimensions, and can be easily completed in large samples. Based on the current findings, future work concerning the abnormal factors may use more specific scales for further investigation. Third, although the nurses and controls have similar education background, their working environment was quite different. Thus, it was unknown whether the high risk of mental deficits in nurses were specific to nursing service or could be generally observed in other staffs of hospital. Finally, this study focused on signals of gray matter and excluded white matter components as the most ICA studies. However, new advances indicated that the resting-state fMRI signal in white matter may also vary with physiological states (Ji, Liao, Chen, Zhang, & Wang, 2017). Thus, it would be interesting to take white matter signals into account in future studies.

## 5 | CONCLUSIONS

With the growing population and rapid change of social environment, nurses in China are suffering from high rates of stress. In this study, we characterized the mental status of nurses using the SCL-90 scale. The “diet/sleeping” score was significantly correlated to the relative duration between resting states across all participants. The dynamic properties of the functional connectome were different between nurses and controls. In summary, this study emphasized the high risk of mental deficits in nurses and explored the underlying neural mechanism, which will provide valuable information for future psychological interventions.

### ACKNOWLEDGMENTS

The authors thank all the nurses and controls for their participation. The National Natural Science Foundation of China (Grant/Award numbers 82090034, 31970979, 81971689, 31571149, 91232717, 81573017, and 81771456), The Foundation of the First Affiliated Hospital of Anhui Traditional Chinese Medicine University (2019rwyb12), the University Natural Science Research Project of Anhui Province (Grant number: KJ2020A0194), the Doctoral Foundation of Anhui Medical University (Grant/Award number XJ201532), the National Basic Research Program of China (Grant/Award number 2015CB856405), the National Key R&D Plan of China (Grant/Award number 2016YFC1300604), and the Youth Top-notch Talent Support Program of Anhui Medical University funded this research.

### CONFLICT OF INTEREST

The authors declare that no competing financial interests exist.

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author.

### ORCID

Gong-Jun Ji  <https://orcid.org/0000-0002-7073-5534>

Jinmei Sun  <https://orcid.org/0000-0002-9295-2759>

Kai Wang  <https://orcid.org/0000-0002-6197-914X>

### REFERENCES

- Allen, E. A., Damaraju, E., Plis, S. M., Erhardt, E. B., Eichele, T., & Calhoun, V. D. (2014). Tracking whole-brain connectivity dynamics in the resting state. *Cerebral Cortex*, *24*, 663–676.
- Ashburner, J. (2007). A fast diffeomorphic image registration algorithm. *NeuroImage*, *38*, 95–113.
- Bech, P., Bille, J., Moller, S. B., Hellstrom, L. C., & Ostergaard, S. D. (2014). Psychometric validation of the Hopkins symptom checklist (SCL-90) subscales for depression, anxiety, and interpersonal sensitivity. *Journal of Affective Disorders*, *160*, 98–103.
- Bullmore, E., & Sporns, O. (2012). The economy of brain network organization. *Nature Reviews. Neuroscience*, *13*(5), 336–349.
- Calhoun, V. D., Adali, T., Pearlson, G. D., & Pekar, J. J. (2001). A method for making group inferences from functional MRI data using independent component analysis. *Human Brain Mapping*, *14*, 140–151.
- Chen, Q., Liang, M., Li, Y., Guo, J., Fei, D., Wang, L., ... Zhang, Z. (2020). Mental health care for medical staff in China during the COVID-19 outbreak. *Lancet Psychiatry*, *7*, e15–e16.
- Damaraju, E., Allen, E. A., Belger, A., Ford, J. M., McEwen, S., Mathalon, D. H., ... Calhoun, V. D. (2014). Dynamic functional connectivity analysis reveals transient states of dysconnectivity in schizophrenia. *NeuroImage: Clinical*, *5*, 298–308.
- Dosenbach, N. U., Nardos, B., Cohen, A. L., Fair, D. A., Power, J. D., Church, J. A., ... Schlaggar, B. L. (2010). Prediction of individual brain maturity using fMRI. *Science*, *329*, 1358–1361.
- Drysdale, A. T., Grosenick, L., Downar, J., Dunlop, K., Mansouri, F., Meng, Y., ... Liston, C. (2017). Resting-state connectivity biomarkers define neurophysiological subtypes of depression. *Nature Medicine*, *23*(1), 28–38.
- Erhardt, E. B., Rachakonda, S., Bedrick, E. J., Allen, E. A., Adali, T., & Calhoun, V. D. (2011). Comparison of multi-subject ICA methods for analysis of fMRI data. *Human Brain Mapping*, *32*, 2075–2095.
- Friedman, J., Hastie, T., & Tibshirani, R. (2008). Sparse inverse covariance estimation with the graphical lasso. *Biostatistics*, *9*, 432–441.
- Gonzalez-Castillo, J., Hoy, C. W., Handwerker, D. A., Robinson, M. E., Buchanan, L. C., Saad, Z. S., & Bandettini, P. A. (2015). Tracking ongoing cognition in individuals using brief, whole-brain functional connectivity patterns. *Proceedings of the National Academy of Sciences of the United States of America*, *112*, 8762–8767.
- Hilton, M. F., Scuffham, P. A., Sheridan, J., Cleary, C. M., & Whiteford, H. A. (2008). Mental ill-health and the differential effect of employee type on absenteeism and presenteeism. *Journal of Occupational and Environmental Medicine*, *50*, 1228–1243.
- Himberg, J., Hyvarinen, A., & Esposito, F. (2004). Validating the independent components of neuroimaging time series via clustering and visualization. *NeuroImage*, *22*(3), 1214–1222.
- Jenkinson, M., Bannister, P., Brady, M., & Smith, S. (2002). Improved optimization for the robust and accurate linear registration and motion correction of brain images. *NeuroImage*, *17*, 825–841.
- Ji, G. J., Chen, X., Bai, T., Wang, L., Wei, Q., Gao, Y., ... Wang, K. (2019). Classification of schizophrenia by intersubject correlation in functional connectome. *Human Brain Mapping*, *40*, 2347–2357.
- Ji, G. J., Liao, W., Chen, F. F., Zhang, L., & Wang, K. (2017). Low-frequency blood oxygen level-dependent fluctuations in the brain white matter: More than just noise. *Scientific Bulletin*, *62*(9), 656–657.



- Ji, G. J., Ren, C., Li, Y., Sun, J., Liu, T., Gao, Y., ... Wang, K. (2019). Regional and network properties of white matter function in Parkinson's disease. *Human Brain Mapping, 40*, 1253–1263.
- Kim, J., Criaud, M., Cho, S. S., Diez-Cirarda, M., Mihaescu, A., Coakeley, S., ... Strafella, A. P. (2017). Abnormal intrinsic brain functional network dynamics in Parkinson's disease. *Brain: A Journal of Neurology, 140*, 2955–2967.
- Kong, R., Li, J., Orban, C., Sabuncu, M. R., Liu, H., Schaefer, A., ... Yeo, B. T. T. (2019). Spatial topography of individual-specific cortical networks predicts human cognition, personality, and emotion. *Cerebral Cortex, 29*, 2533–2551.
- Li, J., Biswal, B. B., Meng, Y., Yang, S., Duan, X., Cui, Q., ... Liao, W. (2020). A neuromarker of individual general fluid intelligence from the white-matter functional connectome. *Translational Psychiatry, 10*, 147.
- Liang, Y., Chen, M., Zheng, X., & Liu, J. (2020). Screening for Chinese medical staff mental health by SDS and SAS during the outbreak of COVID-19. *Journal of Psychosomatic Research, 133*, 110102.
- Liao, W., Zhang, Z., Mantini, D., Xu, Q., Ji, G. J., Zhang, H., ... Lu, G. (2013). Dynamical intrinsic functional architecture of the brain during absence seizures. *Brain Structure & Function, 219*, 2001–2015.
- Milliken, T. F., Clements, P. T., & Tillman, H. J. (2007). The impact of stress management on nurse productivity and retention. *Nursing Economic\$, 25*, 203–210 quiz 211.
- Motulsky, H. J., & Brown, R. E. (2006). Detecting outliers when fitting data with nonlinear regression—A new method based on robust nonlinear regression and the false discovery rate. *BMC Bioinformatics, 7*, 123.
- Ogino, Y., Kawamichi, H., Kakeda, T., & Saito, S. (2019). Exploring the neural correlates in adopting a realistic view: A neural structural and functional connectivity study with female nurses. *Frontiers in Human Neuroscience, 13*, 197.
- Rabany, L., Brocke, S., Calhoun, V. D., Pittman, B., Corbera, S., Wexler, B. E., ... Assaf, M. (2019). Dynamic functional connectivity in schizophrenia and autism spectrum disorder: Convergence, divergence and classification. *NeuroImage: Clinical, 24*, 101966.
- Smith, S. M., Miller, K. L., Salimi-Khorshidi, G., Webster, M., Beckmann, C. F., Nichols, T. E., ... Woolrich, M. W. (2011). Network modelling methods for FMRI. *NeuroImage, 54*, 875–891.
- Wang, Z. H., Ye, Y., Shen, Z., Sun, L. G., Hu, L., Yu, W. L., ... Sun, X. (2018). A meta-analysis of Symptom Checklist-90 assessment results in Chinese nurses. *Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi, 36*, 129–133.
- Xin, S., Jiang, W., & Xin, Z. (2019). Changes in Chinese nurses' mental health during 1998-2016: A cross-temporal meta-analysis. *Stress and Health, 35*, 665–674.

## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

**How to cite this article:** Bai, L., Ji, G.-J., Song, Y., Sun, J., Wei, J., Xue, F., Zhu, L., Li, R., Han, Y., Zhang, L., Yang, J., Qiu, B., Wu, G.-R., Zhang, J., Hong, J., Wang, K., & Zhu, C. (2021). Dynamic brain connectome and high risk of mental problem in clinical nurses. *Human Brain Mapping, 42*(16), 5300–5308. <https://doi.org/10.1002/hbm.25617>