Functional connectome from phase synchrony at resting state is a neural fingerprint

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Abstract

Coherent oscillatory activity across brain regions provides a variety of individual-specific characteristics, sometimes referred to as a neural fingerprint. This information, however, may not be directly retrieved from raw fMRI time series. In this study, we examined the data of 205 participants who completed two resting-state fMRI scanning sessions, separated by an average of 2.63 years. In the first step, we tested the long-term reliability of functional connectomes derived from amplitude-based functional connectivity (the conventional method) and found that they remained accurate markers ($> 85\%$, $p < 0.001$, permutation test) for identifying individuals, even after a period longer than 800 days. Using the same data set, we further expanded our exploration of the extent to which two analytic components of oscillatory activity (amplitude envelope and instantaneous phase) may function as reliable fingerprints. Both analytic signals—in particular, the instantaneous phase—were identified as useful indices in shaping functional connectivity fingerprints (86%, $p < 0.001$, permutation test). Connectivity profiles derived from the ventral attention, frontoparietal, and default mode networks (DMNs) were the largest contributing factors to identification. The current results suggest that neural synchronization tapped by analytical signal from a low-frequency resting-state fMRI BOLD oscillation could be a reliable and useful fingerprint for identifying individuals and might provide an alternative method for characterizing dynamic functional connectivity profiles.

Abbreviation

BOLD: Blood Oxygen Level-Dependent imaging

DMN: Default mode network

FPN: Frontoparietal network

AFN: Affective network

VAN: Ventral attention network

DAN: Dorsal attention network

SMN: Somatomotor network

VN: Visual network

Introduction

The connections characterizing the human brain consist of patterns that are distinct from one

brain to another (Passingham, Stephan et al. 2002). Due to this unique feature of neural

connections, they are sometimes referred to as neural fingerprints. In a pioneering study,

Miranda-Dominguez et al. (2014) demonstrated that resting-state functional connectivity can

be used to identify a so-called "connectotype" in human and monkey brains. Finn et al.

(2015) further demonstrated the value of functional connectivity as a "fingerprint" capable of

identifying individuals out of a pool of adults, with a 92.9% rate of accuracy, and that

specific connectivity profiles could predict individual differences in fluid intelligence. Waller

et al. (2017) explored the sensitivity, specificity, and generalizability of connectome

fingerprinting and concluded that although connectomes share a certain degree of similarity,

they possess important unique variance from which the discipline of precision psychiatry may

be able to draw valuable inferences. Rosenberg et al. (2016) demonstrated the viable use of

whole-brain functional network connectivity as an applicable neuromarker for predicting

individual differences in sustained attention. Furthermore, delayed adolescent

individualization of functional connectivity patterns was shown to correlate with reduced

mental health in early adulthood (Kaufmann, Alnæs et al. 2017).

Functional connectivity, as derived from the correlation of temporal activity patterns between

brain regions, has been investigated in a wealth of neuroimaging studies within the last

fifteen years (Dijk, Hedden et al. 2010). This amplitude-based functional connectivity holds

promise for translation into the clinical setting (Fox and Greicius 2010). However, recent

studies suggest that neuron synchronization patterns observed via neuroimaging can be

studied at different levels and that each level may represent a discrete behavioral trait

(Glerean, Salmi et al. 2012, Hellyer, Shanahan et al. 2014, Hellyer, Scott et al. 2015).

One approach to measuring neuronal synchronization involves the estimation of their analytical representation (Glerean, Salmi et al. 2012, Pedersen, Omidvarnia et al. 2018). Analytical representation allows for the transformation of a one-time function—a magnetic or electric signal recorded over time—into two time functions with meaningful mathematical properties: the instantaneous phase and instantaneous envelope (Lachaux, Rodriguez et al. 1999). Investigating neuronal synchronization using analytic signals has several strengths. First, the temporal resolution of hemodynamic signals increases, taking each time-point as a unit (Glerean, Salmi et al. 2012, Pedersen, Omidvarnia et al. 2018), which then becomes a powerful exploratory and data-driven mode of analysis for task-driven Blood Oxygen Level-Dependent (BOLD) activity (Bolt, Nomi et al. 2018). Second, there is excellent correspondence between analytic signals derived from BOLD activity and brain structure (Ponce-Alvarez, Deco et al. 2015), which offer a new window into understanding the association between brain structure and function. Third, analytic signals offer a partial explanation of deficits in brain function that give rise to psychiatric and/or neurological disorders (Hellyer, Scott et al. 2015). Fourth, unlike a correlation-based sliding windows analysis, they avoid the mandated (semi-)arbitrary choice of window length and window overlap (Pedersen, Omidvarnia et al. 2018). Finally, analytic signals may bridge the gap between brain cognition and neuron activity communication by examining different neural populations at specific frequencies (Fries 2005, Fries 2015).

Despite the high stability of functional connectivity based on analytic signals from magnetoencephalography and electroencephalography having been investigated (Näpflin, Wildi et al. 2007, Colclough, Woolrich et al. 2016), the extent of the stability of functional connectivity derived from analytical signal using fMRI data remains unclear. To address this question, we studied the longitudinal changes in neural fingerprints in a large sample off 226 subjects from a connectome typing perspective. All subjects underwent two sessions of fMRI

scanning, separated by an average interval of 2.63 years (805-1232 days). We constructed

functional connectivity profiles via two methods: 1) the conventional method, defined by

amplitude-based functional connectivity, and 2) the analytical representation by means of an

instantaneous phase and instantaneous envelope. After generating functional connectivity

profiles, we identified individuals across different sessions via a Pearson correlation. We

hypothesized that 1) patterns of functional connectivity are useful fingerprints for

identification and that 2) functional connectivity within higher-order resting-state network(s)

would provide the largest proportional connections with the largest differential power (DP)

for identification.

Methods

Data acquisition

Data came from 226 healthy participants (age range: 18-22, 135 female/91 male) who

completed two scanning sessions using a 3.0-T Siemens Trio MRI scanner (Siemens Medical,

Erlangen, Germany) at Southwest University Center for Brain Imaging, Chongqing, China.

These data were obtained from the open-access data set (Southwest University Longitudinal

Imaging Multimodal, SLIM data). The average interval between scans was 960 days (range:

805-1232 days). The resting-state BOLD signals were acquired as an 8 min scan of 242

contiguous frames. Data acquisition parameters were as follows: slices = 32; repetition

time/echo time= 2000/30 ms; flip angle = 90°; field of view (FOV) = 220 × 220 mm;

thickness/slice gap = 3/1 mm; and voxel size = $3.4 \times 3.4 \times 4$ mm^3. T1 weighted anatomical

images were collected, with a recorded repetition time of 1900 ms, an echo time of 2.52 ms,

an inversion time of 900 ms, a flip angle of 90°, a FOV of 256 × 256, slices of 176 mm, a

thickness of 1.0 mm, and a voxel size of $1 \times 1 \times 1$ mm^3. The data collection was approved by

the Research Ethics Committee of the Southwest University. For further details of the data

set, refer to Liu et al. (2017).

Data preprocessing

Spatial preprocessing of functional images included slice timing correction, realignment, and normalization using the functional connectivity toolbox CONN (https://www.nitrc.org/projects/conn). Participants were excluded if the translation and rotation of head motion in any direction exceeded 2 mm or 2° This resulted in the exclusion of 21 subjects, leaving a final data set of 205 subjects (122 female/83 male; age range: 18~22 years). To address potentially spurious correlations in resting-state networks due to head motion, we applied a procedure for identifying problematic time points with Artifact Detection Tools (ART; http://www.nitrc.org/projects/artifact_detect; Whitfield-Gabrieli, Ghosh et al. 2016). An image was defined as an outlier if the head displacement in the x, y, or z direction exceeded 0.5 mm of the value of displacement in the previous frame or if the global mean intensity of the image exceeded 5 standard deviations from the mean image intensity for the entire resting scan. The anatomical T1 weighted image was segmented into areas that represented grey matter, white matter, and cerebral spinal fluid, and the resulting masks were eroded (one voxel erosion) to minimize partial volume effects. Head motion parameters (3 rotation and 3 translation parameters, derived from the steps of realignment, along with another 6 parameters representing their first-order temporal derivatives) and artefactual covariates (one covariate per artefactual time point), BOLD time series within white matter (5 PCA parameters), and CSF (5 PCA parameters) were regressed. Mean time series within a region were further extracted from the pre-processed data under a high-resolution atlas that included 1024 regions (AAL1024) (Zalesky, Fornito et al. 2010) (Fig. 1b), which featured a reasonable scale for mapping the brain's functional connectivity (Wang, Wang et al. 2009). Critically, the atlas was restricted within an intersection between a study-specific EPI mask and a gray matter mask based on the probability map in SPM8 (threshold ≥ 0.2). Next, extracted time

series were band-pass filtered with a narrow band from 0.04 to roughly 0.07 Hz to reduce the effects of low-frequency drift and high-frequency noise (Fig. 1d). A narrow frequency band, such as 0.04~0.07, has been shown to be the most reliable frequency band with the most widespread spatial distribution of reliable voxels and is thus optimal for the estimation of functional connectome topology properties (Zuo, Di Martino et al. 2010). Furthermore, this narrow frequency band has been shown to be optimal for exploring the analytical signal patterns from BOLD–fMRI activity (Glerean, Salmi et al. 2012, Pedersen, Omidvarnia et al. 2018).

Subnetwork definition

We divided the AAL1024 atlas into seven resting-state functional network templates that were established in previously published work. As Yeo's networks only included cortical areas, we included the striatum, as done previously by Choi and colleagues (2012). Network labeling was done pursuant to Yeo et al.'s (2011) networks by mapping each node to a network template and counting the number of voxels that belonged to each network. We then identified the network with the largest number of voxels, which represents the primary network label of the given node (Fig. 2a). The DMN, frontoparietal network (FPN), affective network (AFN), ventral attention network (VAN), dorsal attention network (DAN), somatomotor network (SMN), and visual network (VN) were comprised of 262, 148, 84, 111, 101, 164, and 151 nodes, respectively (Supplementary Table S1).

Functional connectivity network estimation

Three different methods were applied to determine the functional connectivity based on the band-pass-filtered time series: amplitude-based functional connectivity (the *conventional method*), analytic signal-based functional connectivity (*instantaneous phase* and *instantaneous envelope*), and functional connectivity joining the conventional method and

analytical signal.

For the *amplitude-based functional connectivity (the conventional method)*, Pearson correlations and a partial correlation were computed between the time series of each node for each participant to characterize the coherence between each node pair (Fig. 1g). We then obtained a 1024 × 1024 symmetric correlation matrix representing the functional connectivity between each node pair. We used Fisher's z transform to normalize the correlation matrix. Moreover, a minimum partial correlation was used to scale the functional connectivity derived from the partial correlation, which is a parameter-free measure for the skeleton of functional connectivity (Nie, Yang et al. 2017). A minimum partial correlation is the minimum of absolute value of the partial correlations and is achieved by controlling all possible subsets of other regions. The code for a minimum partial correlation is offered by Dr. Nie (https://github.com/LNie/ElasticPC).

Analytic signal-based functional connectivity (instantaneous phase and instantaneous envelope) was computed pursuant to previously published methods (Glerean, Salmi et al. 2012). To briefly explain, each real valued band-passed (0.04~0.07 Hz) BOLD time series was converted into analytic signals via the Hilbert transformation, which can be expressed using the following formula: $x_{a(t)} = x(t) + iH[x(t)]$, where, H[.] is the Hilbert transformation, and i is the imaginary unit. The new signal $x_{a(t)}$ has the same Fourier transformations $x(t)$, despite being defined only for positive frequencies. Similarly, let $x(t)$ be expressed as an amplitude signal $a(t)$, with carrier frequency $\emptyset(t)$, so that $x(t) = a(t)\cos[\emptyset(t)]$. Then, the Hilbert transformed analytic signal can be rewritten as the product of two meaningful components: $x_{a(t)=}a(t)e^{i\emptyset(t)}$, where $|a(t)|$ represents the instantaneous envelope and $\emptyset(t)$ is the instantaneous phase. In this study, we used $|a(t)|$ and $\emptyset(t)$ as two analytic components of oscillatory activity and further estimated Pearson correlations between each

pair of ROIs, which are Fisher's *z* transformed (Fig. 1h and i). Furthermore, for each time

instance t, the difference $\Delta\emptyset_{ij}(t)$ between the phases of the respective ROIs was estimated,

while i and j are the indices of each ROI. The phase differences ranged between 0 and π,

such that if $|\emptyset_i(t) - \emptyset_j(t)| < \pi 2\pi - |\emptyset_i(t) - \emptyset_j(t)|, \Delta\emptyset_{ij}(t) = |\emptyset_i(t) - \emptyset_j(t)|$; else,

$\Delta\emptyset_{ij}(t) = \emptyset_i(t) - \emptyset_j(t)$. Instantaneous phase coupling matrices $C(t)$ were then calculated

using the phase differences normalized between 0 and 1, thereby representing perfect

anti-synchronization and perfect synchronization, respectively, such that $C_{ij}(t) = 1 -$

$\Delta\emptyset_{ij}(t)/\pi$. The variability in each pair in $C(t)$ and $C_{ij}(t)$ were considered to be at edge level.

The variability of instantaneous phase coupling was calculated as the index of the dispersion

(variance/mean) of the coupling between each pair for each subject. The variability of

instantaneous phase coupling indicates the dynamic neural activity across time (Demirtaş,

Tornador et al. 2016, Córdova-Palomera, Kaufmann et al. 2017).

To determine whether joining the conventional method and analytical signals increase

fingerprinting accuracy, we performed two separate combinations. First, we combined all

three features—conventional amplitude, instantaneous phase, and instantaneous

envelope—comprising a 3072×3072 functional connectivity matrix for each individual.

Second, we only included conventional amplitude and instantaneous phase, resulting in a

2048×2048 functional connectivity matrix for each individual.

Identification analysis

Whole brain and subnetwork-wise analysis

For this analysis, we used the same methods as Finn et al. (2015). To briefly describe these

methods, we created a database including all individual participants' connectivity profiles

from Time 1 (i.e., Rest 1), $\boldsymbol{D} = [X_i, \; i, 2…S]$, where S is the number of participants in each

data set and X_i is a 1024 × 1024, 3072 ×3072, or 2048 ×2048 matrix. The individual

connectivity matrix of the resting session (Time 2, i.e., Rest 2) was set as the target matrix

(Y_i). To derive and determine the participant's identity, we computed the similarity between

the target matrix Y_i and all other matrices in D and found the predicted identity by detecting

the matrix with the maximal similarity score (Fig. 1i). Similarity was defined as the Pearson

correlation between two vectors of edge values taken from the target matrix and each of the

database matrices. We then conducted nonparametric permutation testing (10,000 times) to

reveal the significance of identification accuracy.

Fig. 1 about here.

Additionally, to clarify the contributions of individual networks (see the Subnetwork

definition section) and to identification accuracy, we used submatrices, each of which

corresponded to a single network. Nodes of the predefined networks defined the submatrix of

a network ($1 \dots j = 7$), and only connections within the selected network were included for an

identification analysis (Fig. 2a).

Edge contribution to identification

To determine which edge(s) represented the largest contribution to identification, we used an

edgewise product. A Pearson correlation was employed to estimate the similarity between the

target matrix and the database, and the matrix with the largest correlation coefficient was

assigned a subject identifier. Given that vectors are z-scored normalized, the Pearson

correlation of the vectors is the sum of the element-wise product. As such, with two z-scored

normalized matrixes, X_i and Y_i, in two sessions, the edgewise product can be defined as

follows: $\varphi_{ii}(\text{e}) = X_i(e) \times Y_i(e), e = 1, 2 \dots M$，where *i* represents the subject, *e* indicates

the edge, and *M* is the number of edges of the whole brain (or the selected network). Thus,

the Pearson correlation is summed as $\varphi(e)$. If the subject's subscript is not the same ($i \neq j$), the edgewise product can be expressed as follows: $\varphi_{ij}(e) = X_i(e) \times Y_j(e), e = 1,2 \dots M, and\ i \neq j$. If an edge e is correlated both within a subject and between different subjects, it would not be regarded as a contribution toward the subject identification. Thus, for an edge to be regarded as a contributor to identification, it had to meet the following criteria: $\varphi_{ii}(e) > \varphi_{ij}(e)$ and $\varphi_{ii}(e) > \varphi_{ji}(e)$. Therefore, the empirical probability that quantified the DP of each edge toward subject identification was computed as follows:

$P_i(e) = \frac{|\varphi_{ij}(e) > \varphi_{ii}(e)| + |\varphi_{ji}(e) > \varphi_{ii}(e)|}{2 \times (S-1)}$. As S is the subject's number in the data set (SLIM data, S = 205), and $P_i(e)$ is the DP used to identify a single subject (similar to the p value in a statistical test), the overall DP of an edge, across all subjects, can be defined as follows:

$DP(e) = \sum_i^S \{-\ln(P_i(e))\}$. In contrast to DP, we used φ as an index characterizing group consistency, which was estimated as the mean of $\sum \varphi_i(e)$ across subjects. A large positive φ stands for agreement within a subject and across subjects. We estimated the DP and φ for all edges across the whole brain and regarded edges as significant contributors, only if each value fell within the 99.9[th] percentile on each index.

Validation analyses

Time course effect

To test whether the scanning duration affected the identification accuracy using analytic signals, we varied the scan time between the first and the last time point within a defined time, ranging from 4 min to 8 min, using 60 s increments. We repeated the identification analysis using the same steps described above and generated a re-estimation of the identification accuracy rate.

Anatomical differences

Despite the functional nature (i.e., BOLD) of the data used, subtle anatomical variability may lead to a preference for the same subjects across different sessions (days/years). To reduce the bias introduced by registration, pursuant to a previous study (Finn, Shen et al. 2015), we re-extracted the time series, using data smoothed out with different-sized smoothing kernels (4 mm, 6 mm, and 8 mm) and ran the identification analysis again. Using higher kernel size has been found to eliminate or reduce any potential bias for the same subject's brain relative to a different brain during registration (Finn, Shen et al. 2015).

Results

Conventional method

Using the conventional functional connectivity matrix with a full correlation, we observed success rates of 91% and 87% based on the target database of Rest1–Rest2 and the reverse, Rest2–Rest1, respectively (Fig. 2b). While using the conventional functional connectivity matrix with a partial correlation, we observed success rates of 88 % and 87% based on the target database of Rest1–Rest2 and the reverse, Rest2–Rest1, respectively. Accuracy rates were highly significant ($p < 0.00001$), as determined using non-parametric permutation testing (10,000 times). The results are in line with previous studies (Finn, Shen et al. 2015, Miranda-Domínguez, Feczko et al. 2017, Waller, Walter et al. 2017) and suggest that functional connectivity is a stable and reliable fingerprint for discriminating among individuals.

Fig. 2 about here, please.

Analytic signal-based functional connectivity

Whole brain identification

The connectivity matrix derived from instantaneous phase, instantaneous envelope, and

variability of instantaneous phase coupling demonstrated good identification accuracy

(success rates > 50%) (Table 1). In particular, the functional connectome based on

instantaneous phase had success rates of 86% and 86% based on a target database of

Rest1-Rest2 and the reverse Rest2-Rest1, respectively (Fig. 2c and d). Nonparametric

permutation testing (10,000 times) showed the identification accuracy across various

strategies of connectivity construction had a value of $p < 0.00001$.

Table 1 about here, please.

Subnetwork identification

We further tested which functional network(s) represented a greater contribution to the

project of individual identification and found that higher-order functional networks,

especially the FPN and VAN, demonstrated high rates of identification accuracy either based

on a target database of Rest1-Rest2 or the reverse Rest2-Rest1 (accuracy range = 83% ~

89%) (Fig. 2 c, d, and Table 1). Moreover, we found that the DMN also demonstrated

excellent identification accuracy among different brain connectivity profiles with the

accuracy score ranging between 74% and 91%.

Edgewise contribution to identification

As with the subnetwork identification, we found that the functional brain connectivity fell

into the 99.9th percentile of DP when located in the FPN, VAN and DMN, or interconnected

among these three networks (Fig. 3a and Table S5 in Supplementary). Further, the results

were found to be stable across different percentile thresholds (99th percentile and 99.5th

percentile) (Table S3 and S4 in Supplementary). These results confirmed our results from the

subnetwork identification analysis and demonstrated that connections involving a

higher-order association cortex with rich cognitive involvement are the most typical features

shaping individual brains. In addition, we found that among different strategy-derived brain

connections, brain connectivity with high φ is distributed in VN and SMN, which suggests that sensory processing does not make a significant contribution to individual identification.

Fig. 3 about here.

Identification analysis combining conventional amplitude and analytic signal-based functional connectivity

Joining conventional amplitude, instantaneous phase, and instantaneous envelope decreased the identification accuracy. Instead, joining conventional amplitude and instantaneous phase resulted in a higher/similar identification accuracy compared to accuracies using the two features separately (Table 1). On a subnetwork level, combined identification analysis showed that high-order functional networks (e.g., frontoparietal and dorsal attention networks) showed high rates of identification accuracy, irrespective of whether the analysis is based on a target database of Rest1-Rest2 or Rest2-Rest1 (accuracy range = 86% ~ 91%) (Table 2).

Table 2 about here, please.

Validation analyses

Global signal effects

We found that when the global signal was regressed out, the identification accuracy remained fairly high; however, it did show some decline compared to those results for which the global signal was not regressed out (Fig. S1a and Table S2 in Supplementary).

Anatomical differences

Identification accuracy slightly dropped with increased smoothing kernel but remained highly significant, even at a kernel size of 8 mm (Fig. S1 and Table S2 in Supplementary). The DMN, VAN and FPN, however, remained the most powerful features contributing to the

identification analysis (Fig. S1 and Table S2 in Supplementary).

Time course effects.

Identification accuracy remained significantly greater than random efforts at identification, regardless of the scanning length, although identification accuracy scores increased as scanning times grew longer (Fig.S2). This suggests that resting-state fMRI data scanned over 4 min to 8 min does not significantly affect identification, based on brain connectivity patterns.

Discussion

The findings of this study confirm that analytic signals derived from functional connectivity (i.e., instantaneous phase and instantaneous envelope) demonstrated good accuracy in identifying individuals from a large sample over an average longitudinal time span of 818 days. This suggests that neural synchronization from low-frequency resting-state fMRI BOLD oscillation is reliable and may be a useful neural fingerprint for identifying individuals. Our findings support previous findings (Finn, Shen et al. 2015, Miranda-Domínguez, Feczko et al. 2017, Waller, Walter et al. 2017), which demonstrated that functional connectivity originating from amplitude is a reliable fingerprint for distinguishing between individuals, even after a period of more than 2 years. Together, these findings confirm the long-term consistency of functional connectomes derived from the use of two different techniques (amplitude and analytic signals) to promote the identification of individuals and highlight their potential importance for precision psychiatry.

Previous work indicated the importance of analytic signals in explaining individual differences in higher-order functioning (Fries 2005, Fries 2015) and demonstrated a high degree of correspondence between brain structure and function (Ponce-Alvarez, Deco et al.

2015). Our results significantly add to this knowledge by showing that brain functional

connectivity that originates from these analytic signals is a stable and reliable feature

discriminating individuals. Our results may have clinical significance. Indeed, previous

studies illustrated that analytic signals are meaningful indices for characterizing brain deficits

associated with neuropsychiatric disorders and the impact of genetic effects on depression (C

órdova‐Palomera, Tornador et al. 2015, Córdova-Palomera, Tornador et al. 2016). Hence,

approaches that employ these signals may even provide new insights into tailored

interventions for psychiatric and neurological disorders (Arbabshirani, Plis et al. 2017) .

From a methodological perspective, the phase-based dynamic functional approach has several

advantages relative to conventional approaches to identification. First, using the

instantaneous phase allows for the identification of full temporal dynamics without the need

for time-windowed averaging (Glerean, Salmi et al. 2012), and as a nonlinear measure it may

be more suitable for identifying complex dynamic processes in the brain (Pereda, Quiroga et

al. 2005). Second, this approach has been established as having good stability across a long

time span; the findings of this study further validate this. Third, instantaneous-phase-based

functional connectivity could be applied to characterize unique time-varying connectivity

networks, or "chronnectome" fingerprinting (Calhoun, Miller et al. 2014). Chronnectome is

used to describe connectivity metrics allowing a dynamic view of coupling. For example, Liu

et al. (2018) found robust individual variability in human brain chronnectome that predicted

individual differences in cognitive performance. Compared with amplitude-based functional

connectivity, instantaneous-phase-based functional connectivity does not mandate a

(semi-)arbitrary choice of window length and window overlap, thus increasing the sensitivity

of the functional dynamic (Pedersen, Omidvarnia et al. 2018). Hence,

instantaneous-phase-based functional connectivity offers a new and promising tool for

chronnectome fingerprinting. This is supported by our identification analysis based on the variability of instantaneous phase coupling, which showed high identification accuracy either based on a target database of Rest1-Rest2 or the reverse Rest2-Rest1 (Table 1). Together, this work highlights the importance of considering different components of neuronal activity waves (i.e., instantaneous phase and instantaneous amplitude) as "fingerprints" for identification. Thus, analytic signals, especially instantaneous phase, may provide a useful alternative tool for studying dynamic functional connectome architecture and individual differences in cognition, potentially in clinical outcomes (Uhlhaas and Singer 2006, Hutchison, Womelsdorf et al. 2013, Tewarie, Hunt et al. 2018).

Furthermore, our results indicate that only functional connectivity based on instantaneous phase but not based on instantaneous envelope shows identification accuracies that are comparable with the conventional method. Indeed, instantaneous envelope is always discarded from an analytical signal because it is uncorrelated with the actual phase dynamics (Glerean, Salmi et al. 2012). Moreover, Daffertshofer et al. (2011) found that instantaneous envelope contaminates the instantaneous-phase-based functional connectivity if two connected regions have different magnitudes in amplitude. Testing the magnitude of whole brain nodes is beyond the scope of this study. However, we found decreased identification accuracy in our data when combining conventional amplitude, instantaneous phase, and instantaneous envelope, as compared to when only combining conventional amplitude and instantaneous phase.

The findings of this study need to be considered in light of several limitations. First, all participants in this study were adults whose brains were relatively mature and therefore likely subject to minimal functional changes. Several studies have, however, suggested that factors such as illness (Woodward and Cascio 2015) and cognitive training (Voss, Erickson et al.

2010) may impact functional connectivity profiles. As such, it is important that future research explores the extent to which such factors only shape the general profile of brain connectivity, or whether they also shape more specific connectivity organization profiles. Second, functional connectivity is severely affected by head motion artifacts, which have been shown to modulate the relationship between functional connectivity and behavioral measures, such as fluid intelligence, weight, etc. (Siegel, Mitra et al. 2016, Satterthwaite, Ciric et al. 2017). Although the cutting-edge data processing strategies we applied largely reduced the influence of head motion (i.e., 12 head motion parameters and artifactual covariates detected by ART as regressors) (Power, Barnes et al. 2012), it is impossible to eliminate the head motion effects entirely. Future research may consider systematically exploring head motion effects on the functional connectivity derived by analytic signal to further understand this relationship. Third, limited by the data resources, we were unable to address any association between brain and behavior. Previous studies suggested that static and dynamic functional connectivity (tapped by a sliding window approach) can predict cognitive performance (Finn, Shen et al. 2015, Liu, Liao et al. 2018). Whether neural synchronization characterized by analytical signal can serve as a predictor of cognitive performance needs to be addressed in a future study.

Conclusion

Our findings confirm that functional connectivity based on resting-state fMRI can be used to map individual brain differences. Furthermore, we have demonstrated that analytic signal-derived functional connectivity, in particular the instantaneous phase, is also a useful "fingerprint" for identifying individuals. This may represent an alternative mode for characterizing the dynamic functional connectivity organization profile and provide different individual specific information relative to the conservative method commonly employed.

Acknowledgement

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Table 1 Identification results across whole brain/subnetwork

	Conventional method						Analytic signal			
	Full correlation		Partial correlation		Instantaneous phase		Instantaneous envelope		Variability of instantaneous phase coupling	
	R1-R2	R2-R1	R1-R2	R2-R1	R1-R2	R2-R1	R1-R2	R2-R1	R1-R2	R2-R1
Whole brain	0.91	0.87	0.88	0.87	0.86	0.86	0.53	0.51	0.87	0.86
Visual Network	0.60	0.57	0.61	0.59	0.58	0.55	0.34	0.30	0.53	0.53
Somatomotor network	0.70	0.70	0.69	0.64	0.62	0.66	0.31	0.28	0.62	0.63
Dorsal attention network	0.88	0.85	0.80	0.81	0.84	0.85	0.62	0.64	0.86	0.85
Ventral attention network	0.88	0.86	0.67	0.68	0.86	0.83	0.53	0.53	0.86	0.84
Affective network	0.51	0.50	0.27	0.23	0.33	0.34	0.09	0.13	0.33	0.34
Frontoparietal network	0.90	0.89	0.83	0.82	0.89	0.89	0.71	0.78	0.91	0.88
Default mode network	0.93	0.89	0.87	0.87	0.91	0.86	0.74	0.74	0.92	0.87

Note: R1-R2 identification analysis based on a target database of Rest1-Rest2; R2-R1 identification analysis based on a target database of Rest2-Rest1.

Table 2 Identification results by fusing the conventional method and analytical-based signal

	Conventional method+ Instantaneous phase + Instantaneous envelope		Conventional method+ Instantaneous phase	
	R1-R2	R2-R1	R1-R2	R2-R1
Whole brain	0.84	0.79	0.87	0.88
Visual Network	0.31	0.25	0.61	0.58
Somatomotor network	0.29	0.32	0.71	0.71
Dorsal attention network	0.71	0.70	0.88	0.86
Ventral attention network	0.63	0.57	0.88	0.86
Affective network	0.13	0.17	0.50	0.51
Frontoparietal network	0.77	0.81	0.91	0.90
Default mode network	0.83	0.80	0.93	0.89

Note: R1-R2 identification analysis based on a target database of Rest1-Rest2; R2-R1 identification analysis based on a target database of Rest2-Rest1.