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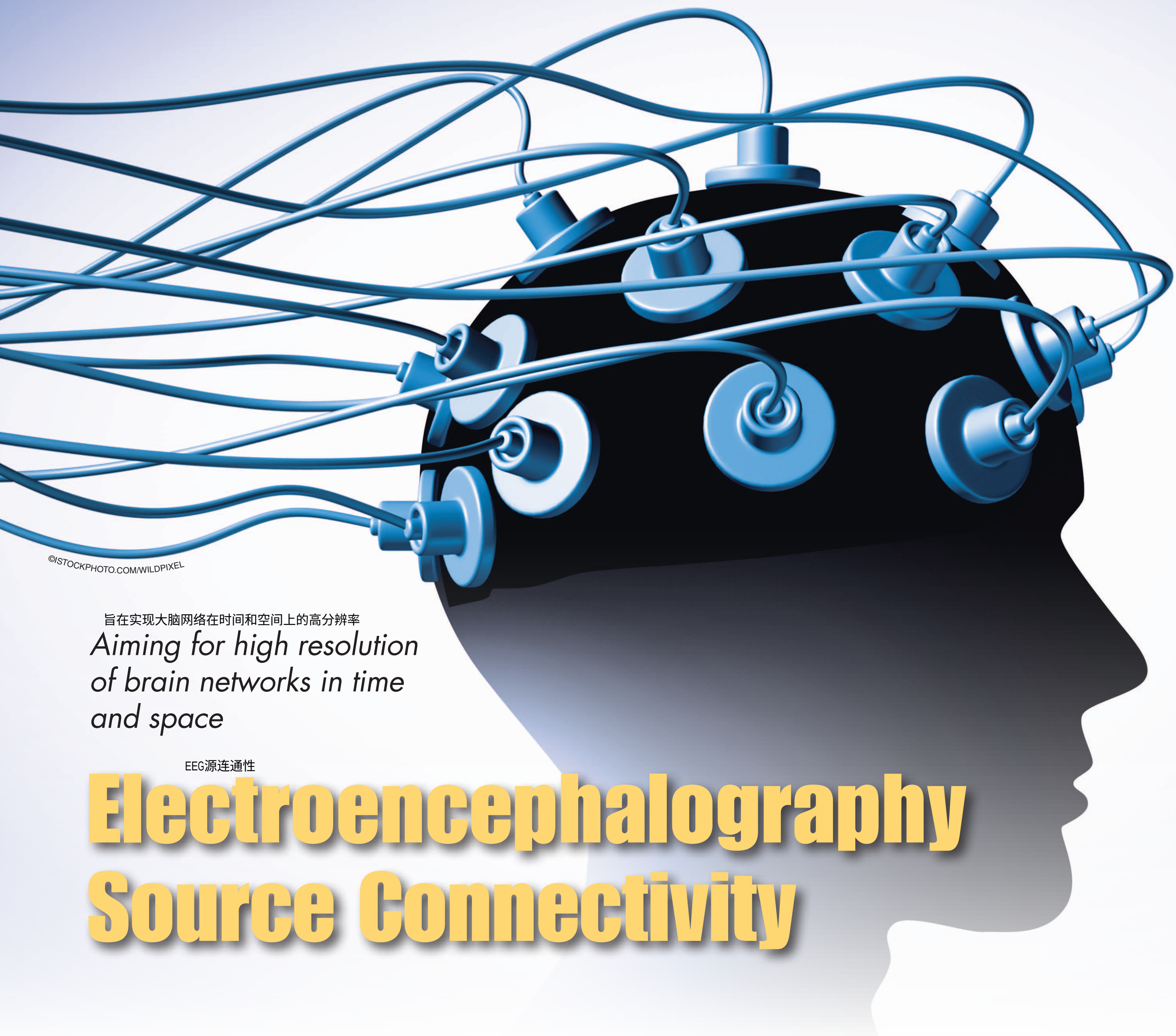

旨在实现大脑网络在时间和空间上的高分辨率

Aiming for high resolution of brain networks in time and space

EEG源连通性

Electroencephalography Source Connectivity

人脑是一个大规模的网络，其功能依赖于空间分布区域之间的动态相互作用。

The human brain is a large-scale network the function of which depends on dynamic interactions between spatially distributed regions. In the rapidly evolving field of net-
在快速发展的网络神经科学领域，有两个尚未解决的挑战有望取得突破。
work neuroscience, two unresolved challenges hold the promise of potential breakthroughs. First, functional brain net-
首先，应该使用非侵入性和易于使用的神经成像技术来识别功能性脑网络。
works should be identified using noninvasive and easy-to-use neuroimaging techniques. Second, the time–space resolution of
其次，这些技术的时间-空间分辨率应足以评估所识别网络的动态特性
these techniques should be good enough to assess the dynamics of the identified networks. Emerging evidence suggests that the
现有证据表明，只要对头皮EEG信号进行适当处理，EEG源连通性方法可以解决这两个问题
electroencephalography (EEG) source-connectivity method may offer solutions to both issues, provided that scalp EEG signals are appropriately processed. Therefore, this technique's
因此，该技术的性能很大程度上依赖于不同方法的信号处理，如预处理方法、逆向求解、信号间的统计耦合以及网络科学
performance strongly depends on signal processing that involves various methods, such as preprocessing approaches, inverse solutions, statistical couplings between signals, and network science.

本教程的主要目的是提供EEG源连通性的概述
The main objective of this tutorial is to provide an overview of EEG source connectivity. We describe the major contribu-
我们描述了信号处理对这一研究领域的主要贡献
tions that the signal processing community has brought to this research field. We emphasize the methodological issues that
强调需要认真处理方法问题，以取得相关成果
need to be carefully addressed to obtain relevant results, and

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we stress the current limitations that need further investigation. We also report results obtained in concrete applications in both normal and pathological brain states. Additionally, we discuss future directions in terms of signal processing methods and applications.

Introduction

Over the past decades, neuroscience research has significantly improved our understanding of the normal brain. There is now a growing body of evidence suggesting that brain functions are generated by large-scale networks of highly specialized and spatially segregated areas of the nervous system. From a theoretical viewpoint, network science in general and graph theory in particular have progressively entered the fields of neuroscience and neurology. A relatively new research field, referred to as *network neuroscience* [1], offers researchers a unique opportunity to assess, quantify, and ultimately understand the multifaceted features of complex brain networks. This interdisciplinary field has also been accelerated by enormous advances in neuroimaging techniques, which now allow for the visualization of brain structure and function at unprecedented space and time resolution using, e.g., functional magnetic resonance imaging (fMRI), magnetoencephalography (MEG), and EEG.

In this rapidly growing and thought-provoking context, the identification of normal and pathological functional networks from neuroimaging data has become one of the most promising prospects in brain research [2]. Among the neuroimaging techniques that are able to provide relevant information about the dynamics of functional brain networks, EEG has considerably progressed over the past two decades. A key advantage of EEG systems is the noninvasiveness and the relative ease of use. Information conveyed in EEG signals can be highly informative about the underlying functional brain networks if those signals are appropriately processed to extract the relevant information. In addition, an important advantage of EEG is its excellent temporal resolution, which offers the irreplaceable opportunity to not only track large-scale brain networks over very short durations like in many cognitive tasks [3] but to also analyze fast, dynamic changes that can occur during the resting state [4] or in brain disorders, such as epilepsy, typically during interictal periods (between seizures) or ictal events (seizures).

Studying the role of neural synchrony in brain function using EEG has been reviewed in depth [5]. Most of the reported studies on EEG functional connectivity analyses were performed at the sensor level. However, the interpretation of corresponding networks is not straightforward, as signals are strongly corrupted by the volume conduction effect due to the electrical conduction properties of the head [6], [7] and the fact that multiple scalp electrodes, to some extent, collect the activity arising from the same brain sources. These two factors can result in an inaccurate estimation of the real functional connectivity between brain areas. Several recent studies have clearly reported the limitations of computing connectivity at the EEG scalp level (see [8] for a review). Recent years have witnessed a significant increase of interest in the EEG analysis of functional brain networks at the cortical source level. A proposed approach to reducing the aforementioned limitations is called *EEG source connectivity*. It is conceptually quite attractive, as high spatiotemporal resolution networks can be directly identified in the cortical-source space, provided that some methodological aspects are carefully accounted for to avoid pitfalls.

Practically, the transition from the electrode space into the source space involves solving an ill-posed inverse problem, the biophysical basis of which relies on dipole theory. Among the many inverse methods proposed so far (see the review in [9]), some make use of physiologically relevant a priori knowledge about both the location and orientation of dipole sources at the origin of signals collected at the scalp. When this information is combined with an accurate, possibly subject- or patient-specific representation of the volume conductor (the realistic head model [10] obtained by MRI segmentation), these methods considerably increase both the precision of localized sources and the estimation of associated time series, which are analogous to local field potentials. These time series then become the input information for so-called connectivity methods, which aim to estimate brain networks directly in the source space. Such networks are much more informative from the application viewpoint (e.g., cognitive sciences and clinics) [11], [12].

EEG source connectivity approaches involve several steps, each related to important topics in signal processing, such as the preprocessing of raw EEG data (e.g., artifact removal and denoising), EEG inverse solutions (e.g., source localization and reconstruction, spatial/temporal hypothesis, sparsity, and regularization constraints), estimation of statistical couplings between signals [e.g., phase synchronization (PS)/entropy, mutual information, coherence function, and linear/nonlinear regression analysis], and graph theory-based analysis (e.g., network segregation/integration and hubness). However, a complete overview of EEG source connectivity in terms of methodological choices and limitations at each stage and the available tools is still missing. The main objective of this tutorial is to address this issue by providing a comprehensive description of the main contributions of the signal-processing community to this relatively new research field. From the methodological viewpoint, we also address future advances that could likely overcome some limitations of the current techniques.

From the application viewpoint, we focus on results obtained so far with EEG source-connectivity methods applied to data recorded during either normal or pathological brain states. We also present new results using this method in the tracking of the dynamics of brain networks during cognitive activity at a subsecond timescale. In particular, we highlight recent studies reporting attempts to use EEG source connectivity to reveal clinically valuable information about the topology and dynamics of dysfunctional networks involved in epilepsies and neurodegenerative diseases. Finally, we address some expectations in the field of cognitive and clinical research.

The volume-conduction problem

Let $\mathbf{X}(t)$ be the time series recorded at the surface of the brain using M scalp EEG electrodes. These M sensors record the activity of N brain sources $\mathbf{S}(t)$. The computation of the statistical couplings directly between the $\mathbf{X}(t)$ time series produces an $M \times M$-dimensional functional network at the scalp level. Scalp-EEG-based networks were widely used in the past [5]. However, interpretation of connectivity from sensor-level recordings is very difficult, as these recordings are severely corrupted by the effects of field spread and volume conduction [6]–[8]. Ideally, if each electrode measures only the neuronal activity below it, then any statistical coupling measured from signals recorded from two electrodes $\mathbf{X_1}$ and $\mathbf{X_2}$ would reflect the connectivity between two physically distinct brain regions $\mathbf{S_1}$ and $\mathbf{S_2}$ [Figure 1(a)].

Unfortunately, this ideal situation cannot always be assumed for EEG recordings. The biophysics of the forward problem of EEG shows that each scalp electrode, to a certain degree, measures the activity arising from all brain sources, depending on 1) the source-to-sensor distance and 2) the orientation of the equivalent dipoles associated with these sources. Therefore, scalp EEG signals correspond to a complex mixture of overlapping signals arising from distinct brain regions. A direct consequence is that statistical couplings measured in the electrode space (whatever the signal processing method used to this end) cannot be interpreted in a straightforward manner as a brain connectivity measure between the underlying cortical regions [Figure 1(b)].

Several methods have been proposed to manage the volume-conduction problem when computing connectivity at the scalp level, such as the use of a spatial filter prior to computing connectivity (Laplacian montages), the computation of the time-lagged connectivity that would reflect a propagation process between distant areas, and the use of measures less sensitive to volume conduction, such as the imaginary part of the coherence. However, none of the proposed methods has shown itself to be capable of completely overcoming the limitations of the volume-conduction and the field-spread problems. See [8] for more details concerning these approaches.

From EEG signals to cortical network

The computation of the statistical couplings between EEG cortical sources reconstructed from the M channels is one of the best methods so far for alleviating the volume-conduction problem, as the connectivity is computed at the level of the sources $S(t)$. This can produce a network (at the cortical level) of $N \times N$ sources. Practically, this network is often reduced to $R \times R$ brain regions, where R represents the number of regions of interest (ROIs), which can vary depending on the segmentation parameters for the cortical surface (this issue will be considered in the following sections). The key idea of the EEG source-connectivity method is the reconstruction of functional networks at the neocortical level from scalp recordings (see Figure 2).

EEG data can be recorded during task-related or task-free paradigms, and the recordings can be performed on medical patients as well as healthy subjects. Signals are preprocessed using, e.g., artifact removal and filtering techniques. The resulting signals constitute the input to the source connectivity

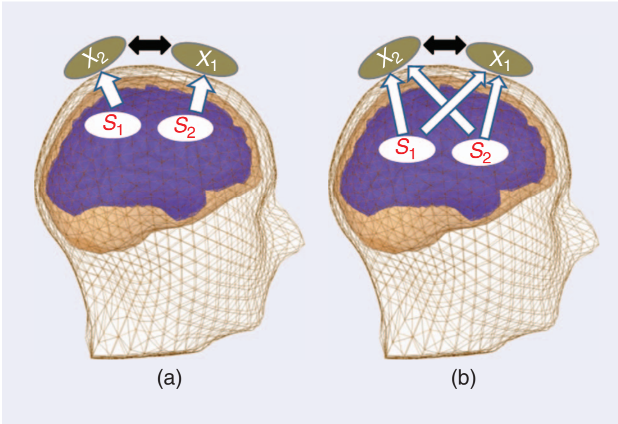

FIGURE 1. An illustration of the volume-conduction problem for interpreting scalp-level connectivity. X_1 and X_2 represents the electrodes, S_1 and S_2 represent the brain sources, the black arrow represents the measured functional connectivity between X_1 and X_2, and the white arrows represent the pathway of electrical activity from S_1 and S_2. (a) Ideally, each electrode measures brain activity below the electrode, and, thus, the connectivity between electrodes reflects the connectivity between distinct brain regions. (b) In practice, both brain sources S_1 and S_2 contribute to signals recorded at each electrode. Due to this mixing phenomenon, the statistical couplings measured in the electrode space cannot be directly interpreted in terms of brain connectivity between the underlying cortical regions.

method. Figure 2(b) details the necessary elements required to reconstruct the EEG sources. A lead field matrix is needed and can be computed from a multiple-layer head model and the position of the scalp electrodes. Figure 2(b) also illustrates the boundary element method, which is classically used in the case of realistic multiple-layer head models (the skin, skull, cerebrospinal fluid, gray matter, and white matter layers). Using segmented MRI data, the source distribution is constrained to a field of current dipoles homogeneously distributed over the cortex and normal to the cortical surface. The dynamics of the reconstructed sources are then estimated by solving the inverse problem, which consists of estimating the remaining free parameter, i.e., the moment of the dipoles. A source space with defined ROIs is most often used given a number of regional time series (68 ROIs extracted from a Desikan atlas [20] in this example).

Figure 2(c) and (d) details the subsequent steps that occur once the regional time series are reconstructed. The functional connectivity can be estimated by computing the statistical couplings between these time series. This produces an adjacency matrix that represents the pairwise functional connections between all of the ROIs. Finally, once the nodes and edges have been defined, network topological properties can be studied by graph theory-based analysis. These quantitative metrics can be used for cognitive research or with a clinical perspective, such as in the localization of abnormal epileptic networks or the computation of biomarkers of cognitive decline in neurodegenerative diseases. The full pipeline from EEG recordings to cognitive/clinical markers of brain functions and dysfunctions involves four main steps, which are detailed in the following sections.

数据记录和预处理

Data recording and preprocessing

如前所述，与任务相关或无任务(静止状态)范式中可以记录EEG数据。 As previously stated, EEG data can be recorded in a task-related or task-free (resting state) paradigm. 根据上下文(临床或认知研究)，在患者或健康受试者中使用密集电极排列(64-256个传感器)进行这些记录[图1(a)]。 Depending on the context (clinical or cognitive research), these recordings can be performed using dense electrode arrays (64–256 sensors) either in patients or in healthy subjects [Figure 1(a)]. MEG和EEG是非常相似的技术。 MEG and EEG are quite similar techniques. 从生物物理学的角度来看，记录的电场和磁场源的现象略有不同(EEG同时检测径向电流和切向电流，MEG只检测切向电流)。 From a biophysics viewpoint, the phenomena at the origin of recorded electric and magnetic fields are slightly different (EEG detects both radial and tangential currents, while MEG detects tangential currents only). 除了成本问题,直接从测量磁场的技术困难的顺序1英尺(10 – 15 T),差异也与这两种方法的敏感性深源,容积传导在重建源的影响,并易于使用有关。 Besides cost issues that stem directly from the technical difficulty of measuring magnetic fields to the order of 1 fT (10–15 T), differences are also related to the sensitivity of both methods to deep sources, to the impact of volume-conductor modeling on the reconstruction of sources, and to ease of use. 虽然本文将重点讨论EEG源连通方法，但两种技术的分析步骤是相同的 While this article will focus on the EEG source connectivity method, the analysis steps remain the same for both techniques.

Number of channels 通道数量

头皮电极数量是EEG源连通方法的性能的重要参数 The number of scalp electrodes is a crucial parameter for the performance of EEG source connectivity methods. 不同的研究已表明通道数量对局部源或根据EEG数据重构网络的质量具有很强的影响 Different studies have shown that the number of channels has a strong impact on the quality of the localized sources [13] or the networks reconstructed from scalp EEG data [14]. 现有系统的使用(从原来的19-32通道到新的64-256通道)会对源重构步骤的性能产生显著影响(参见"EEG源重构"一节)。 The use of the available systems (going from the former 19–32 channels to the newer 64–256 channels) can have a dramatic impact on the performance of the source reconstruction step (see the section "Reconstruction of EEG Sources"). 越来越多的证据表明，增加EEG通道的数量可以提高源估计的准确性。 There is growing evidence that increasing the number of EEG channels provides greater accuracy in source estimations. 所需电极的最小数量也与管道中使用的其他参数有关，主要是用于重建脑源动态的算法。 The minimal number of electrodes required is also related to the other parameters used in the pipeline, mainly the algorithm used to reconstruct the dynamics of brain sources. 许多研究表明，至少需要128个电极才能获得满意的结果，特别是当使用最小范数类逆向方法来定位源或识别功能网络时。 Many studies have shown that at least 128 electrodes are needed to obtain satisfactory results, typically when the minimum norm class of inverse methods is used for localizing sources [13] or identifying functional networks [14].

Preprocessing 预处理

EEG经常受到各种生理或非生理活动来源的污染，如心电、眼动和眨眼、肌电和头部/电缆运动。 EEGs are often contaminated by various physiological or non-physiological sources of activity, e.g., cardiac signals, eye movements and blinks, muscle activity, and head/cable movements. 在应用EEG源连接之前，去除这些伪迹是产生无噪信号的关键步骤。 Removing these artifacts is a crucial step in producing noise-free signals prior to applying EEG source connectivity per se. 基于伪迹的类型，检测可以是可视化的，也可以是半自动或全自动化的 The detection can be done visually or semi- or fully

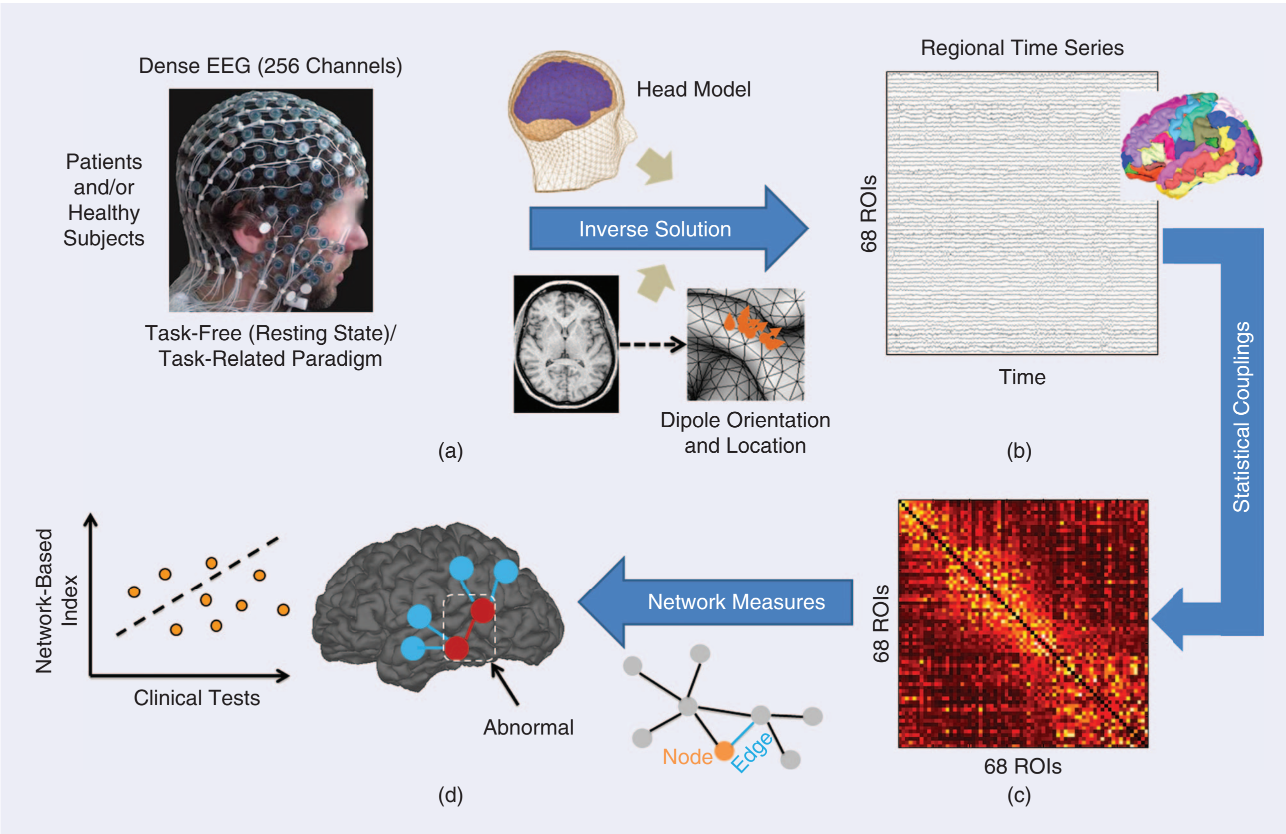

图2 从EEG记录和预处理到脑网络和应用的过程。 (a)脑电图数据可在任务相关(诱发反应)或无任务(静息态)范式中记录。 (b)为了重建脑电图源，需要导场矩阵(每个皮层源对头皮传感器的贡献)。 计算方法为:1)多层头部模型(容积传导)，由MRI分割得到; 2)头皮电极位置。边界元法是一种有效的数值方法。 (c)一旦重建了区域时间序列，就可以通过计算这些时间序列之间的统计耦合来估计功能连接性。 (d)一旦定义了节点和边，就可以通过基于图论的分析研究网络拓扑特性(组织)。

FIGURE 2. The process from EEG recording and preprocessing to brain networks and applications. (a) EEG data can be recorded during task-related (evoked response) or task-free (resting state) paradigms. (b) To reconstruct EEG sources, the lead field matrix (the contribution of each cortical source to the scalp sensors) is required. It is computed from 1) a multiple-layer head model (volume conductor), which is obtained from MRI segmentation, and 2) the position of the scalp electrodes. The boundary element method is one of the available numerical methods. (c) Once the regional time series are reconstructed, the functional connectivity can be estimated by computing the statistical couplings between these time series. (d) Once nodes and edges have been defined, network topological properties (organization) can be studied by graph theory-based analysis.

automatically, depending on the type of artifact. A simple way
一个简单的方法是剔除包含视觉上清晰的伪迹的数据段
is to reject the data segment where the artifact is visually
例如，对于在给定时间内同时影响大量通道的运动伪迹（实验过程中被试的头动）
clear. This is the case, for instance, for movement artifacts (a participant's head moving during an experiment) that simultaneously affect a large number of channels over a given time
这一步仍然是主观的，因为视觉检测取决于用户
period. This step is still subjective, as the visual inspection is user dependent.

还可以自动检测和剔除伪迹。
Artifacts can also be detected and removed automatical-
最简单的方法是比较EEG信号幅度和任意定义的阈值信号，去除非物理的、与背景活动的80μV振幅相比通常饱和段非常高的振幅。
ly. The simplest method involves comparing the EEG signal amplitude to an arbitrarily defined threshold signal to remove nonphysiological, often saturated segments of very high amplitude compared to the usual ±80 μV amplitude of
坏的通道也可以通过插值恢复，使用周围的电极（当密集的电极阵列可用时，这是更有效）
the background activity. Bad channels also can be recovered by interpolation, using the surrounding electrodes (which is more efficient when dense electrode arrays are available).
更复杂的方法包括滤波，这是现在任何EEG检查软件广泛采用的。
More sophisticated methods include filtering, which is now widely available with any EEG reviewing software. Eye
EEG实验中经常出现眨眼，采用独立成分分析方法通过手动或自动方法可以剔除。
blinks are often present during EEG experiments, and they can be removed using the independent component analysis method, which is performed manually or automatically
将EOG信号与EEG信号同时记录下来可以准确、自动地去除眨眼。
[4]. Recording the electrooculography signal simultaneously with the EEG signals could help to precisely and automatically remove the eye blinks. In this case, adaptive filtering
在这种情况下，自适应滤波已被证明是相对有效的。
has proven to be relatively efficient [15]. Muscle artifacts can
肌电伪迹也能严重破坏EEG信号。
also severely corrupt EEG signals. They are more difficult to
由于与EEG频率的重叠，使其更难去除。
remove because of the overlap with the EEG frequency band.
一些对模拟数据和真实数据的研究表明，使用盲源分离方法，如典型相关分析，是去除肌电伪迹的有力工具
Several studies on simulated and real data have shown that the use of blind source separation methods, such as canonical correlation analysis, are powerful tools for removing muscle artifacts [16], [17].

Reconstruction of EEG sources EEG源重构

为了定位脑源并重建它们的时间进程，需要以下数据：
To localize brain sources and reconstruct their time courses, the following data are required:

- 头皮记录的EEG信号
  the scalp-recorded EEG signals
- 位于头部的电极3D位置
  the three-dimensional (3-D) positions of the electrodes positioned on the head
- 头部模型，包含头部的电极和几何特征信息
  the head model, which contains information about the electrical and geometrical characteristics of the head
- 源模型，提供关注被估计偶极子的位置和朝向信息
  the source model, which provides information about the location and orientation of the dipole sources to be estimated.

在采集系统中，通常有一个3D电极位置的模板文件
A template file for the 3-D electrode locations is often available with the acquisition systems. However, in a patient- or subject-
然而，在特定病人或被试的情况中，可能需要实际的位置
specific context, the actual position may be required. A number
许多3D数字设备可以对头部的电极位置进行配准，如Fastrack数字仪和Geodesic摄影测量系统
of 3-D digitizing devices allow for the registration of the electrode positions on the head, such as Fastrak Digitizer (Polhemus Inc.) and Geodesic Photogrammetry System (EGI Inc.).
采用边界元法（表面情况）或有限元法（体积情况）的现实头模型可以精确计算大脑中的电场
Realistic head models employing the boundary element method (surfacic case) or the finite element method (volumic case) allow for an accurate calculation of the electrical fields in the
与简单的球形头部模型相比，改进的头部集合形状描述的真实感，已经在组织中与其相关的电
brain. Compared to simple spherical head models, improved
导率，提高了EEG正向/逆向解
realism in the description of the head geometry and in the tissues with their associated conductivities increases the quality of the EEG forward/inverse solution. The source model is comput-
源模型是通过结构MRI（特定被试的模板）分割计算得到的
ed from the segmentation of the anatomical MRI (template or
通常，白质/灰质界面是被选为对EEG作用最大的皮层源的源空间
subject specific). Usually, the white/gray matter interface is chosen as the source space for the neocortical sources that mostly contribute to EEG. The MRI anatomy and channel loca-
采用相同的结构标志（左、右耳前的点和鼻尖）将MRI结构与电极位置配准
tions are coregistered using the same anatomical landmarks (the left and right preauricular points and the nasion). In the fol-
在接下来的工作中，我们将用更形式化的方式来补充前面提到的EEG源重构的定性描述
lowing, we complement the aforementioned qualitative description of EEG source reconstruction with more formal aspects.

根据偶极子模型，M通道记录的EEG信号X(t)可视为P时变电流偶极子源S(t)的线性组合
According to the dipole theory, EEG signals $\mathbf{X(t)}$ recorded from M channels can be considered as linear combinations of P time-varying current dipole sources $\mathbf{S}(t)$:

$$X(t) = \begin{pmatrix} x_1(t) \\ \cdots \\ x_M(t) \end{pmatrix} = G.\begin{pmatrix} s_1(t) \\ \cdots \\ s_P(t) \end{pmatrix} + N(t) = G.S(t) + N(t),$$

其中G（M*P）为引线场矩阵，N(t)为噪音
where $\mathbf{G}$ $(M \times P)$ is called the *lead field matrix* and $\mathbf{N}(t)$ is
G反映了每个脑源对传感器的贡献
the noise. $\mathbf{G}$ reflects the contribution of each brain source to
它是由头部模型（体积传导）和电极位置计算出阿里的
the sensors [9]. It is computed from a head model (volume conductor) and from the positions of the electrodes. In the
当源分布受限于均匀分布于皮层上且垂直与皮层表面的电流偶极子场时，定义了源的位置和方向
case where the source distribution is constrained to a field of current dipoles homogeneously distributed over the cortex and normal to the cortical surface, the position and the orientation of the sources are defined. For the methods described next, the
对于下面介绍的方法，EEG逆向问题包括估计源信号的幅度
EEG inverse problem consists of estimating the source magnitude of

$$\hat{S}(t) = W.X(t). \tag{1}$$

已经提出了几种算法来解决这个问题，并基于与源的时空特性和正则化约束相关的不同假设来估计W。
Several algorithms have been proposed to solve this problem and estimate W based on different assumptions related to the spatiotemporal properties of the sources and regularization constraints (see [9] for a review). Here, we describe two
在此，我们描述了两种广泛应用于EEG连通性分析的方法，分别基于最小范数估计和波束形成滤波器。
methods widely used in EEG source connectivity analysis, based respectively on a minimum norm estimate and a beamformer filter.

加权最小范数估计（wMNE）时最常用的方法之一
Weighted minimum norm estimation (wMNE) is one of the most popular approaches. Here, $\mathbf{W}$ is estimated in such a way
这里，W的估计方法时，以符合最小二乘误差测量值的最小功率产生源分布
as to produce the source distribution with the minimum power that fits the measurements in a least-square error:

$$W_{\mathrm{wMNE}} = BG^T(GBG^T + \lambda C)^{-1},$$

其中lamda为正则化参数，C为噪声协方差矩阵
where λ is the regularization parameter and C represents the
wMNE算法补偿了MNE偏好微弱和表面源的趋势
noise covariance matrix. The wMNE algorithm compensates for the tendency of MNE to favor weak and surface sources
矩阵B通过减小标准MNE解固有的偏差来调节解的性质
[18]. Matrix $\mathbf{B}$ adjusts the properties of the solution by reducing the bias inherent to the standard MNE solution.
通常，B是由矩阵G构造的一个对角矩阵，起非零项与导场向量的范数成反比
Classically, $\mathbf{B}$ is a diagonal matrix built from matrix $\mathbf{G}$ with nonzero terms inversely proportional to the norm of the lead
主义，当权重为空时，B=I
field vectors. Note that $\mathbf{B} = \mathbf{I}$ in the case where the weighting
实际上，lamda是根据信噪比（SNR）计算的
is null. Practically, λ is computed based on the signal-to-noise ratio (SNR): $\lambda = 1/\mathrm{SNR}$.

信噪比取决于数据类型。
The SNR depends on the data type. For instance, in the task-
例如，在任务相关范式中，前刺激通常被认为是噪声，后刺激被认为是有用的信号。
related paradigm, the prestimuli are usually considered to be noise and the poststimuli to be the useful signal. The SNR can
信噪比可以用这两个周期内信号方差的比值来计算。
be computed using the ratio of the signal variance over these
此外，刺激前周期还可以用来计算噪声协方差矩阵C。
two periods. In addition, the prestimuli period can also be used to compute the noise covariance matrix $\mathbf{C}$. In resting-state data,

在静息态数据中，由于信号和基线间的差异非常小，因此计算更难

the computation is more difficult, as the difference between the signal and baseline is very small. 传统上采用长EEG分段来估计C矩阵 A long EEG segment is traditionally used to estimate the $\mathbf{C}$ matrix. 当噪声在所有通道位置上为空间均匀时，则C=1 When the noise can be assumed as spatially uniform across all channel sites, then $\mathbf{C} = \mathrm{I}$.

另一个流行的逆解是波束形成。 Another popular inverse solution is beamforming. 这里，波束形成滤波器提取具有特定空间特征的信号成分。 Here, the beamformer filter extracts the components of a signal with some specific spatial features. 更具体地说，它允许扫描每个源位置并保留来自该空间位置的信号贡献，同时拒绝来自其他位置的任何贡献。 More particularly, it allows for scanning each source location and for retaining a signal contribution that originates from that spatial location, while it rejects any contribution stemming from other locations. 因此，矩阵W中的权值(对应每个特定的源位置)是由数据一个一个地估计出来的。 The weights in matrix $\mathbf{W}$ (which correspond to each specific source location) are therefore estimated one by one from the data. 数据协方差矩阵C用于此目的。 The data covariance matrix $\mathbf{C}$ is used for this purpose. 最广泛使用的波束形成器之一是线性约束最小方差(LCMV)[19]，它对给定位置的源进行如下权重估计： One of the most widely used beamformers is the linearly constrained minimum variance (LCMV) [19], which makes use of the following weight estimation for the source placed at a given location:

$$\mathbf{W}_{\text{beamformer}} = [(\mathbf{G}^T.\mathbf{C}^{-1}).\mathbf{G}]^{-1}.(\mathbf{G}^T.\mathbf{C}^{-1}).$$

上述两种方法都属于一套广泛的信号处理方法，旨在解决EEG信号逆向问题，如估计矩阵W，利用 (1) 重建脑源的动态

The two previously described methods belong to a wide set of signal processing methods aimed at solving the EEG inverse problem, i.e., estimating matrix $\mathbf{W}$, from which the dynamics of the brain sources can be reconstructed using (1). 通常在高分辨率的表面网格(如8000或15000个顶点)上进行估计。 This estimation is usually done on high-resolution surface mesh (e.g., 8,000 or 15,000 vertex). 然而，重构源的数量太大，无法执行连接性分析的第二步。 However, this number of reconstructed sources is too great to perform the second step of the connectivity analysis. 因此，实际上，空间封闭的脑源是基于一组预定义的R roi进行聚类的， Therefore, in practice, spatially closed brain sources are clustered based on a set of $\mathbf{R}$ predefined ROIs, with $\mathbf{R}$ 相对于估计的源的数量R选择为小 chosen as small with respect to the number of estimated sources.

为了定义ROI，有许多结构和/或功能坐标集可用，例如图1(b)中演示示例中使用的Desikan-Killiany坐标(有68个ROI)和Destrieux坐标(有148个ROI)。 To define ROIs, many anatomical and/or functional atlases are available, such as the Desikan–Killiany atlas, with 68 ROIs, used in the illustrative example in Figure 1(b), and the Destrieux atlas, with 148 ROIs. 这个过程产生R个区域时间序列R(t)，每个序列表示由预定脑区R之一生成的平均大脑活动。 This procedure leads to $\mathbf{R}$ regional time series $\mathbf{R}(t)$, each one representing the average brain activity generated by one of the $\mathbf{R}$ predefined brain regions. 注意，新皮质板块的3D表面是折叠的。 Note that the 3-D surface of neocortical patches is folded. 为了避免由于偶极子源方向相反而导致的活动抵消，对偶极子矩的绝对值进行平均。 To avoid activity cancellation due to the opposite direction of the dipole sources, the averaging is performed on the absolute value of the dipole moments. 对整个ROI的时间序列求平均是一种简单的方法，可以生成一个表示给定扩展脑源(ROI)活动的单一时间序列。 Averaging the time series across ROIs is a simple way to produce a single time-series representative of the activity of a given extended brain source (ROI). 注意，绝对值转换有点轶事性质。 Note that the absolute value transformation is a bit anecdotal. 它解释了影响极少量源的计算错误，这些源在平均之前被翻转到主导(和正确)方向。 It accounts for calculation errors that affect an extremely small number of sources that are flipped to the dominant (and correct) direction before averaging. 然而，当然也存在一些其他方法来估计与给定ROI相关的活动，例如使用降维技术，如主成分分析。 Nevertheless, there certainly exist some other approaches to estimate the activity associated with a given ROI, e.g., the use of a dimensionality reduction technique, such as principal component analysis.

Functional and effective connectivity 功能性和有效性连接

一旦重建了R(t)时间序列，就可以估计出这些区域时间序列之间的统计耦合。 Once the $R(t)$ time series are reconstructed, the statistical couplings between these regional time series can be estimated. 当估计量只与耦合程度有关时，该方法称为功能连接。 When the estimated quantity is related only to the degree of coupling, the method is referred to as *functional connectivity.* 当目标是估计这种耦合或考虑时间序列之间因果关系的方向性时，该方法被称为有效性连接。 When the objective is to estimate directionality in this coupling or causality between considered time series, the method is referred to as *effective connectivity*. 在过去的二十年中，功能和有效性连接方法一直是深入研究的主题，现在有许多可用的度量标准 Both functional and effective connectivity methods have been the topic of intensive research over the past two decades, and many metrics are now available (a review is in [21]).

在EEG功能连接方面，应用最广泛的方法是基于线性/非线性相关、相干函数、PS、互信息和幅度包络相关(AEC)的方法(综述见[22]，比较研究见[23])。 Concerning functional connectivity, the most widely used approaches in the EEG context are those based on linear/nonlinear correlation, the coherence function, PS, mutual information, and amplitude envelope correlation (AEC) (see [22] for a review and [23] for comparative studies). 一个关键的问题是性能，而且，关于这一点，无论在何种背景下(认知研究或临床应用)，每种方法都有自己的优势和局限性，对于一种标准方法是否优于其他方法还没有达成共识。 A key issue is performance, and, in regard to this, whatever the context (cognitive research or clinical application), each method has its own advantages and limitations, and there is no consensus about one standard approach that would outperform the others. 在本节中，我们介绍了三种主要的方法：线性相关、PS和AEC，因为它们代表了EEG源连接中最常用的技术 In this section, we present three main families of methods: linear correlation, PS, and AEC, as they represent the most-used techniques in the context of EEG source connectivity.

互相关系数(r2xy)是衡量两个时间序列之间相互依赖关系的最古老、可能也是最经典的方法之一。 The cross-correlation coefficient (r_{xy}^2) is one of the oldest and probably the most classical measure of interdependence between two time series. 从概念上讲，它非常接近统计学中所谓的皮尔逊相关系数，它是对两个信号(x和y)之间线性相关的一种度量，可能被x延迟 Conceptually very close to the so-called Pearson's correlation coefficient in statistics, it is a measure of the linear correlation between two signals, x and y, possibly delayed by τ:

$$r_{xy}{}^2(\tau) = \frac{\operatorname{cov}^2(x(t), y(t+\tau))}{(\sigma_{x(t)}\sigma_{y(t+\tau)})^2}, \tag{2}$$

其中delta和cov分别表示标准差和方差

where σ and cov denote the standard deviation and the covariance, respectively. 由 (2) 开始，矩阵r2xy表示x与y耦合的经典度量 Starting from (2), the metrics r_{xy}^2 classically used to characterize the coupling between x and y are given by

$$r_{xy}^2 = \max[r_{xy}^2(\tau)]$$
$$-\tau_{\max} < \tau < \tau_{\max},$$

式中 为两个信号之间的最大时移

where $\tau_{\max}$ denotes the maximum time shift between the two signals.

第二种方法是PS。 The second family of methods is PS. 众所周知，两个时间序列的相位可以同步，即使它们的振幅是独立的。 It is well known that the phases of two time series can be synchronized, even if their amplitudes are independent. PS的一般原理是检测定义为的两个系统之间是否存在相位锁定 The general principle of PS is to detect the presence of a phase locking between two systems defined as

$$\varphi(t) = |\Phi_x(t) - \Phi_y(t)| \leq C,$$

其中Ux(t)、Uy(t)为信号x和y在时间t处的展开相位，C为常数。

where $\Phi_x(t)$, $\Phi_y(t)$ are the unwrapped phases of the signals x and y at time bins t, and C is a constant. 第一步是提取每个信号的瞬时相位。 The first step is to extract the instantaneous phase of each signal. 可以使用两种不同的技术：希尔伯特变换和小波变换。 Two different techniques can be used: the Hilbert transform and the wavelet transform. 这两种方法都产生了相对接近的结果。 Both approaches produce relatively close results. 第二步是定义度量估计阶段之间同步程度的度量标准。 The second step is the definition of a metric that measures the synchronization degree between the estimated phases. 提出了几种测量信号间PS的方法。 Several measures have been proposed to measure the PS between two signals.

锁相值 (PLV) 定义为 The phase-locking value (PLV) [24] is defined as

$$\mathrm{PLV} = |\langle e^{i\varphi(t)} \rangle|,$$

其中 表示时间和试次的均值

where $\langle\cdot\rangle$ denotes the average over time and trials.

The phase-lag index (PLI) [25] quantifies the asymmetry of the phase difference, rendering it insensitive to shared signals at zero phase lag:

$$\mathrm{PLI} = |\langle \operatorname{sign}\varphi(t) \rangle|.$$

Another method used in MEG/EEG source connectivity is AEC. It consists of estimating the amplitude correlation between signals using the linear correlations (or partial correlations) of the envelopes of filtered signals. The envelopes of the signals can be computed using the Hilbert transform [26]. The r^2, PLV, PLI, and AEC values range from zero (independent signals) to one (fully correlated/synchronized signals).

The aforementioned functional connectivity methods consider only the degree of coupling. In contrast, effective connectivity methods aim to estimate the causality (in the sense of Granger causality) or the directionality of coupling between the signals. Several techniques have been proposed based on the multivariate autoregressive model (MVAR), such as the directed transfer function (DTF) and partial directed coherence (PDC) [27].

As an example, we describe here the method based on the parametric representation of multichannel time series, which is widely used to study causal brain interactions. For signals $X(t)$ with M dimensions, the MVAR with order p can be defined as

$$X(t) = \sum_{i=1}^{p} A(i)X(t-i) + \varepsilon(t),$$

where $\varepsilon(t)$ denotes the additive noise and $A(i)$ are the model coefficients $(M \times M)$. This time-domain representation can be transformed into a frequency-domain model:

$$X(f) = A^{-1}(f)\varepsilon(f) = H(f)\varepsilon(f),$$

where $H(f)$ is the transfer function and $A(f)$ is the Fourier transform of the coefficients. Using MVAR coefficients, the PDC estimator, characterized by the outflow from channel j to channel i at frequency f, is defined as

$$\mathrm{PDC}_{ij}^2 = \frac{A_{ij}^2(f)}{\sum_{r=1}^{k} A_{rj}^2(f)},$$

and the DTF estimator, which describes the causal influence of channel j on channel i at frequency f, is defined as

$$\mathrm{DTF}_{ij}^2(f) = \frac{|H_{ij}(f)|^2}{\sum_{r=1}^{k} |H_{ir}(f)|^2}.$$

Other methods are also available to compute the effective connectivity. They are based on a directionality index derived from nonlinear regression analysis [28], on the transfer entropy [29], or on the combination of effective connectivity with neural mass models identified from time series. This latter method is known as *dynamic causal modeling* [30]. Due to space constraints, these techniques are not described in this article. Readers may refer to [21] for a review.

Network measures

From the previous step, and whatever the connectivity method being used (functional or effective), an $\mathbf{R} \times \mathbf{R}$ adjacency matrix is produced. This matrix represents the pairwise connections between all of the ROIs. An example of a functional connectivity matrix for $R = 68$ is presented in Figure 2(c). To retain significant interactions, these matrices are usually thresholded (e.g., keeping only the top 10% of connections) to distinguish real functional connections from spurious ones. A variety of thresholding methods are available, but none is free of bias. It is then prudent to perform studies across different threshold values (in addition to using alternative strategies) to ensure that the obtained findings are robust to this methodological factor. In the context of EEG, other techniques are also available to test the significance of interactions, such as the use of surrogate data analysis. Readers can check [31] for a complete overview of most network-related methodological issues.

Interestingly, this $\mathbf{R} \times \mathbf{R}$ adjacency matrix can be characterized and quantified using network measures derived from graph theory. Graph theory is a branch of mathematics focused on the analysis of systems consisting of interconnected elements. Such a system can be represented as a graph in which nodes (or vertices) are connected by edges (or links). In the context of brain networks, the nodes represent the brain regions and the edges reflect the functional and/or effective connections. Once nodes and edges are defined, network topological properties can be studied by graph-theory metrics. As illustrated in Figure 1, these quantitative metrics can be used to characterize the normal brain network architecture during rest or during cognitive functions. They can also be used in a clinical perspective, such as the localization of epileptic zones [Figure 2(d), right] or the development of neuromarkers for other brain disorders [Figure 2(d), left].

A simple graph can be represented by $\mathbf{G} = (V, E)$ where V is the set of nodes and E is the set of edges. In the weighted undirected graph, each node can be identified by an integer value $i = 1, 2, \ldots, N$, and an edge can be identified by (i,j), which represents the connection going from node I to node j, to which a weight A_{ij} can be associated. We now briefly describe some of the main network measures, illustrated in Figure 3.

- The degree d denotes the total number of links connected to a given node [Figure 3(a)].
- The clustering coefficient C reflects the tendency of a network to form topologically local circuits [Figure 3(b)]. For a given node i with degree d, the local C_i is defined as

$$C_i = \frac{2L_i}{d_i(d_i - 1)},$$

where L_i denotes the number of links between the d_i neighbors of node i. C_i varies between zero and one, and it is considered the main graph metric of information

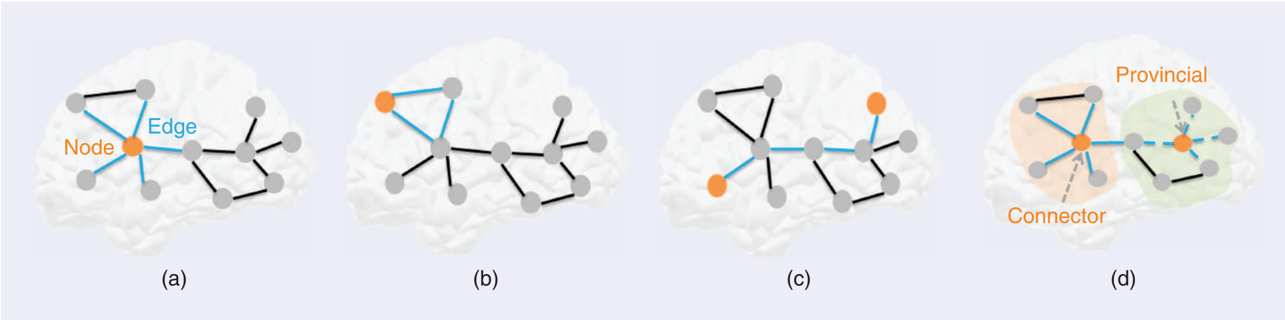

图3 将连接方法应用于EEG重构的脑源，建立无向图，并使用一些度量方法。

(a)度：相对于其他节点而言度较高的节点。

(b)聚类系数：节点的聚类系数计算为节点上附加的三角形数量，相对于可能的三角形总数。

(c)最短路径长度：两个节点之间的最短路径。网络的特征路径长度是每对节点之间的平均路径长度。

(d)模块性：说明网络的模块分解。已经确定了两个模块，用不同的背景颜色表示。

一个模块内的节点彼此紧密相连，而与其他模块内的节点稀疏相连。

这种分解允许分析节点角色和hub类别。省级集线器在其自己的模块内高度连接，而连接器集线器的连接分布在多个模块之间。

FIGURE 3. Some metrics used in undirected graphs built from connectivity methods applied to brain sources reconstructed from EEG. (a) Degree: A node with high degree compared to other nodes. (b) Clustering coefficient: The clustering coefficient of a node is computed as the number of triangles attached to a node, relative to the total possible number of triangles. (c) Shortest path length: The shortest path between two nodes. The characteristic path length of a network is the average path length between every pair of nodes. (d) Modularity: An illustration of a modular decomposition of the network. Two modules have been identified, as represented by the different background colors. Nodes within a module are strongly connected with each other and sparsely connected with nodes in other modules. Such decomposition allows for analysis of node roles and hub category. A provincial hub is highly connected within its own module, while a connector hub has connections distributed across modules.

节点i的邻域互联越紧密，其局部聚类系数越大。

segregation in networks. The more the neighborhood of node i is densely interconnected, the higher is its local clustering coefficient.

这个网络度量将在下面的实际应用程序中使用(图4)。

This network measure will be used in a real application described next (Figure 4).

路径长度是平均加权最短路径长度，常用来衡量网络的全局集成。

定义为网络中所有可能顶点对之间最短路径的调和平均，其中两个顶点之间的最短路径定义为总权值最大的路径。

- The path length is the average weighted shortest path length often used as a measure for the global integration of the network. It is defined as the harmonic average of the shortest paths between all possible vertex pairs in the network, where the shortest path between two vertices is defined as the path with the largest total weight.

网络的全局效率EG与特征路径长度成反比。

一些研究已经使用EG作为信息处理能力的一种度量。

全局效率是对集成和并行信息处理的度量[图3(c)]

- The global efficiency E_G of a network is the inverse of the characteristic path length. Several studies have used E_G as a measure of information processing capability. The global efficiency is a measure of integrated and parallel information processing [Figure 3(c)].

一般来说，在网络中，节点的功能值与节点所参与的路径数成正比。

寻找脑网络中关键节点的一种方法是计算每个节点之间的中心性。

该值定义为网络中通过节点的最短路径数，该节点由最短路径总数标准化。

- Generally speaking, in a network, the functional value of a node is proportional to the number of paths in which it participates. A way to find the critical nodes in a brain network is to calculate the betweenness centrality of each node. This value is defined as the number of shortest paths in the network that pass through the node normalized by the total number of shortest paths.

用于描述网络拓扑的另一个度量是模块性，它表示将关联图划分为集群或模块(也称为社区)。

网络模块定义为图中节点的子集，这些节点与同一模块中的其他节点的连接比与其他模块

中的节点的连接更为紧密

- Another metric used to characterize network topology is modularity, which denotes the partitioning of the associated graph into clusters or modules (also called *communities*). A network module is defined as a subset of nodes in the graph that are more densely connected to other nodes within the same module than to the nodes in the other modules.

中心度可以通过模型内连通性Z和参与系数PC来测量。

一旦计算了模块性并确定了最优模块，就可以计算每个节点的Z和PC指标。

如果节点Z大于定义的阈值T，则将节点划分为集线器；否则，它们被归类为非hub

- Hubness can be measured based on the intramodular connectivity Z and participation coefficient PC. Once the modularity is calculated and optimal modules have been identified, the Z and PC metrics are computed for each node. The nodes are classified as hubs if their Z is higher than a defined threshold T; otherwise, they are classified as nonhubs.

使用PC，集线器可以分为省级集线器(其中节点大多连接到自己模块中的节点)和连接器集线器(其中

节点在网络中多个不同模块之间具有不同的连接性)[图3(d)]。

对于动态网络，可以使用多级网络模块化算法计算模块性[32]

- Using PC, a hub can be classified as a provincial hub, where the nodes are mostly connected to nodes within its own module, or as a connector hub, where the nodes have diverse connectivity across several different modules in the network [Figure 3(d)]. For dynamic networks, the modularity can be computed using the multislice network modularity algorithm [32].

Software

开发了EEGLAB、CARTOOL、Fieldtrip、Brainstorm等EEG信号处理软件包。

此外，还提出了各种用于分析和可视化复杂网络的工具箱，如Brain Connectivity Toolbox (BCT)、

BrainNet Viewer (BNV)、GCCA Toolbox、connectommapper、Gephi、connectomviewer、eConnectome、

EEGNET、connectomvisualization Utility和GraphVar。

然而，从EEG处理到脑网络分析与可视化的完整流程，目前还缺少一个全面的工具。

表1列出了一系列基于matlab的工具，以及它们在EEG预处理和逆向求解、功能性和有效性的连通度量、网络

表征和可视化方面的主要功能。

Several software packages have been developed to process EEG signals, such as EEGLAB, CARTOOL, Fieldtrip, and Brainstorm. In addition, various toolboxes have been proposed to analyze and visualize complex networks, such as the Brain Connectivity Toolbox (BCT), BrainNet Viewer (BNV), the GCCA toolbox, the Connectome Mapper, Gephi, the Connectome Viewer, eConnectome, EEGNET, the Connectome Visualization Utility, and GraphVar. However, a comprehensive tool that implements the complete pipeline from EEG processing to analysis and visualization of brain networks is still missing. Table 1 provides a list of MATLAB-based tools, along with their main functionalities in terms of EEG preprocessing and inverse solutions, functional and effective connectivity measures, and network characterization and visualization.

功能性脑网络的动态重构

Dynamic reconfiguration of functional brain networks

脑网络的时间动态跟踪是认知和神经病理学研究的热点问题。

“大脑网络重构”一词指的是一生中由于经历和对外界刺激或干扰[33]的快速自发或诱发变化而发生的缓慢变化。

例如，一个重要的挑战是，在一个亚二级的持续时间内，暂时跟踪与认知任务有关的大脑功能网络的变化。

脑电图的一个关键优势是其出色的时间分辨率，这为跟踪大规模的大脑网络提供了独特的机会。

这种出色的时间分辨率允许分析大脑加工过程的动态特性，到目前为止，只有少数研究涉及认知活动或静息

状态(参与者不参与特定任务)，才解决了这个问题。

Tracking the temporal dynamics of brain networks is an issue of great interest in cognition and neuropathology. The term *brain network reconfiguration* refers to slow changes across a lifetime due to experiences and to rapid spontaneous or evoked changes in response to external stimuli or perturbations [33]. For instance, an important challenge is to temporally follow, over a subsecond-level time duration, changes in functional brain networks involved in a cognitive task. A key advantage of EEG is its excellent temporal resolution, which offers the unique opportunity to track large-scale brain networks over time. This outstanding temporal resolution permits the analysis of the dynamic properties of brain processes, an issue so far addressed in only a few studies dealing with cognitive activity or with the resting state (where participants are not involved in a particular task).

许多研究报告，即使在受试者休息时(闭上或睁开眼睛)，一些大脑区域仍然保持着高度的功能连接

Many studies have reported that some brain regions remain highly functionally connected even when subjects are at rest

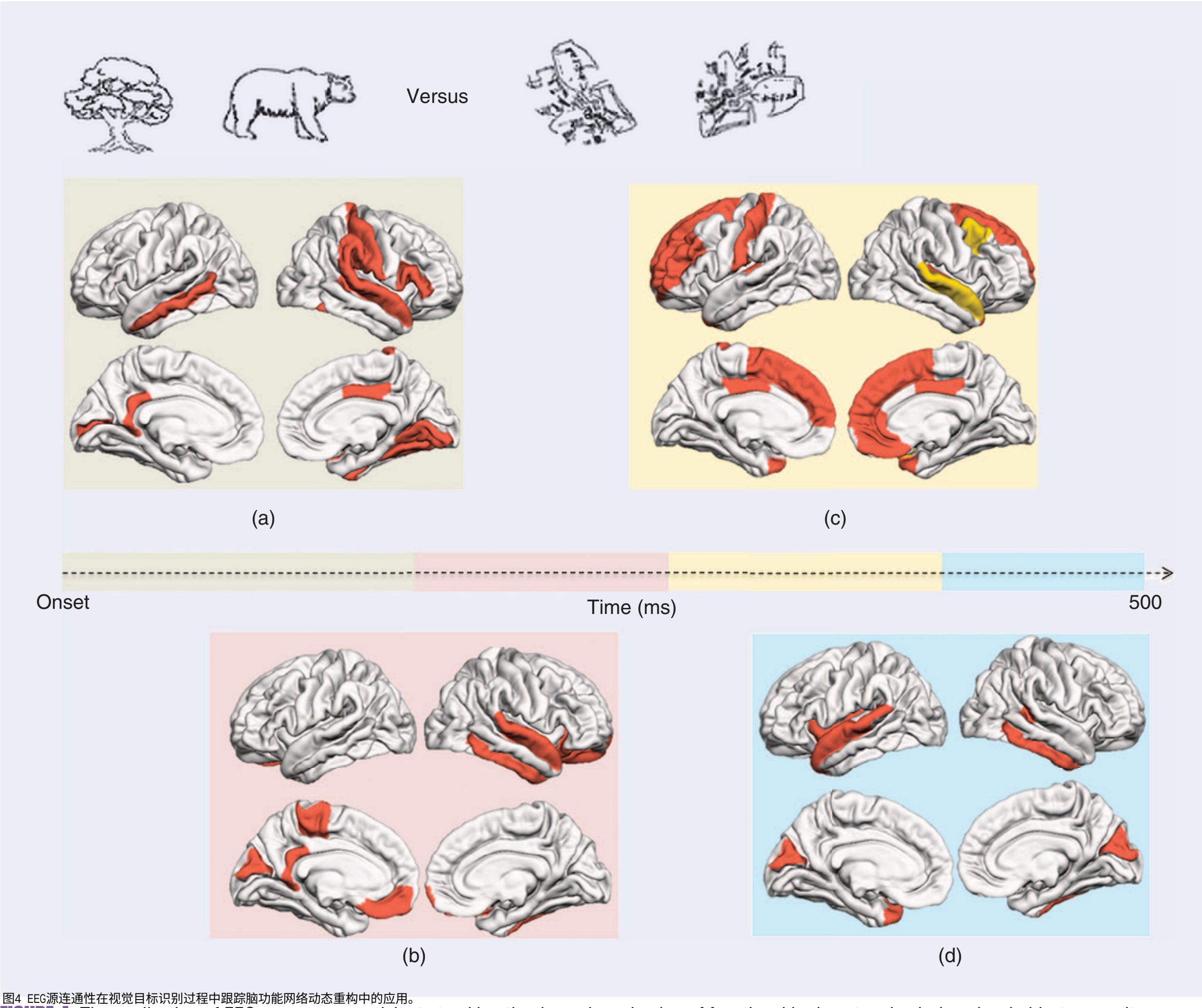

图4 EEG源连通性在视觉目标识别过程中跟踪脑功能网络动态重构中的应用。
FIGURE 4. The application of EEG source connectivity to tracking the dynamic reshaping of functional brain networks during visual object recogniton.
(a) BNS 1，(b) BNS 2，(c) BNS 3，和(d) BNS 4。 两类物体(有意义的图像，如左上方的图像和无意义图像)在不同时间段的聚类系数(采用k-means聚类算法得到，如[39]所示)的脑区差异有统计学意义(p<0.05)。
(a) BNS 1, (b) BNS 2, (c) BNS 3, and (d) BNS 4. Brain regions show significant differences ($p < 0.05$) in terms of clustering coefficient over time periods (obtained using a k-means clustering algorithm as described in [39]) between the two categories of objects (meaningful images such as those at top left versus meaningless ones).
橘红色表示多次比较的未矫正的数据，金色表示使用FDR方法进行多次比较矫正的数据。
Orange red indicates uncorrected data for multiple comparisons, and gold indicates corrected data for multiple comparisons using the false discovery rate approach.
这些结果显示了EEG源连通性方法在跟踪非常短的认知任务(<1s)和揭示大脑区域的能力，这些区域将意义与人类大脑中识别的视觉对象联系起来。
These results show the power of the EEG source connectivity method to track very short cogitive tasks (< 1 s) and to reveal brain regions that associate the meaning to visual objects recognized in the human brain.

在这种情况下，EEG允许在亚秒级跟踪静息态网络的时间动态，而这一结果是fMRI无法实现的。
(with closed or open eyes). In this context, EEG allows for the tracking of the temporal dynamics of resting state networks at a subsecond timescale, a result that is not attainable using fMRI.
在这些研究中，结果显示了一些特定的大脑区域，如后扣带皮层和前额叶皮层(形成所谓的默认模式网络)，
在维持整个大脑有效的时间通讯方面的关键作用。
In these studies, the results showed the key role of some specific brain regions, such as the posterior cingulate cortex and the prefrontal cortex (forming the so-called default mode networks), in maintaining efficient temporal communication in the whole brain.
其他的研究集中在评估主要静息态网络之间的时间转换，如视觉、听觉和背侧注意网络[4]。
Other studies have focused on assessing the temporal transitions between the main resting-state networks, such as the visual, audio, and dorsal attentional networks [4].
近年来，EEG源连通性方法也被应用于追踪任务相关网络，如跟踪人类大脑在短时间(亚秒)认知任务开始
到结束时的信息处理轨迹。
Recently, the EEG source connectivity method was also used to track the task-related networks, i.e., following the trajectory of the information processing in the human brain from the beginning to the end of a short-duration (subsecond) cognitive task.
在视觉任务、运动任务和记忆任务[3]、[34]、[35]期间，对大脑网络重构进行跟踪。
The brain network reconfiguration was tracked during visual, motor, and memory tasks [3], [34], [35].
使用聚类算法(如k-means算法)，这些研究表明，任何认知功能都可以被分解成一组反映底层认知过程
(如视觉或语义处理和记忆获取)的大脑网络状态(BNSs)。
Using clustering algorithms (such as a k-means algorithm), these studies showed that any cognitive function can be decomposed into a set of brain network states (BNSs) that reflect the underlying cognitive processes (e.g., visual or semantic processing and access to memory).

在图4中，我们报告了一些新的结果，显示了在视觉认知任务中EEG源连接方法的性能。
In Figure 4, we report some novel results showing the performance of the EEG source connectivity method within the context of a visual cognitive task.
我们在屏幕上呈现了两类视觉刺激:有意义的图像(如动物和工具)和无意义的图像(打乱)。
We presented two categories of visual stimuli on a screen: meaningful images (e.g., animals and tools) and meaningless ones (scrambled).
我们要求参与者(N = 20)说出所呈现的视觉刺激。
We asked the participants ($N = 20$) to name the presented visual stimuli.
通过试次计算(n = 120)将wMNE和PLV(见"EEG源重建"和"功能和有效连通性")相结合，得到EEGgamma
波段(30 - 45 Hz)的功能网络
By using a combination of the wMNE and PLV (see the sections "Reconstruction of EEG Sources" and "Functional and Effective Connectivity") computed over the trials ($n = 120$), we obtained functional networks in the EEG gamma band (30–45 Hz).
然后应用k-means聚类算法对EEG进行分割，最终识别出4个BNSs。
We then applied a k-means clustering algorithm to segment the EEG responses, which led to identifying four

Table 1. Some MATLAB-based toolboxes for preprocessing, source estimation, functional/effective connectivity measures, and network analysis/visualization.

Software	Web Page	EEG Preprocessing	EEG Inverse Solution	Functional Connectivity/ Effective Connectivity	Network Measures	Network Visualization
Brainstorm	http://neuroimage.usc.edu/brainstorm/	✓	✓	✓		
EEGLAB	https://sccn.ucsd.edu/eeglab/	✓	✓			
FieldTrip	http://www.fieldtriptoolbox.org/	✓	✓	✓		
eConnectome	http://econnectome.umn.edu/	✓	✓	✓		✓
EEGNET	https://sites.google.com/site/eegnetworks/		✓	✓	✓	✓
Conn	https://www.nitrc.org/projects/conn/			✓	✓	✓
FCT	https://sites.google.com/site/functionalconnectivitytoolbox/				✓	
BCT	https://sites.google.com/site/bctnet/				✓	✓
BNV	https://www.nitrc.org/projects/bnv				✓	✓
GraphVar	https://www.nitrc.org/projects/graphvar/				✓	✓
NBS	https://www.nitrc.org/projects/nbs/				✓	✓

FCT: functional connectivity toolbox; NBS: network-based statistic.

有关在图片命名任务中开发的分割算法的详细信息可以在[3]中找到

BNSs. Details about this segmentation algorithm developed in the context of the picture-naming task can be found in [3].

然后，我们对这两种类别之间的网络拓扑结构的差异感兴趣。

We were then interested in the difference in terms of network topology between both categories.

我们对每个脑区(R = 68,Desikan Killiany坐标轴)计算了反映局部信息处理的聚类系数，并保留了导致两种情况之间存在显著差异的区域(t检验，p < 0.01,使用FDR方法对多次比较进行矫正)。

We computed the clustering coefficient reflecting the local information processing, as defined previously, for each brain region ($R = 68$, Desikan–Killiany atlas), and we retained regions leading to significant differences between both conditions (t-test, $p < 0.01$, corrected for multiple comparisons using the false discovery rate method).

图4显示，随着时间的推移，这两种类别的网络聚类系数并不相同，说明在两种情况下(有意义的图像和无意义的图像)，大脑中信息分离的过程是不同的。

Figure 4 shows that the clustering coefficient of the network is not the same for both categories over time, suggesting that the process of information segregation in the brain is different in the two conditions (meaningful versus meaningless images).

有趣的是，该方法还显示了颞叶对所有状态的作用，这被广泛报道与大脑中的语义处理有关

Interestingly, the method also showed the implication of the temporal lobe for all of the states, which is widely reported to be related to semantic processing in the brain.

EEG source connectivity in brain disorders 脑功能障碍中的EEG源连接

越来越多的证据表明，大脑中的扰动很少局限于一个区域。

Converging evidence suggests that perturbations in the brain are rarely limited to a single region.

由于大脑是一个由结构和功能相互联系的区域组成的复杂网络，局部功能障碍往往会传播和影响其他区域，导致大规模的网络改变[2]。

As the brain is a complex network of structurally and functionally interconnected regions, local dysfunctions often propagate and affect other regions, resulting in large-scale network alterations [2].

这些功能障碍可能发生在轴突和突触水平。

These dysfunctions likely occur at both the axonal and synaptic levels.

一个典型的例子是癫痫发作时局部(局灶性)癫痫活动的迅速扩散，它迅速波及不同空间区分布的脑区域。

A typical example is the rapid spread of partial (focal) epileptic activity at the onset of seizures, which rapidly involves spatially distributed brain regions [36].

沿着同样的路线，但在更长的时间尺度上，现在已经确定阿尔茨海默病和帕金森病的渐进进化也与大规模网络的病理变化有关，尽管这些神经退行性疾病具有局灶性发作的[37]。

Along the same line but on a longer timescale, it is now established that the progressive evolution in Alzheimer's disease and Parkinson's disease is also related to pathological changes in large-scale networks, although these neurodegenerative diseases have a focal onset [37].

因此，从临床角度来看，对非侵入性和易于使用的方法来识别病理网络(如癫痫相关网络)的需求很高。

Therefore, from a clinical perspective, the demand is high for noninvasive and easy-to-use methods to identify pathological networks such as those involved in epilepsy.

此外，对新型神经标志物的需求也很大，这种标志物能够表征帕金森症和阿尔茨海默症患者的网络变化和相关认知缺陷，尤其是在早期阶段。

In addition, the demand is also great for novel neuromarkers that are able to characterize network alterations and associated cognitive deficits in Parkinson's and Alzheimer's patients, in particular, at the early stages.

在这种背景下，EEG显示出一些主要的优势，因为它是一种无创、易于使用和临床可用的技术。

In this context, EEG exhibits some major strengths, since it is a noninvasive, easy-to-use, and clinically available technique.

因此，我们最近的研究[11]、[38]表明，只要进行适当的信息处理，EEG源连接方法可以对临床需求做出一定的响应。

Therefore, and as shown by our recent studies [11], [38], EEG source connectivity methods could provide some responses to clinical demand, provided that appropriate information processing is performed.

接下来，我们描述EEG连接在神经系统疾病中的主要应用。

Next, we describe the main applications of EEG source connectivity in neurological disorders.

Epilepsy 癫痫

Ding等人率先将功能连通性应用于癫痫患者的EEG源信号。

Ding et al. [40] were the first to apply functional connectivity to EEG source signals in epileptic patients.

作者认为，该方法能较好地区分癫痫发作产生的主要来源和癫痫发作传播的次要来源。

The authors showed that the method was able to distinguish the primary sources responsible for the seizure generation from the secondary sources involved in the seizure propagation.

在后续研究中，Lu等人将该方法应用于部分癫痫患者的EEG记录(76通道)。

In a follow-up study, Lu et al. [41] applied the method to EEG recordings (76 channels) performed in patients with partial epilepsy.

这些作者发现，与侵入性记录相比，EEG源连接方法能正确定位癫痫发作。

Those authors found that the EEG source connectivity method led to correct seizure onset localization as compared to invasive recordings.

他们还报告了需要大量电极来更好地估计癫痫网络。

They also reported the need for a large number of electrodes to better estimate the epileptic network.

Vecchio等人对额颞叶癫痫患者采用结合基于图论分析的EEG源连通性

Vecchio et al. [42] used EEG source connectivity combined with graph theory-based analysis in patients suffering from frontotemporal epilepsy.

作者报道了与对侧半球相比，同侧半球的alpha波段上局部连通性(以聚类系数为特征)和全局连通性(使用特征路径长度计算)显著增加。

The authors reported a significant increase of local connectivity (characterized by the clustering coefficient) and global connectivity (computed using the characteristic path length) in the alpha band in the ipsilateral hemisphere as compared to the contralateral hemisphere.

Coito等人以16例患者为研究对象，应用源水平上的有效性连接方法，研究了在病程间尖峰期间脑区相互作用的方向性。

With 16 patients, Coito et al. [43] investigated the directionality of the interactions between brain regions during interictal spikes estimated with effective connectivity methods applied at the source level.

]除了与侵入性记录达到良好的匹配外，还显示了连接模式与患者获得的神经心理结果之间的关系。

In addition to achieving good matching with invasive recordings, [43] showed a relationship between

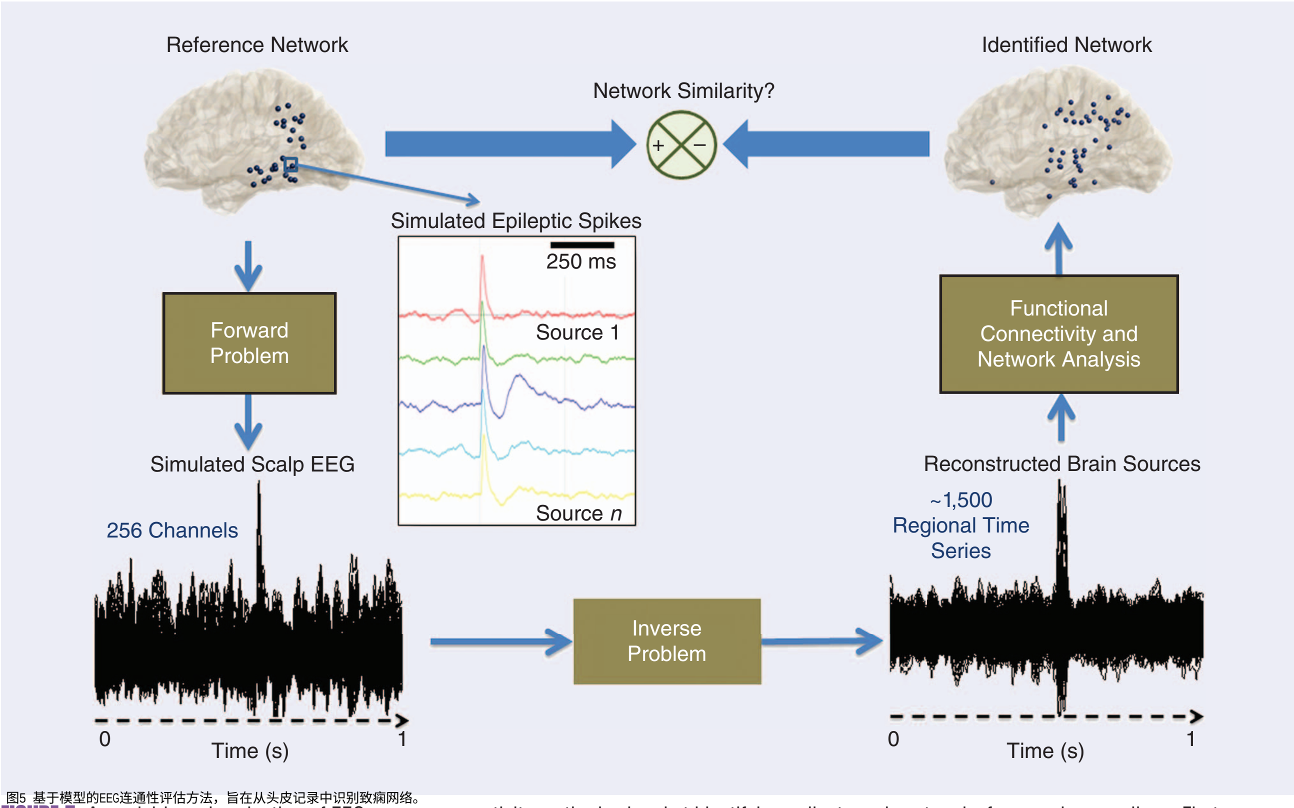

图5 基于模型的EEG连通性评估方法，旨在从头皮记录中识别致痫网络。

FIGURE 5. A model-based evaluation of EEG source connectivity methods aimed at identifying epileptogenic networks from scalp recordings. First, a spatially distributed epileptogenic network is generated by a physiological model (coupled neural masses generating epileptic spikes). This network is considered to be the ground truth. By solving the forward problem, synthetic dense-EEG data are generated. These simulated signals are then used to evaluate the performance of EEG source connectivity methods according to their ability to recover the reference network. Different combinations of methods were used to solve the inverse problem and reconstruct the dynamics of the cortical sources. For each combination, the identified network is compared with the original network using a similarity index accounting for topological features (the 3-D position of nodes and edges) of matched networks.

首先，通过一个生理模型(产生癫痫尖刺的耦合神经团)生成一个空间分布的致痫网络。这个网络被认为是基本事实。通过求解正向问题，生成了合成的致密脑电图数据。然后，根据这些模拟信号对参考网络的恢复能力，对EEG源连接方法的性能进行评估。采用不同的方法组合求解逆向问题，重建皮层源的动力学。对于每个组合，使用说明匹配网络的拓扑特征(节点和边缘的三维位置)的相似性指数，将识别出的网络与原始网络进行比较。

the connectivity patterns and the neuropsychological results obtained in patients.

在这里，我们提出了一种基于模型的评估EEG源连接方法，旨在从头皮记录标识由癫痫引起的网络(图5)。

Here, we present a model-based evaluation of EEG source connectivity methods aimed at identifying epileptogenic networks from scalp recordings (Figure 5). We performed a joint comparison of two inverse solution algorithms [wMNE and dynamic statistical parametric mapping (dSPM)] and two connectivity measures (PLV and r^2) using data simulated from a biophysical/physiological model that allows for the generation at the cortical level of realistic interictal epileptic spikes that also reflect in scalp EEG signals. We used a network-based similarity index to compare the network identified by each inverse/connectivity combination with the original network simulated in the model. The main advantage of this algorithm, called *SimiNet*, is that it takes into consideration the physical locations of the nodes to compute network similarity, which is a crucial element when dealing with brain networks. The nodes shown in Figure 6(b) represent the physical locations of the generated sources, while Figure 6(a) represents the nodes with the 5% highest strength values (the most important nodes in the network). Edges are not shown to enhance visualization.

我们进行了两个逆向解算法[wMNE和动态统计参数映射(dSPM)]和两个连接措施(PLV和r2)的联合比较，使用从一个生物物理/生理模型模拟的数据，允许逼真的癫痫发作间期尖峰的皮层水平的出现，也反映在头皮EEG信号上。我们使用一个基于网络的相似度指数来比较每个反向/连接组合所识别的网络和模型中模拟的原始网络。该算法的主要优点为SimiNet，是考虑节点的物理位置来计算网络相似性，这是处理脑网络时的一个关键因素。图6(b)所示的节点表示生成源的物理位置，图6(a)表示具有5%的最高强度值的节点(网络中最重要的节点)。边缘不显示以增强可视化。

整体上，结果显示，逆向/连通组合的选择对头皮EEG信号识别的网络有显著影响[图6(a)]。

Globally, the results revealed that the choice of the inverse/connectivity combination can have a significant impact on the networks identified from scalp EEG signals [Figure 6(a)]. They also showed that methods based on PS (e.g., PLV) combined with the wMNE inverse algorithm show better performance in terms of similarity between the reference network and identified network as compared with other combinations [Figure 6(c)]. Other methods and other network scenarios were tested in [38]. Interestingly, the same combination exhibited the best performance. Finally, applying this combination on real dense (256 channels) EEG data recorded in epileptic candidates for surgery showed excellent matching between scalp EEG-based networks and intracerebral EEG-based networks, as reported in [38].

他们还表明，与其他组合相比，基于PS(如PLV)结合wMNE逆算法的方法在参考网络与已识别网络相似性方面表现出更好的性能[图6(c)]。在[38]中测试了其他方法和其他网络场景。有趣的是，同样的组合表现得最好。最后，将该组合应用于癫痫患者手术候选EEG数据记录的真实致密(256通道)，显示头皮EEG网络与脑内EEG网络具有良好的匹配性，如[38]报道。

Neurodegenerative diseases 神经退行性疾病

神经退行性疾病与不同类型的功能网络功能障碍有关。使用EEG源连接的主要动机是发现认知缺陷的程度与大脑功能网络的改变之间的联系。假设随着大脑功能连接的逐渐改变，认知障碍会逐渐恶化。除了用于神经退行性疾病外，EEG源连通性还被用于其他应用，如精神分裂症[44]、重度抑郁症[45]、疼痛[46]和强迫症。

Neurodegenerative diseases are associated with distinct patterns of functional network dysfunction [37]. The main motivation for using EEG source connectivity here is to find an association between the degree of cognitive deficit on the one hand and the alterations in the functional brain networks on the other. The hypothesis is that cognitive impairment gradually worsens with the progressive alteration of brain functional connectivity. Besides its utilization with neurodegenerative diseases, EEG source connectivity was also used in other applications, such as with schizophrenia [44], major depression [45], pain [46], and obsessive compulsive disorder

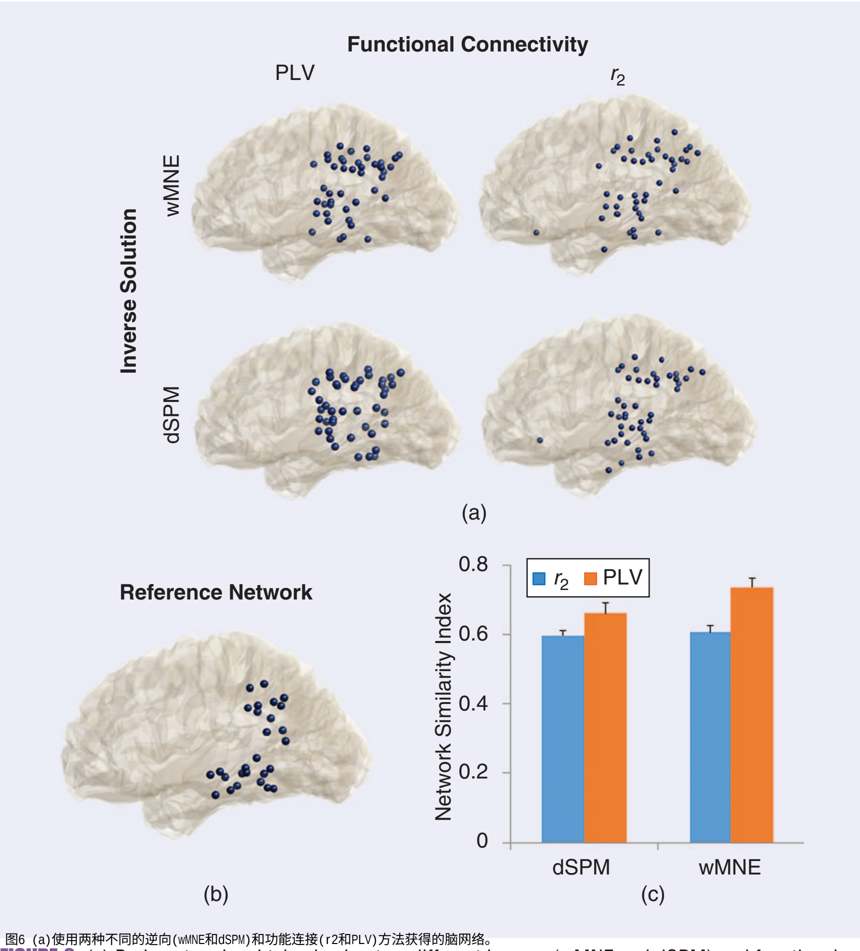

图6 (a)使用两种不同的逆向(wMNE和dSPM)和功能连接(r2和PLV)方法获得的脑网络。 (b)原始网络(地面真相)。 (c)各组合识别的网络与模拟致密EEG数据的参考"致痫"网络计算相似指数值(均值±标准差)。(图片改编自[38]。)

FIGURE 6. (a) Brain networks obtained using two different inverse (wMNE and dSPM) and functional connectivity (r^2 and PLV) methods. (b) The original network (ground truth). (c) Values (mean ± standard deviation) of the similarity index computed between the network identified for each combination and the reference "epileptogenic" network used to simulate dense-EEG data. (Image adapted from [38].)

在本节中，我们将重点介绍利用这种方法治疗帕金森病的一些最新结果。

[47]. In this section, we highlight some recent results obtained with this approach in Parkinson's.

Herz等人对帕金森病患者采用密集EEG(122通道)源连接。 结果显示多巴胺在前额-前运动的连接重构中的作用 使用MEG源连通性，帕金森患者的alpha1(8-10 Hz)和alpha2 (10-13 Hz)频带连通性下降。 大部分的改变发生在时间区域。 在一项为期四年的纵向研究中，该团队还对70名帕金森患者应用MEG源连接来跟踪神经网络的静息态，目的是评估疾病进展[49]可能的随访情况。 作者报告了在多个频段内局部聚类网络测量值的逐步下降，以及在alpha2频段路径长度的下降。 这些变化与运动功能和认知能力的恶化有关。 这项研究首次表明，网络测量(如局部/全局效率)可能导致帕金森病进展的有希望的神经标志物。

Dense EEG (122 channels) source connectivity was used by Herz et al. [48] in patients with Parkinson's. The results revealed the effect of dopamine in the reconfiguration of prefrontal-premotor connectivity. Using MEG source connectivity, decreases in alpha1 (8–10 Hz) and alpha2 (10–13 Hz) frequency band connectivity were observed in Parkinson's patients. Most of the alterations were located in the temporal regions. In a four-year longitudinal study, the same team also applied MEG source connectivity to 70 Parkinson's patients to track the resting state of networks, with the goal of assessing the possible follow-up on the disease progression [49]. The authors reported a progressive decrease in the local clustering network measure in multiple frequency bands, together with a decrease in path lengths at the alpha2 frequency band. These alterations were related to a worsening in motor function and cognitive performance. This study was the first to show that network measures (such as local/global efficiency) may lead to promising neuromarkers of progression in Parkinson's.

利用124名帕金森患者的EEG，我们最近报告了三组患者之间的功能连接逐渐中断:认知完整的患者、轻度认知缺陷患者和重度认知缺陷患者。 我们的研究结果表明，功能连通性随着认知能力的恶化而降低，这表明它可能被用于设计帕金森患者认知障碍的新型神经标志物[11]

Using dense EEG from 124 Parkinson's patients, we recently reported progressive disruption in functional connectivity among three patient groups: cognitively intact patients, patients with mild cognitive deficits, and patients with severe cognitive deficits. Our findings indicate that functional connectivity decreases with the worsening of cognitive performance, suggesting that it can potentially be used to devise novel neuromarkers of cognitive impairment in Parkinson's patients [11].

Discussion

EEG是通过放置在头皮上的电极来测量大脑的电活动。 脑电图的一个关键特征是其固有的良好的时间分辨率，这使得它在跟踪分布在大脑皮层的神经元组合体的功能网络的快速重构方面具有独特性。 现有证据表明，在头皮水平(电极空间)计算的大脑功能连接不允许对解剖学上相互作用的区域进行相关解释，因为体积传导效应严重破坏了估计数(最近的评论见[6]和[7])。 在这篇综述中描述的一个有效的解决方案是在大脑源(源空间)的层次上计算功能连接。 该EEG源连接方法结合了EEG良好分辨率和优于异常空间分辨率的特点，这取决于用于解决EEG逆向问题的源模型的粒度(粗粒到细粒)，然后在皮层水平识别网络。

EEG involves measuring the brain's electrical activity by using electrodes positioned on the scalp. A key feature of EEG is its intrinsically excellent time resolution that makes it unique for tracking the fast reconfiguration of functional networks of neuronal assemblies distributed in the cerebral cortex. Emerging evidence shows that functional brain connectivity computed at the scalp level (the electrode space) does not allow for the relevant interpretation of anatomically interacting areas, as estimates are severely corrupted by the volume-conduction effect (see [6] and [7] for recent comments). An efficient solution, described in this review, is to compute the functional connectivity at the level of the brain sources (the source space). This EEG source connectivity method combines the excellent resolution of EEG with a superior to exceptional spatial resolution, depending on the granularity (coarse to fine grain) of the source model that is used to solve the EEG inverse problem and subsequently identify networks at the cortical level.

*Spatial leakage*空间渗漏

在计算源级的连通性时，经常遇到的一个关键问题是空间泄漏。 由于源估计在空间上是相关的，推断出的源泄漏到它们的本地邻居中经常发生。 当连通性方法忽略这一影响时，计算出的不同源之间的假连通性值可能被解释为功能连通性，尽管它们只反映了源共享同一传感器信号的成分这一事实。 为了解决这一问题，提出了几种策略，在进行连接分析之前消除零延迟相关性。 其他研究表明，只保持长期联系。 然而，这些解决方案可能会抑制重要的相关性，这些相关性可能发生在零延迟，甚至在紧密区域之间。

A critical issue often raised in the computation of connectivity at the source level is the spatial leakage. As source estimates are spatially correlated, a leakage of inferred sources into their local neighborhood often occurs. When the connectivity method ignores this effect, false connectivity values computed between distant sources may be interpreted as functional connectivity, although they only reflect the fact that sources share components of the same sensor signal. To address this issue, several strategies have been proposed to remove zero-lag correlations before performing connectivity analyses. Other studies suggest that only the long-range connections should be kept. However, these solutions may suppress important correlations that might occur at zero lag or even between close regions.

与fMRI连接分析相比，脑电图源连接仍然是一个相对较新的领域，需要更多的方法学努力来完全克服如混合和空间泄漏等问题。

As EEG source connectivity is still a relatively new field compared to fMRI connectivity analysis, more methodological efforts are still needed to completely overcome issues such as mixing and spatial leakage. 我们还建议使用多模态记录，如EEG/fMRI，这可以受益于发NRI良好空间分辨率和EEG良好时间分辨率，并有助于交叉验证这两种技术的结果。 We also advise the use of multimodal recordings, such as EEG/fMRI, which can benefit from the excellent spatial resolution of the fMRI and the excellent time resolution of the EEG and can help to cross-validate the results from both techniques.

Consistency of inverse/connectivity measures 逆向/连通性标量的一致性

虽然所有报道的EEG研究都包括两个主要步骤(EEG逆问题，然后是源连接估计)，但从方法论的角度上它们是不同的。 Although all reported EEG studies include two main steps (an EEG inverse problem followed by a source connectivity estimation), they differ from a methodological perspective. 事实上，不同的算法被用来重建皮质源。 Indeed, different algorithms were used to reconstruct cortical sources. 在这些算法中，利用各种数学假设对病态逆问题进行正则化。 In these algorithms, various mathematical assumptions are used for the regularization of an ill-posed inverse problem. 主要假设与能量最小的源、时间/空间稀疏性以及重建源之间可能存在的相关性有关。 The main assumptions relate to sources with minimum energy, time/space sparsity, and possible correlation between the reconstructed sources. 此外，还提出了大量的功能和有效的连通性度量方法来度量区域时间序列之间的统计耦合。 A plethora of functional and effective connectivity measures were also proposed to measure statistical couplings between regional time series. 因此，自然提出的问题是：应该使用什么反逆/连接方法的组合来提高整体性能，并确保结果与已确定的大脑网络的相关性? Therefore, the question naturally raised is: What combination of inverse/connectivity methods should be used to enhance global performance and to guarantee the relevance of results in terms of identified brain networks? 不幸的是，这个问题没有答案。 Unfortunately, there is no answer to this question. 由于每一种逆向方法和功能性的/有效性的方法都有其自身的假设和特点，因此对于最佳组合还没有达成共识。 As each of the inverse and functional/effective methods has its own assumptions and characteristics, there is no consensus, yet, about the best combination.

这一关键问题已在各种研究中得到解决，这些研究表明所选择的方法(如逆向解法和连接性标量)直接影响EEG表面信号识别的网络拓扑/统计特性。 This crucial issue has been addressed in various studies showing that the selected methods (i.e., the inverse solution and connectivity measure) directly impact the topological/statistical properties of networks identified from EEG surface signals. 最近，Mahjoory等人评估了解剖模板、头部模型、逆向解和软件实现的效果。 Recently, Mahjoory et al. evaluated the effect of the anatomical templates, head models, inverse solutions, and software implementations. 结果表明，两种逆向解算法(主要是LCMV和wMNE)之间存在一定的差异。 The authors showed the variability between the inverse solution algorithms (mainly LCMV and wMNE). 此外，与使用有效性连通方法得到的测量值相比，功能性连通的测量值在各变量间的一致性要高得多。 Also, the functional connectivity measures were much more consistent across the variables as compared with measures obtained with effective connectivity methods.

我们还对最优逆/连通组合方法的选择进行了两项比较研究。 We also conducted two comparative studies regarding the choice of the optimal inverse/connectivity combination method. 在这两项研究中，我们的目的都是最大化关于大脑网络的先验信息(基本事实)，这些大脑网络本应通过密集的脑电图来识别。 In both studies, our intent was to maximize the a priori information (ground truth) regarding the brain networks that were supposed to be identified from dense EEG. 在第一个[14]中，我们关注的是一个广泛使用的认知任务(图片命名)，它有很强的文献基础，主要来自fMRI研究。 In the first [14], we focused on a widely used cognitive task (picture naming) for which a strong literature background was available, essentially coming from fMRI studies. 在第二项研究[38]中，我们采用了一种建模方法，使用致痫网络来模拟致密EEG数据，然后用这些数据来评估EEG源连接。 In the second study [38], we pursued a modeling approach in which epileptogenic networks were used to simulate dense-EEG data that were subsequently used to evaluate EEG source connectivity. 然后，我们使用我们团队最近提出的网络相似度指数，将每个逆向/连通性组合得到的网络与参考网络进行比较。 We then compared the network obtained by each inverse/connectivity combination with the reference network, using a network-similarity index recently proposed in our team.

有趣的是，两项比较研究有趣的是，两项比较研究都得出了相同的结论：在被测试的组合中观察到很强的变异性，但是wMNE/PLV组合提供的结果显示出一致性，并且在估计值与参考网络的匹配方面总是表现得最好。 Interestingly, both comparative studies led to the same conclusion: a strong variability was observed among the tested combinations, but the results provided by the wMNE/PLV combination displayed consistency and always exhibited the best performance in terms of matching between the estimated and the reference network. 这一结果可能是由于wMNE依赖于合理的生理假设(源的位置和方向)。 This result might be explained by the fact that wMNE relies on reasonable physiological assumptions (the position and orientation of sources). 唯一的数学假设是解的能量最低。 The only mathematical assumption is that the solution has the lowest energy. 这一假设也可以用大脑在执行任务或静息时的最低能量消耗来解释。 This assumption could also be interpreted physiologically in terms of minimal energy cost in the brain during task performance or at rest [50]. 第二步，用PLV方法估计EEG振荡之间的PS。 Regarding the second step, the PLV method estimates the PS between EEG oscillations. 因此，这种方法符合大脑中通过一致性进行交流的概念，其中局部产生的信号之间的同步是大脑功能的关键机制。 Therefore, this method is in line with the concept of communication through coherence in the brain in which synchronization between locally generated signals is a crucial mechanism in brain function. 在EEG源连通性的背景下，尤其是PLV方法，更普遍地说，PS方法，准确地反映了不同源产生的脑信号之间潜在的同步。 In the context of EEG source connectivity, the PLV method, in particular, and, more generally, the PS methods, precisely reflect the underlying synchronization between the brain signals generated by distant sources [25]. 总之，这些特征可以解释这种方法组合的良好性能，特别是在涉及认知活动的大脑网络的评估中。 Altogether, these features may explain the good performance of this combination of methods, particularly within the assessment of brain networks involved in cognitive activity.

Clinical impact 临床应用

越来越多的证据表明，大脑疾病与大脑区域之间功能连接的改变有关，这些改变破坏了正常的大规模大脑网络组织和功能[2]、[51]。 A growing body of evidence suggests that brain disorders are related to alterations in functional connections between brain regions that disrupt the normal large-scale brain network organization and function [2], [51]. 本教程的第一个结论是，从EEG中提取有价值的病理大脑网络信息是具有挑战性的，但却是可以实现的。 A first conclusion from this tutorial is that the extraction of valuable information about pathological brain networks from EEG is challenging but obtainable. 第二，临床实践在未来几年肯定会发生变化。 A second remark is that clinical practice will certainly change in coming years. 此外，虽然EEG源连通性与网络科学的结合仍是一个年轻的研究领域，但近年来报道的结果在临床上非常有前景。 Furthermore, although the combination of EEG source connectivity with network science is still a young research field, results reported over the last few years are, clinically, very promising. 利用新工具对已识别的网络进行表征和量化(这是现代网络科学使用基于图论分析的情况)，很可能会发展并推广到临床。 It is likely that the use of novel tools allowing for the characterization and quantification of identified networks (which is the case in modern network science using graph theory-based analysis) will develop and spread to clinics.

然后，在本回归中报告和讨论的大多数研究一般在相对小的病人组中进行。 However, most of the studies reported and discussed in this review were generally performed on relatively small groups of patients. 由于方法方法的多样性(例如，候选逆向解算法和功能性/有效性的连接度量，以及电极数量的影响)和可能条件的数量(例如，任务相关和无任务范式)，对结果进行比较仍然很困难。 Because of the diversity of methodological approaches (e.g., candidate inverse-solution algorithms and functional/effective connectivity measures, and the impact of the number of electrodes) and the number of possible conditions (e.g., task-related versus task-free paradigms), a comparison of results is still difficult. 对更大的患者群体的进一步研究必将有助于标准化分析条件。 Further studies on larger cohorts of patients will certainly contribute to standardizing the analysis conditions.

在癫痫情况下，主要的医学挑战之一是 Within the context of epilepsy, one of the main clinical challenges is the delineation of the epileptogenic zone (EZ), electrophysiologically defined as the primary zone of organization of ictal discharges. 在耐药的部分癫痫患者中，切除EZ足以显著减少癫痫发作的发生，甚至能使患者摆脱癫痫。 In drug-resistant partial epilepsies when surgery can be indicated, resectioning the EZ showed it to be sufficient to significantly reduce the occurrence of seizures and even to lead to freedom from them. 然而，没有可用的技术可以精确地定义EZ。 Yet, there exists no available technique able to precisely define the EZ. 在此情况下，EEG源连接方法显示了令人鼓舞的结果，从无创记录估计致痫网络。 In this context, the EEG source connectivity method showed encouraging results to estimate epileptogenic networks from noninvasive recordings. Some studies could obtain a good matching with intracerebral invasive recordings [38], [43], [52].

部分研究可与脑内侵袭性记录[38]、[43]较好匹配,

For neurodegenerative and psychiatric disorders, the main challenge is to develop methods that establish a relationship between 1) the degree of cognitive deficit and 2) the alterations within the functional connectivity of brain networks. To have direct clinical impact, these new methods should be noninvasive, easy to use, and widely available in clinics. This is already the case with EEG (MEG is still more research oriented). These disorders share a common feature, i.e., they are characterized by disturbances in large-scale neuronal networks. In this context, EEG source connectivity methods seem to have the potential to not only identify dysfunctional networks but also open new perspectives in terms of neuromarkers for cognitive impairment. Results reported so far and synthetized in this article show that this objective is reachable, provided that appropriate data processing is applied to sufficiently large databases [49].

对于神经退行性疾病和精神疾病来说，主要的挑战是开发一种方法，在认知缺陷的程度和大脑网络功能连接的改变之间建立联系。为了产生直接的临床影响，这些新方法应该是无创的，易于使用，并广泛应用于临床。EEG已经是这样了(MEG 仍是研究方向)。这些疾病有一个共同的特征，即，其特征是大规模神经元网络的干扰。在此背景下，EEG源连接方法似乎不仅具有识别功能障碍网络的潜力，而且在认知障碍的神经标志物方面开辟了新的前景。到目前为止报告的结果和本文综合的结果表明，只要对足够大的数据库应用适当的数据处理，这个目标是可以实现的。

*Limitations and future directions*局限性和未来展望

In this section, we review some recent developments based on EEG source connectivity, which is considered to have great potential for brain research. This field is not yet mature, and it lacks a complete validation procedure. However, this absence of validation is not insuperable and should not prevent us from increasing our research efforts in this field. For instance, progress will certainly be made with future developments such as the simultaneous recording of intracerebral and scalp EEG data that will be further used as a ground truth to evaluate proposed algorithms, at least in patients with drug-resistant epilepsy. Some limitations and future directions are summarized hereafter.

在这一节中，我们回顾了基于EEG源连通性的一些最新进展，这些进展被认为具有很大的脑研究潜力。这个领域还不成熟，也缺乏完整的验证过程。然而，缺乏验证并不是不可克服的，也不应该阻止我们在这一领域加大研究力度。例如，未来的发展必将取得进展，如同时记录脑内和头皮EEG数据，这些数据将被进一步用作评估拟议算法的基本事实，至少在耐药癫痫患者中是如此。在此基础上总结了一些不足之处和未来的发展方向

Dipole models偶极子模型

EEG signals reflect a mixing of activities generated by neuronal sources arranged as assemblies. As described by bioelectromagnetic models [19] and experimental studies [20], it is known that synaptic activation leads to the formation of a sink and a source at the neuronal level that can then be viewed as elementary current dipoles. In the case where neurons are geometrically aligned (as with pyramidal cells organized in palisade in cortical structures), the dipole contributions tend to sum up instead of cancel out. These biophysical considerations explain why summed postsynaptic potentials (PSPs)—either excitatory or inhibitory—generated at the level of pyramidal cells located in the cerebral cortex are the major contributors to EEG signals recorded distantly from sources (typically with electrodes positioned on the head). These issues explain why the dipole model is the most suitable for solving the inverse problem. Nevertheless, more efforts to overcome some of the limitations of the dipole model (mainly the spatial limitations) will certainly improve EEG forward/inverse solutions. Note that from a biosignal processing viewpoint, the generation mechanisms of EEG signals are considered to be random (nondeterministic) processes.

脑电图信号反映了一种以集合体的形式排列的神经元源产生的混合活动。正如生物电磁模型[19]和实验研究[20]所描述的，我们知道突触激活导致神经元水平上的一个渗透和一个源的形成，这些可以看作是基本电流偶极子。在神经元呈几何排列的情况下(就像皮质结构中栅栏状的锥体细胞)，偶极子的贡献趋向于累加而不是抵消。这些生物物理学的考虑解释了为什么位于大脑皮层的锥体细胞水平上产生的兴奋性或抑制性突触后电位(PSPs)是远距离记录的EEG信号的主要来源(通常电极位于头部)。这些问题解释了为什么偶极子模型最适合求解逆向问题。然而，更多的努力克服偶极子模型的一些限制(主要是空间限制)肯定会改进EEG的正向/逆向解。注意，从生物信号处理的角度来看，EEG信号的产生机制被认为是随机(非确定性)过程。

Moreover, the generation of action potentials and PSPs in neuron networks results from complex nonlinear processes that cannot be analytically described. Consequently, local field potentials (recorded by intracerebral electrodes) and EEG signals (recorded by scalp electrodes) are random signals, i.e., they take random values at any given time, they cannot be predicted, and they can be characterized only statistically. Nevertheless, at a given time t, the relationship between the neuronal sources and the sensors is fully determined by biophysical factors, i.e., the position and orientation of equivalent dipoles, the source/sensor distance, and the volume-conductor properties (conductivity of the various layers). Typically, for EEG, the equation $X(t) = \mathbf{G}S(t) + N(t)$ describes the relationships between the cortical sources $S(t)$ and the signals collected at scalp electrodes $X(t)$. In this equation, $S(t)$ is the random fraction of the EEG signal. $\mathbf{G}$ is the lead field matrix that describes the deterministic quasi-instantaneous projection of signal sources on the scalp electrodes. $N(t)$ is the measurement noise inherent in any acquisition procedure.

此外，神经元网络中动作电位和突触后电位的产生是由复杂的非线性过程引起的，无法用解析的方法描述。因此，局部场电位(由脑内电极记录)和EEG信号(由头皮电极记录)均为随机信号，即它们在任何给定的时间取随机值，它们不能被预测，只能用统计学来描述。然而，在给定的时间t，神经元源与传感器之间的关系完全由生物物理因素决定，如等效偶极子的位置和方向、源/传感器距离、以及容积导容特性(各层的电导率)。通常，对于EEG，方程X(t) =GS(t)+ N(t)描述了皮层源S(t)与头皮电极X(t)处采集的信号之间的关系。式中，S(t)为EEG信号的随机分数。G为描述信号源在头皮电极上的确定性准瞬时投影的引线场矩阵。N(t)是任何采集过程中固有的测量噪声。

Volume-conduction effects 容积传导效应

Volume-conduction effects are prominent in the electrode space. Connectivity analysis at the source level was shown to reduce the effect of volume conduction, as connectivity methods are applied to local time series (analogous to local field potentials) generated by cortical neuronal assemblies modeled as current dipole sources. Nevertheless, these so-called mixing effects can also occur in the source space but can be reduced by an appropriate choice of connectivity measures. Inverse methods are characterized by their own spatial resolution, i.e., their ability to separate spatially closed sources, which depends on methodological assumptions. Therefore, one should be cautious when interpreting brain connectivity measures even when they are performed at the source level, since the hypothesis that part of the measured coupling is also caused by the mixing of sources cannot be ruled out.

容积传导效应在电极空间中非常明显。在源水平上的连通性分析被证明可以减少容积传导的影响，因为连通性方法被应用于局部时间序列(类似于局部场电位)，这些时间序列是由皮层神经元集成模型为电流偶极子源产生的。然而，这些所谓的混合效应也可以发生在源空间中，但是可以通过适当选择连接度量来减少。逆向方法具有自身的空间分辨率，如它们分离空间封闭的源的能力，这依赖于方法论上的假设。因此，在解释大脑连通性度量时，即使是在源水平上，也应该谨慎，因为不能排除部分测量到的耦合也是由源混合引起的假设。

Functional and effective connectivity measures功能性和有效性的连接测量

Every functional/effective connectivity measure has its own strengths and weaknesses. False functional couplings can be generated by some connectivity methods when applied to mixed signals, such as estimated brain sources. To address this issue, various methods were developed based on the rejection of zero-lag correlation. In particular, unmixing methods, known as *leakage correction*, have been reported that force the reconstructed signals to have zero cross-correlation at lag zero [53]. Although handling this problem theoretically helps interpretation, a quite recent study showed that the current correction methods also produce erroneous human connectomes under very broad conditions [54].

每个功能性/有效性的连接度量都有自己的优缺点。当将一些连接方法应用于混合信号时，例如估计脑源，可能会产生错误的功能耦合。为了解决这一问题，人们开发了各种基于零滞后相关抑制的方法。特别是，据报道，被称为泄漏校正的非混合方法迫使重构信号在滞后于零时具有零互相关。虽然从理论上解决这个问题有助于解释，但最近的一项研究表明，目前的纠正方法在非常广泛的条件下也会产生错误的人类连接体[54]

Graph theory图论

Over the past decade, graph theory has become a well-established approach in the network neuroscience field [1]. It provides complementary information to source connectivity methods by quantifying structural, functional, and/or statistical aspects of identified brain networks. This field is moving very fast, so we stress the need for more validation studies regarding the use of graph theory-based approaches in the context of

在过去的十年中，图论已经成为网络神经科学领域[1]中一个非常稳定的研究方法。它通过量化已识别的大脑网络的结构、功能和/或统计方面，为源连接方法提供补充信息。这一领域的发展非常迅速，因此我们强调，在EEG/MEG源连接性分析的情况下，需要对基于图论的方法进行更多的验证研究。

EEG/MEG source connectivity analysis. This issue is in line with a few recent attempts to evaluate other parameters involved in EEG source connectivity, such as inverse/connectivity measures, the number of scalp electrodes, the head model, the toolboxes used to perform the analysis, and intra-/intersubject reproducibility of the identified networks [14], [38], [55]. The network measures and other issues, e.g., the preprocessing techniques, should also necessarily be the subjects of further validation and investigation. More precisely, the field needs studies that thoroughly evaluate graph theoretic approaches in combination with different inverse solution and connectivity measures.

这个问题符合一些近期试图评估参与EEG源连接其他参数，如逆向/连接指标、头皮电极的数量、头部模型、用于执行分析的工具箱和识别网络的内部/主体间再现性[14]，[38]，[55]。
网络测量和其他问题，例如预处理技术，也必须成为进一步验证和研究的主题。
更准确地说，这个领域需要结合不同的逆向求解和连通性测量，对图论方法进行全面的评估。

Conclusions

As long as there is technological progress in EEG systems and there are advances in signal processing, there will always be new information to extract from EEG. In this article, we presented one of the latest advances in identifying brain networks, with high spatiotemporal resolution from dense-EEG recordings: EEG source connectivity. We provided an overview of this approach and presented the main processing aspects of a signal problem consisting in estimating brain networks at the level of neuronal sources from surface EEG recordings.

只要EEG系统的技术不断进步，信号处理技术不断进步，就一定会有新的信息从REEG中提取出来。
在这篇文章中，我们介绍了识别大脑网络的最新进展之一，具有高时间空间分辨率的致密EEG记录：EEG源连接。
我们概述了这种方法，并介绍了一个信号问题的主要处理方面，包括从表面EEG记录的神经元源水平估计大脑网络。

We also reviewed applications of this new neuroimaging technique within the context of normal brain functions and brain disorders. However, this review has not been exhaustive. The emphasis has been placed on the fundamental aspects of a new neuroimaging technique that provides a good time/space resolution for identifying functional brain networks. A number of issues have not been addressed, as our intent was to provide a didactic guide for researchers interested in EEG source connectivity. By pointing out some methodological issues, our intent was also to help these researchers to choose/design the methods capable of extracting relevant information from EEG data in a given application context.

我们也回顾了这种新的神经成像技术在正常大脑功能和大脑疾病中的应用。
然而，这项审查并非详尽无遗。
重点已放在一项新的神经成像技术的基本方面，该技术为识别大脑功能网络提供了良好的时间/空间分辨率。
许多问题还没有得到解决，因为我们的目的是为对EEG源连接感兴趣的研究人员提供教学指导。
通过指出一些方法上的问题，我们的目的是帮助这些研究人员选择/设计能够在特定的应用背景下从EEG数据中提取相关信息的方法。

In terms of the future, the signal processing community is directly involved with new advances mainly in the development of fully automatic preprocessing algorithms, more realistic inverse solutions algorithms, and unbiased effective connectivity measures. Efforts will likely lead to the development of novel signal processing methods that are able to assess the dynamics of brain networks on short and long timescales. At the same time, the rapid progress in the network analysis community will certainly improve existing methods for analyzing the brain networks identified from dense EEG.

就未来而言，信号处理领域直接参与的新进展主要是开发全自动预处理算法、更现实的逆向解算法和无偏效应的连接措施。
这些努力可能会导致新的信号处理方法的发展，这些方法能够在短时间和长时间尺度上评估大脑网络的动态。
与此同时，网络分析领域的快速发展必将完善现有的分析致密EEG所识别的脑网络的方法。

Recent trends in open-source neuroimaging data will undoubtedly accelerate the validation of the current techniques, such as the huge database of the human connectome project (HCP) (http://www.humanconnectome.org/). The MEG HCP data could be used to test new methods and validate existing ones. In addition, the structural connectome from the HCP (mainly the diffusion tensor imaging data) could certainly be used as a constraint in the inverse solutions, which could lead to an improvement of the spatial precision of the identified functional networks.

最近开源神经成像数据的发展趋势无疑将加速现有技术的验证，比如人类连接体项目(HCP)的大型数据库(http://www.humanconnectome.org/)。
MEG HCP数据可用于测试新方法和验证现有方法。
此外，来自HCP的结构连接体(主要是弥散张量成像数据)当然可以作为逆向解的约束，从而提高所识别的功能网络的空间精度。

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