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Recent developments in representations of the connectome

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ABSTRACT

Research into the human connectome (i.e., all connections in the human brain) with the use of resting state functional MRI has rapidly increased in popularity in recent years, especially with the growing availability of large-scale neuroimaging datasets. The goal of this review article is to describe innovations in functional connectome representations that have come about in the past 8 years, since the 2013 NeuroImage special issue on 'Mapping the Connectome'. In the period, research has shifted from group-level brain parcellations towards the characterization of the individualized connectome and of relationships between individual connectomic differences and behavioral/clinical variation. Achieving subject-specific accuracy in parcel boundaries while retaining cross-subject correspondence is challenging, and a variety of different approaches are being developed to meet this challenge, including improved alignment, improved noise reduction, and robust group-to-subject mapping approaches. Beyond the interest in the individualized connectome, new representations of the data are being studied to complement the traditional parcellated connectome representation (i.e., pairwise connections between distinct brain regions), such as methods that capture overlapping and smoothly varying patterns of connectivity ('gradients'). These different connectome representations offer complimentary insights into the inherent functional organization of the brain, but challenges for functional connectome research remain. Interpretability will be improved by future research towards gaining insights into the neural mechanisms underlying connectome observations obtained from functional MRI. Validation studies comparing different connectome representations are also needed to build consensus and confidence to proceed with clinical trials that may produce meaningful clinical translation of connectome insights.

1. Introduction

The goal of mapping the human connectome (i.e., building a model of all connections in the human brain) can be tackled at different scales ranging from single neurons to macroscale brain regions/networks (Betzel and Bassett, 2017), and using different modalities such as structural and functional measurements. In this review article we focus on macroscale functional connectomics as measured with functional magnetic resonance imaging (fMRI), most commonly obtained while participants are at rest. Propelled by major investment from the National Institute of Health (NIH), the success of the young adult Human Connectome Project (HCP-YA; 2010–2016 (Van Essen et al., 2013)) has paved the way for subsequent consortia efforts to study the connectome in disease populations (Tozzi et al., 2020), and across the lifespan (Harms et al., 2018). Advances and insights from the HCP-YA have also informed recent population neuroimaging studies such as the UK Biobank imaging study (N = 100,000 older adults; (Miller et al., 2016)) and the longitudinal ABCD study (N = 10,000 children followed up for 10 years; (Casey et al., 2018)). Across these big data efforts, connectome research plays a central role to study individualized prediction (Finn et al., 2015; Tavor et al., 2016), correlates of behavior (Smith et al., 2015), and markers of disease (van den Heuvel and Sporns, 2019).

Modern connectomic research builds on a rich history that has developed from early microscopy and mapping insights from the 19th and 20th century (Brodmann, 1908; Catani et al., 2013; Nieuwenhuys, 2013; Triarhou, 2007; Van Essen and Glasser, 2018; Vogt and Vogt, 1903), through the early days of functional PET and MR connectivity (Biswal, 2012; Snyder and Raichle, 2012), to the riches of present day big data (whether it is 'deep' with many data points per subject or 'wide' with many subjects) and computational resources (Smith and Nichols, 2018). In this article, we present an overview of the new developments that have occured over the past eight years, since the last NeuroImage special issue on 'Mapping the Connectome' (Smith, 2013).

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We discuss how approaches and ideas about connectome representations of fMRI data have advanced and the remaining open questions and challenges that lie ahead.

By studying the macroscale functional connectome with fMRI, the field has gained substantial insights into the inherent organizational principles of the human brain. Early work focused on uncovering group-level gross patterns of connectivity, including the discovery of the default mode network (Raichle et al., 2001), and additional reproducible networks that mimic task-related activation patterns (Smith et al., 2009), and that are linked to underlying structural connectivity (Honey et al., 2009). Recent years have seen a shift from these landmark early efforts to map group-level patterns of connectivity towards between-subject studies of behavior (Kashyap et al., 2019; Smith et al., 2015), and interrogations of individualized functional organization (Bijsterbosch et al., 2018; Braga and Buckner, 2017; Gordon et al., 2017; Kong et al., 2019; Wang et al., 2015). This shift is critical because there exists substantial inter-individual variability in brain functional organization, especially in the association cortices (Mueller et al., 2013). Inter-individual variability is a fundamental property of the human brain that is already prominent in newborn infants (Stoecklein et al., 2020). Moreover, similar spatial distribution of inter-individual variability may be present in macaque monkeys and humans which differentiates the multimodal association areas from primary areas (Ren et al., 2020), suggesting that this phenomenon has an evolutionary history. In line with this group-to-subject shift in applied scientific findings, methodological efforts are slowly shifting away from the creation of group-based functional atlases (Craddock et al., 2012; Power et al., 2011; Yeo et al., 2011), towards methods that capture unbiased individualized connectome variation in healthy subjects as well as in patients (Bijsterbosch et al., 2019; Brennan et al., 2019; Glasser et al., 2016a; Hacker et al., 2013; Harrison et al., 2020; Haxby et al., 2020; Lebois et al., 2021; Li et al., 2019; Wang et al., 2020a; Wang et al., 2020b). In parallel with this appreciation of between-subject differences, the field has also started to move beyond focusing only on the view of the brain as a modular set of regions/networks with clear boundaries to also study smooth gradients of organization (Huntenburg et al., 2018; Margulies et al., 2016; Valk et al., 2020), and complex spatio-temporal modes of function (Abbas et al., 2019; Vidaurre et al., 2018). These different representations of the functional connectome offer complimentary (rather than mutually exclusive) insights into brain organization, which is recognized in the modern (Bijsterbosch et al., 2020; Glasser et al., 2016a; Van Essen and Glasser, 2018), and historical literature (Mesulam and Mufson, 1985). The goal of this review article is to provide a brief primer on the various representations of the human connectome that have emerged in recent years.

We begin by reviewing advances in preprocessing strategies to address systematic confounds in functional connectomes (Section 2). We summarize the traditional conceptualization of the functional connectome based on parcellating the brain into a set of distinct regions (Section 3), and then discuss non-parcellated connectome representations such as gradients (Section 4). The shift towards individualized connectome representations and associated challenges is the topic of Section 5. In the conclusion (Section 6), we highlight future areas of research that will be important next steps towards the maturation of the field of rfMRI connectomics.

2. Advances in data preprocessing

Selective yet effective fMRI data clean up is critically important for all connectome representations, especially for individual subject representations of brain connectivity and activity (see Section 5). For example, the HCP's approach to brain imaging preprocessing and analysis relies on multiple denoising stages. The overall goal is to remove the fMRI fluctuations that are related to head motion, respiratory and cardiac physiology, scanner artifacts, and thermal noise without removing neurally related fMRI activation. Validating such an approach is challenging and we recommend the use of experimental modulation of the expected neural signal (i.e., a task-based paradigm) to ensure that denoising steps are only removing noise and retaining all neural signals. Indeed, we have shown that the use of spatial ICA (ideally combining across fMRI runs in each individual subject) and the machine learning component classifier FIX (Griffanti et al., 2014; Salimi-Khorshidi et al., 2014) are highly accurate at removing spatially specific artifacts from head motion, physiology, and scanner artifacts (Glasser et al., 2018). This approach is analogous to the popular "scrubbing" approach advocated by others (Power et al., 2020; Power et al., 2012), but ICA has the advantage of removing variance in proportion to the amount of noise in a given frame (a weighted or "soft" scrubbing rather than an all or nothing approach) and also cleaning those timepoints that lie below a scrubbing threshold without removing neural signal (Glasser et al., 2018). Indeed, recent work has shown that physically restraining subjects results in additional noise reduction benefits above and beyond scrubbing even in low motion, unscrubbed timepoints (Power et al., 2019), indicating that cleaning the non-scrubbed timepoints is also important. Although both scrubbing and spatial ICA-based denoising reduce temporal degrees of freedom, so long as there is shared information amongst the artifacts, ICA-based denoising will remove fewer temporal degrees of freedom than scrubbing, which will improve statistical power. Residual image distortions remain after standard methods of rigid image alignment (Montez et al., 2021) arising from head motion changing the magnetic field inhomogeneity and slice-to-volume mis-registrations in gradient echo EPI data.These distortions will require explicit susceptibility by motion interaction modeling (Andersson et al., 2001; Andersson et al., 2018) and slice-to-volume alignment (Andersson et al., 2017) for optimal correction (and to avoid showing up as artifacts in ICA). Relevant tools already exist for spin echo diffusion MRI and are coming in the future for gradient echo fMRI in FSL and the HCP preprocessing pipelines.

Importantly, multiple publications have shown that spatial-ICA-based denoising does not remove artifactual global blood flow changes related to blood partial pressure of CO2 arising from changes in respiratory rate and depth (Burgess et al., 2016; Glasser et al., 2018; Power, 2017; Power et al., 2017; Siegel et al., 2017). Early work often confused the causality of these global respiratory effects, attributing them to subject motion given that they are at times correlated (Power et al., 2015; Power et al., 2014; Satterthwaite et al., 2012). However, more recent work with multi-echo fMRI has shown that spatially specific artifacts related to head motion arise from different S0-dependent mechanisms,[1] and global respiratory artifacts arise from a $T2^*$-dependent mechanism just like the neural signal does (Power et al., 2018). Moreover, head motion, like any other "task" or behavior, produces both $T2^*$-dependent neural BOLD and artifactual S0-related effects on the fMRI timeseries (Glasser et al., 2018; Power et al., 2020).

In the HCP's denoising approach, individual subject spatial ICA-based denoising is applied immediately after spatial minimal preprocessing (Glasser et al., 2013), and prior to cross-subject areal-feature-based registration (Robinson et al., 2018; Robsinson et al., 2014), ensuring that spatially specific artifacts that might influence cross-subject registration are removed and at the same time avoiding changes to the neural signal that might influence such registration. Using areal-feature-based cross-subject registration has an additional advantage with group-defined parcellations because it ensures that most differences in the size, shape, and position of cortical areas are represented as spatial differences in the registration, rather than differences in measured brain functional activity or connectivity. Notably, such spatial bias in connectivity can be substantial when considering network-level organiza-

[1] For example due to T1-recovery related spin history effects, due to interactions between the head coil receive field and head motion, due to head motion breaking the assumptions of the pulse sequence such as differential excitation and readout locations in space, and due motion changing the magnetic field inhomogeneities magnetic leading to differential susceptibility induced gradient echo signal loss.

tion (Bijsterbosch et al., 2018), and limiting the information 'leakage' at the level of cortical areas is therefore an important step towards disambiguating spatial and connectivity information. This may have important implications for identifying brain measures that are relevant to behavior or other traits outside the scanner, and avoid inaccurately attributing areal differences as functional connectivity or activity differences. Thus, measures of brain areal size, shape, and position (which can be represented at the areal level as surface areas or volumes or at the grayordinate level as isotropic and anisotropic distortion maps or registration induced displacement maps) represent a fertile untapped resource for biomarkers (Kong et al., 2019; Li et al., 2019).

Subsequent to cross-subject areal-feature-based registration, the HCP's denoising approach has been extended to perform group level denoising of global respiratory noise with temporal ICA (Glasser et al., 2018; Power et al., 2020), making use of the improved cross-subject correspondence. Temporal ICA is used because, in contrast to spatial ICA, it is able to represent spatially global fluctuations in a single or a few components, rather than mixing them across all components so as to satisfy a spatial orthogonality constraint (instead, the components are constrained to be temporally orthogonal). ICA performs best when there are many samples along the axis being orthogonalized, which is why spatial ICA-based denoising is done at the individual subject level where hundreds of thousands of voxels are available and temporal ICA works best at the group level where again hundreds of thousands of timepoints are available in large datasets. Components representing global respiratory noise can thus be removed selectively using temporal ICA while retaining neural signal in its unchanged form. Indeed, this is a key advantage of temporal ICA over global signal regression (Glasser et al., 2018), which removes task-related neural signal (Glasser et al., 2018) and spuriously increases anti-correlations in functional connectivity (Glasser et al., 2018; Murphy et al., 2009). Interestingly, the use of aggressive regression of movement regressors (i.e., regressing out all variance explained by movement regressors) has also been shown to remove task-related neural signal (Glasser et al., 2019), and thus, is no longer recommended in the HCP approach to brain imaging. Similarly, other unselective approaches to functional MRI denoising including band-pass filtering, tissue-based nuisance regressors, and blind tissue-based PCA decompositions have yet to be validated using task-fMRI-based paradigms with a known ground truth and likely are not beneficial above and beyond spatial and temporal ICA cleanup. For example, head motion also causes neurally driven BOLD changes in the timeseries because motor and sensory cortices activate during head motion (Glasser et al., 2018; Power et al., 2020). There are also neural signals that correlate with respiration during a task or resting state (e.g. stimulus correlated breathing) (Glasser et al., 2018). Overall ICA-based cleanup for HCP-style high spatial and temporal resolution data aims to retain all neural signal in the fMRI scan (including the neural activation resulting from to e.g., head motion or neural signal that is correlated with respiration), while removing all temporal artifacts arising from head motion or respiration. One can always then choose the neural signal that one wants to look at according to the goals of one's study after such selective denoising (e.g., choosing to remove all traces of head motion from the data including those that arise from neural activation and thereby reducing fluctuations in the head sensorimotor functional network accordingly). We recommend that such study paradigm choices about which neural signal to retain should be conscious decisions that are justified in a study's methods rather than being silently imposed by non-selective denoising approaches. Datasets without the emerging standards of high spatial and temporal resolution may be more limited in their denoising options because neural and artifactual contributions cannot be fully separated, and such limitations should be carefully considered when planning new fMRI studies.

Finally, thermal noise presents an interesting challenge for data cleanup. Although methods have been developed to reduce thermal noise while at the same time not spatially or temporally smoothing the data (Glasser et al., 2016b), similar to temporal smoothing, these methods reduce temporal degrees of freedom, which reduces statistical efficiency. Thus, the optimal approach for thermal noise removal likely depends on the planned analysis approach, with correlation-based approaches (e.g. the pairwise correlation of two noisy signals when computing a dense connectome) potentially benefiting more from thermal noise removal than regression-based approaches such as dual regression (the relationship between noisy data and relatively noise free component timeseries derived from weighted averages across the brain). That said, the most effective approach across a wide spectrum of analyses likely involves neuroanatomically-informed spatial smoothing (e.g., as achieved in good-quality parcellations) (Glasser et al., 2016a), because it reduces thermal noise without reducing temporal degrees of freedom.

3. The parcellated connectome

To achieve the connectomics goal of mapping all connections in the brain, an important first step is to set the units of the map (i.e., the elements between which connections will be drawn). As an intuitive example, say we want to map out all social interactions in a country. If we treat each person as a unit and draw out all interactions amongst all people, this 'social connectome' of a country would be very dense and difficult to interpret. Therefore, we may want to group people together so that we can map out connections between households, families, neighborhoods, or other social groupings like school/work departments or institutions. As the units become bigger, the number of connections in the social connectome as a whole reduces because social interactions within a unit are no longer considered as between-unit connections. The same holds for the functional connectome, such that there is ambiguity between representing connectivity information as part of the unit definition or as between-unit connections. This analogy also points to ambiguities in the criteria used to determine the units. For example, should a college student who lives on campus during the week and returns home on weekends be included in the family-home household unit or in the college dorm household unit, or both? Similar questions and ambiguities exist when determining brain units for functional connectomics.

The smallest possible units in fMRI are the measurement voxels, or gray matter vertices after surface-based preprocessing (Glasser et al., 2013). Notably, these smallest measurement units already contain thousands of neurons and are therefore far removed from the smallest relevant biological units of individual neurons or even synapses. It is less common in functional connectomics to map connections between all voxels/vertices and instead voxels are typically grouped together into larger regions, although recent findings suggest that fine-scale "dense" connectivity may contain behaviorally relevant information that is lost in the coarse-scale regional connectome (Feilong et al., 2020). Nevertheless, analyses are often performed at the 'areal' level to gain computational, statistical, and interpretational efficiencies (Eickhoff et al., 2018; Glasser et al., 2016b). Such grouping of data is reasonable as each brain area is thought to contribute distinctly to the neural computations carried out within the functional network underlying a given behavior (Van Essen and Glasser, 2018). Brain areas also often have specialized architecture (i.e., internal organization and local connectivity), a unique pattern of distant connectivity with other areas, and may spatially represent topographic maps of sensory or motor systems (Sereno et al., 1995), or cognitive systems (Huth et al., 2016). Therefore, a lower rank parcellation of the brain into a smaller number of units each made up of many voxels/vertices is most frequently used for the functional connectome. Of note, variation of size within a given parcellation may influence the discoverability and polygenicity across parcels (van der Meer et al., 2020). Thus, depending on the study goal a parcellation with more or less equally sized parcels may be preferred.

For brevity, we present a brief overview of the main criteria for brain parcellations in Table 1 and summarize the characteristics of several widely used publicly available parcellations in Table 2 (for further detail see (Bijsterbosch et al., 2017b)). The nomenclature for brain units defined by brain parcellations is diverse, and units may be referred

Table 1.
Overview of the main criteria that brain parcellations can be characterized by.

Parcellation criteria	Options	
Hard vs Soft	Binary parcels have voxel values of either zero (not in parcel) or 1 (in parcel). These "hard" parcellations often do not allow for overlap (i.e., voxels being part of more than one parcel).	Weighted parcels have voxel values across a range. These "soft" parcellations therefore have fuzzy borders and allow for overlap (i.e., a voxel with high weights in multiple parcels).
Areal/regional vs Network	Areal/regional (contiguous) parcels are blobs of spatially neighboring voxels. Bilateral homologous brain regions are therefore separate parcels.	Network (non-contiguous) parcels are whole-brain patterns of multiple blobs that are not all interconnected.
Dimensionality	A wide range of dimensionalities have been used ranging from 6 to 10 parcels at the lower end to 1000 parcels at the higher end. It is possible to define a hierarchical parcellation with a low number of combined parcels at the top and increasing splits into smaller parcels further down the hierarchy.	
Sample	Publicly released high quality parcellations are mostly derived from young healthy participants.	Deriving a parcellation from a specific study sample may fit the population better (especially if different ages or if psychopathology is present).
Modality	Parcellations defined based on functional data are more relevant to functional studies than those based on gyral and sulcal landmarks.	Consensus across imaging modalities (e.g., thickness, myelin, resting state, task) can be used for a multimodal parcellation.

Table 2.
Summary of several commonly used publicly available functional brain parcellations.

Parcellation	Voxel values		Spatial dispersion		Parcel	#Population	Modality		Coverage
	Binary	Weight	Areal/regional	Network			rfMRI	Multi-modal	
Smith (Smith et al., 2009)		✔		✔	10	Young healthy	✔		Whole brain
Yeo, Krienen (Yeo et al., 2011)	✔			✔	7/17/98	Young healthy	✔		Cortical
Power (Power et al., 2011)	✔		✔		103/226	Young healthy	✔		Cortical
Craddock (Craddock et al., 2012)	✔		✔		353	Young healthy	✔		Whole brain
Shen (Shen et al., 2013)	✔		✔		213	Young healthy	✔		Whole brain
Wang (Wang et al., 2015)	✔			✔	18	Young healthy	✔		Cortical
Gordon (Gordon et al., 2016)	✔		✔		422	Young healthy	✔		Cortical
Glasser (Glasser et al., 2016a) = HCP-MMP1.0	✔		✔		360	Young healthy		✔	Cortical
Schaefer (Schaefer et al., 2018)	✔		✔		100 - 1000	Young healthy (HCP)	✔		Cortical

to as nodes, parcels, networks, or regions. Naming conventions based on anatomical principles have been suggested for low-dimensional network parcellations (Uddin et al., 2019), and for higher dimensional areal/regional parcellations (Glasser et al., 2016a).

Once the units for the functional connectome have been defined, the subsequent steps for defining the parcellated connectome involve extraction of node time series and defining the method to estimate pairwise connections between nodes (also known as edges). For binary parcellations, the node time series is often defined as the average time series across all voxels within the parcel. For weighted parcellations such as those derived using Independent Component Analysis (ICA, (Beckmann and Smith, 2004)), the node time series can be extracted using dual regression (Nickerson et al., 2017) or back projection (Calhoun et al., 2001). Once the node time series have been extracted, edges are often defined as either the full correlation (Pearson's), the partial correlation (after residualizing the two node time series with respect to all other nodes) with or without regularization, or the covariance (Smith et al., 2013).

Over the past eight years, there have been a number of important advances for parcellated representations of the connectome. The development of the HCP-MMP1.0 brain parcellation based on multimodal HCP-YA data (task, rest, myelin, cortical thickness) bridges between anatomical and functional mapping efforts and highlights examples of atypical topological organization (Glasser et al., 2016a). Although some parcellations treat "homogeneity" as the end goal to be optimized (Gordon et al., 2016; Schaefer et al., 2018), it should be noted that brain areas are often not homogeneous (Van Essen and Glasser, 2018) and spatially overlapping weighted components such as those from ICA or probabilistic functional modes will therefore achieve higher homogeneity (see Section 4). Nevertheless, the HCP's parcellation provides an alternative somatotopic subregional parcellation for sensorimotor cortex that is already being used together with the areal parcellation in translational studies (Chandrasekaran et al., 2020). It also provides a cortical areal classifier that enables mapping cortical areas in individual subjects, even when those areas are atypical in layouts and not aligned with the best available surface registration methods (see Section 5). Furthermore, the characterization of the parcellated connectome as a fingerprint has been a valuable catalyst for efforts to predict behavior and clinical symptomatology (Brennan et al., 2019; Finn et al., 2015; Lebois et al., 2021; Li et al., 2019; Wang et al., 2020a; Wang et al., 2020b). Related to these efforts, recent work has shown that transformations of parcellated connectivity estimates (such as tangent space projections) can improve performance when using subsequent machine learning methods for behavioral prediction (Dadi et al., 2019; Pervaiz et al., 2020). Although the parcellated connectome is still the most common representation for functional connectomics, criticisms have also started to emerge. For example, it has been shown that between-subject connectivity differences in the parcellated connectome are mixed with spatial variability in network topography (Bijsterbosch et al., 2018; Li et al., 2019), which has led to increased interest in non-parcellated and/or individualized connectome representations (Sections 4 and 5). There has also been increased interest in node-based analysis that investigate signal fluctuation instead of signal correlations (Bijsterbosch et al., 2017a; Duff et al., 2018; Miller et al., 2016). Lastly, although causal inference on the directionality of connections is of great interest (Reid et al., 2019), the temporal slowness of fMRI and regional variability in the hemodynamic response function (Friston, 2009) limit the accuracy of many causal connectivity estimates, especially lag-based methods (Smith et al., 2011). Nevertheless, recent methodological advances such as Bayesian Nets and dynamic causal models for resting state may hold promise for causal inferences (Mumford and Ramsey, 2014; Park et al., 2018).

4. Non-parcellated connectome representations

The parcellated connectome approaches discussed in the previous section provide an intuitive framework for mapping the functional connections in the brain. At the same time, in many cortical parcels, borders vary depending on the chosen modality and may not show clear borders in all modalities or with all analysis approaches (Haak and Beckmann, 2020; Huntenburg et al., 2018; Von Bonin and Bailey, 1947). Simply averaging within parcels assumes that connectivity profiles are homogeneous within a specific parcel, with only one dominant pattern (Haak and Beckmann, 2020). However, function and microstructure are often highly variable within a region, and inconsistent across modalities. Moreover, variations in both function and structure display "multiplicity" (i.e., overlap) and are organized along more than one meaningful axis of variance (Haak and Beckmann, 2020). Such challenges of diverse and overlapping functional organization cannot be overcome by using finer grained parcellations (Bijsterbosch et al., 2020), but rather may be best studied by multidimensional connectome representations.

One approach to account for multiplicity is to allow for spatial overlap in the definition of network organization. For example, Probabilistic Functional Modes (PROFUMO) is a Bayesian dimensionality reduction algorithm that estimates network structure using temporal and spatial priors, thereby avoiding the spatial independence constraint that is enforced either explicitly or implicitly in other parcellation methods (such as ICA) (Harrison et al., 2020; Harrison et al., 2015). The definition of potentially overlapping networks adds a spatial overlap correlation matrix in addition to the temporal correlation matrix, and previous work has shown that individual differences in spatial network overlap may be more strongly associated with behavior than individual differences in temporal correlation (Bijsterbosch et al., 2019).

Another way to address multiplicity is by profiling cortical organization based on the relationships between voxels or vertices, and extracting multiple axes of eigenvariance within that organization (Haak and Beckmann, 2020; Huntenburg et al., 2018; Margulies et al., 2016; Marquand et al., 2017; Paquola et al., 2019). Such methods can be applied at the regional (Haak et al., 2018; Marquand et al., 2017; Vos de Wael et al., 2018), or at the global level to study so-called gradients or natural axes in functional brain organization (Huntenburg et al., 2018; Margulies et al., 2016). These approaches capture the similarity of connectivity profiles between two given units (voxels, vertices, parcels) and order them as a function of their similarity. E.g. two units with similar gradient values have similar functional connectivity profiles, and can be interpreted as integrated, whereas two units with maximally differing gradient scores have different connectivity profiles, and can be interpreted as functionally segregated (Shine et al., 2019). Gradients can be reliably derived from connectome information (Hong et al., 2020) and capture both functional and structural features of brain organization (Huntenburg et al., 2018). The resulting overlapping axes of organization known as smooth connectivity 'gradients' capture the internal organizational principles of a certain region or assembly of regions, and provide a low dimensional coordinate system of neural organization.

Genetic, transcriptomic, and evolutionary patterns have been shown to follow gradual axes of change along the cortex and hippocampus (Burt et al., 2018; Margulies et al., 2016; Valk et al., 2020; Vogel et al., 2020; Xu et al., 2020), supporting the intrinsic relationship between the physical layout of the brain and its function (Fornito et al., 2019; Mesulam, 1998). For example, at the global level, it has been shown that the principal axis of intrinsic functional organization follows a trajectory from unimodal, primary, regions to transmodal association cortices (Margulies et al., 2016), aligning with cortical expansion and functional reorganization in primate evolution (Van Essen and Dierker, 2007; Xu et al., 2020). A different, tertiary, organizational pattern juxtaposes the default mode network with the multi-demand network (Assem et al., 2021; Assem et al., 2020; Duncan, 2010), possibly reflecting a balance that underlies working memory performance and goal-directed cognition (Murphy et al., 2020; Spreng et al., 2010). Conversely, at the regional level it has been shown that functional organizational axes within the hippocampus align with anterior to posterior patterns and functional co-activation, whereas lateral-medial patterning is associated with cortical microstructure as measured by T1w/T2w contrast (Vos de Wael et al., 2018). Also the internal organization of the human striatum seems to be governed by smooth axes within intrinsic functional organization, reflecting its connections to the cortex and capturing behavioral variability (Marquand et al., 2017). Although the understanding of how different gradients organize brain regions and their interrelationship is still at its beginning, it has provided novel information and understanding of brain organization, its development, evolution and disorder. For example, Hong and colleagues have been able to show alterations of functional organization along the principal functional gradient in Autism Spectrum Disorders, aligning with notions of altered cortical development in ASD (Hong et al., 2019).

Additional connectome representations that incorporate dynamic temporal information have also emerged, including hidden markov models (Vidaurre et al., 2018), and quasi periodic waves (Abbas et al., 2019). Parcellated and non-parcellated connectome representations provide complementary insights, and may even be meaningfully combined (Dohmatob et al., 2021). At the same time, integrating the complementary insights across connectome representations becomes increasingly challenging because the implications of new results obtained using one connectome representation for other representations are often not clearcut. Increased comparative and collaborative efforts are therefore needed to ensure cumulative growth and avoid siloing (Bijsterbosch et al., 2020).

In summary, this section described a number of advances in connectome representations that move beyond the traditional parcellated approach. In Table 3 we provide a summary of some key advantages and disadvantages of these non-parcellated connectome representations compared to the traditional parcellated approach. Overall, although there certainly has been a historical tension between the functional segregation versus holistic views of brain function have engendered debate for over 100 years (Zilles and Amunts, 2010) with early physicians such as Broca, Wernicke, and Lichtheim finding that brain functions were lost when specific parts of the brain were damaged and classical neuroanatomists like the Vogts and Brodmann working to identify cortical areas based on differences in microscopically visible properties (myelo and cytoarchitecture). Then other neuroanatomists such as Bailey and von Bonin or Lashley and Clark expressed skepticism of many of Brodmann's and the Vogts' boundaries and favored coarser, more gradual and "gradient-like" subdivisions. Although the juxtaposition between sharp boundaries and smooth gradient-based approaches might appear as a more modern version of this debate. There can be well-defined boundaries between cortical areas (e.g. visual areas) and yet riding on top of these more gradual gradients in functional connectivity from early to late areas along the dorsal and ventral visual streams. Thus, these concepts are not in our view mutually exclusive. Indeed Van Essen and Glasser (Van Essen and Glasser, 2018) attempted to bridge the cortical area and functional network concepts in relation to human behavior by positing that "any specific behavior might have a distinctive functional network, similar behaviors may have largely overlapping functional networks, and each cortical area may be responsible for a portion of the computations necessary to produce a behavior when working in concert with its partners in that behavior's functional network.".

5. The individualized connectome

Brain maps are often instantiated first at the group level and this is particularly valid if there has been care taken to ensure that individual subjects' brain areas line up as well as is possible (Coalson et al., 2018; Glasser et al., 2016a). The use of group averages helps to define what is typical in a population, achieves correspondence across subjects to enable like-for-like comparisons, and averaging across subjects can markedly improve the contrast-to-noise ratio for subtle effects.

Table 3.
Summary of relative advantages and disadvantages of parcellated and non-parcellated connectome representations.

Connectome representation	Advantages	Disadvantages
Parcellated	Intuitive to interpret Relatively simple analysis	Hard, non-overlapping parcels do not capture smooth variation or overlapping functional organization Group-defined parcellations do not match individualized organization
PROFUMO	Hierarchical model achieves between-subject correspondence and accurately captures individual subject organization	Relatively more difficult to interpret Network decomposition is relatively sensitivity to potentially minor changes in the data (similar to ICA)
Global gradient	Continuous space captures fundamental organization axes Spatial relationships between regions/networks can be revealed	Alignment of gradients between individuals and across studies is not trivial May miss out on nuanced differences (if only the top eigenvectors are explored) Difficult to disentangle global from local effects when performing brain-wide gradient analysis.
Local (areal) gradient	Identifies overlapping patterns of organization that is overlooked in other representations	Localized (within-region) analysis that doesn't easily integrate with whole-brain connectome studies

Those advantages aside, it is well known that even when areal-feature-based cortical surface registration is used to precisely align cortical areas (Robinson et al., 2018; Robinson et al., 2014), a significant fraction of individual subjects will have atypical layouts of at least some cortical areas (Glasser et al., 2016a). Thus, individualized representations of connectomes will likely be most accurate for most subjects. This accuracy will represent a tradeoff between correctly capturing true individual variability in cortical areal borders and the inherently increased uncertainty of mapping individual subject areal boundaries using a limited amount of data with lower contrast-to-noise ratio than group level data. Indeed, recent explorations of this tradeoff (Laumann et al., 2015; Mueller et al., 2015), showed that increasing the amount of resting state fMRI data markedly improved the reliability of individual estimates of brain connectivity. Further work is needed to evaluate the effects of differing amounts, paradigms (e.g., resting state vs traditional task vs naturalistic movies), and field strengths (e.g., 3T vs 7T) of fMRI data on the accuracy of cross-subject areal feature based registration and individual subject areal classification.

Individual subject parcellation may be achieved using a variety of approaches. One approach relies on learning the multi-modal areal fingerprint of each human cortical area and using grayordinate-wise multimodal maps in individuals to find each cortical area using a machine learning areal classifier (Glasser et al., 2016b; Hacker et al., 2013). Importantly, such an approach is capable of identifying cortical areas even in individuals whose areas have atypical layouts and thus will not be aligned with areal-feature-based surface registration. Similar to such registration, and as mentioned above, the optimal amount, type, and field strength of fMRI used for areal classification has not yet been characterized and ongoing work seeks to do this. Additionally, accurate individual subject areal classification will enable exploration of the neurobiological significance of atypical brain areas and answer the question of whether humans all have the same set of brain areas or if some have extra areas and some are missing areas. Accurate fMRI denoising (Section 2) will be critical to ensuring that noise does not "create a brain area" in an individual subject and that neural signal is not removed to cause a "missing brain area."

Another approach attempts to identify functional networks defined at the group-level in each individual subject's brain (Wang et al., 2015). Functional organization for each individual is determined based on functional connectivity using an iterative adjusting algorithm guided by the group-level atlas and inter-subject variability pre-estimated in the population (Mueller et al., 2013). The central idea is to allow idiosyncrasies of the individual to drive the network solution. Critically, the influence of the population-based atlas on the individual brain parcellation is not identical for every subject or every brain region, and is flexibly adjusted based on the known distribution of individual variability and the signal-to-noise distribution in the particular subject. Specifically, a weighting strategy is applied where the population-based atlas will have less impact than the individual subject's data on brain regions known to have high levels of inter-subject variability, or brain regions showing good SNR in a particular subject. It has been shown that functional networks localized using this technology may be validated by invasive cortical stimulation mapping in surgical patients (Shen et al., 2020; Wang et al., 2015). A further hierarchical Bayesian approach that iteratively optimizes functional networks at the group and individual levels is probabilistic functional modes (PROFUMO) (Harrison et al., 2020; Harrison et al., 2015).

A final approach to brain alignment, hyperalignment, is worth mentioning here. The area-feature-based approach to cross-subject registration mentioned above clearly improves the correspondence of brain areas across subjects (Coalson et al., 2018), but is limited in that it cannot account for topology-breaking cross-subject differences. For example, if brain areas swap positions or split and join as does area 55b in 11% of subjects (Glasser et al., 2016a), areal feature-based registration is unable to align them. The HCP's approach to brain imaging preprocessing and analysis relies on the areal classifier to handle such topologically incompatible differences at the brain area level, but what if one wants to align across subjects at an even more fine-grained level while at the same time allowing topological incompatibilities? Hyperalignment promises such alignment (Haxby et al., 2020), and indeed does show improvements beyond and above areal-feature-based registration (Feilong et al., 2020). Hyperalignment forgoes the traditional spatial alignment goals of achieving voxel-to-voxel or vertex-to-vertex correspondence across individuals, and instead aligns subjects based purely on activation or correlation information. A hybrid strategy might use the areal classifier to identify corresponding areal searchlights across subjects to enable well constrained within-area hyperalignment, as topological cross-subject correspondence is unlikely at neurobiologically lower levels of the hierarchy than cortical areas, given the break down at this level already in many subjects.

Moving from group-parcellations to individualized connectome representations offers many advantages. Firstly, the mean time series extracted from a parcel forms the basis of many connectomic analyses, and this average time series does not represent a meaningful functional unit if the boundaries of the parcel do not functionally align for the individual (Allen et al., 2012). Secondly, studying the individualized connectome offers insights into previously untapped sources of between-subject variation such as differences in the size, shape, position and non-topological variation of brain areas and networks (Bijsterbosch et al., 2018; Glasser et al., 2016a; Kong et al., 2019). Thirdly, accurately capturing individualized areal/network boundaries helps to disambiguate between spatial and temporal origins of individual differences, which is important to ensure appropriate interpretation of results (Bijsterbosch et al., 2019). In general, the importance of accurately modeling individual connectomes increases along with increased interest in individual difference research such as correlations with behavior, individual-level predictions, and clinical biomarker studies.

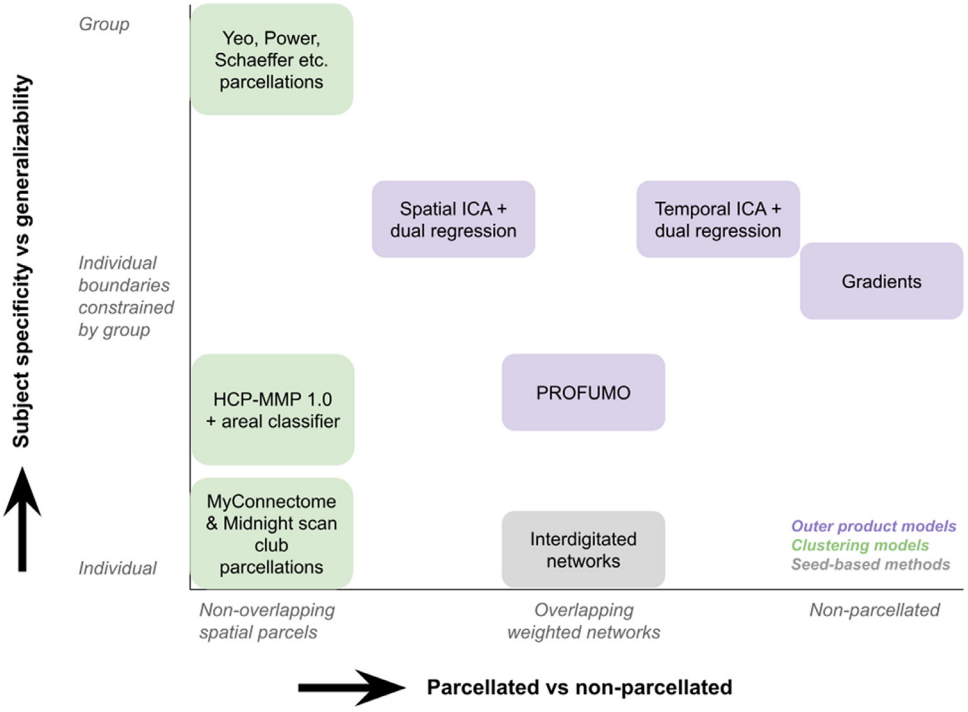

Fig. 1.. Overview of methods and parcellations as a function of algorithmic constraints (x-axis; parcellated to non-parcellated) and input data (y-axis; individual subject to group).

For individual difference research, sample size is another important consideration because sampling variability leads to inflated and inconsistent correlations between connectome representations and non-imaging variables such as behavior/ lifestyle/ cognition/ symptoms (Marek et al., 2020). Importantly, we have to adjust our expectations and appreciate that realistic and reproducible effect sizes of brain-behavior correlations are likely (much) smaller than previously reported (Lindquist, 2021), and accordingly larger samples are needed to reliably and reproducibly detect these effects. In the past, most studies had relatively small sample sizes and therefore required high thresholds for significance due to simple power restrictions and by definition any findings that passed significance had a relatively high effect size. However, these findings have often failed to replicate in new samples (Ioannidis, 2017; Poldrack et al., 2017), because they are largely driven by sampling variability (Marek et al., 2020). The availability of large-scale neuroimaging datasets offers opportunities for addressing past challenges with reproducibility. However, this requires an acceptance that small, but reproducible, effect sizes are the norm and are worthy of investigation (Lindquist, 2021).

6. Conclusion

The field has come a long way in the years since the last NeuroImage special issue on the connectome. The way the functional connectome is conceptualized (both theoretically and analytically) has expanded to take into consideration overlapping networks and multiple organizational axes/gradients. These different representations of resting state fMRI data offer very valuable and complementary insights into the organizational principles of brain function. Additionally, greater awareness of between-subject variability has driven detailed assessments of the individualized connectome and methodological advances in preprocessing, cross-subject registration, and individualized parcellation. In Fig. 1, we provide a schematic of recent brain representations positioned along the two major axes of innovation (i.e., non-parcellated and individualized representations). The positioning of connectome representations along this schematic are relative and approximate based on implementations and examples in the current literature (i.e., axes do not represent quantifiable units). Nevertheless, we hope that this schematic - along with the summary Tables in this article - will aid the reader in their understanding of the relationships between different representations of the connectome.

Given the expansive landscape of definitions, methods, and trade-offs in studying the connectome, the term 'functional connectivity' has become overly broad and perhaps inaccurate. Therefore, greater specificity is needed to describe how we represent the brain, which assumptions and constraints are required, and how these might affect results and interpretation (Bijsterbosch et al., 2020).

Looking ahead, many unanswered questions about the functional connectome remain. Further research is needed to better understand the biological basis of fMRI-derived connectomes. For example, detailed comparisons of non-invasive functional connectomes to invasively defined structural connectomes or invasive functional recordings in non-human primates may enable validation of the best ways to model functional connectivity (Bentley et al., 2016; Hayashi et al., 2021). Additionally, more work is needed to establish the clinical utility of connectomic measures, for example for early diagnosis (e.g., in Alzheimer's Disease), and prediction of treatment response (e.g., in Major Depressive Disorder). Although existing small-scale studies are suggestive of meaningful effects, full-scale clinical trials are needed to achieve meaningful clinical translation and impact patients. One factor that reduces the likelihood of such clinical trials is the lack of white-paper agreement on appropriate preprocessing and analysis approaches. To move towards such agreement, more comparative benchmarking research (Botvinik-Nezer et al., 2020; Ciric et al., 2017; Dadi et al., 2019), standardization (e.g., BIDS), and collaboration is needed.

Author contributions

JDB wrote the introduction section, parcellated connectome section, conclusion section, and parts of the individualized connectome section, and created the figure and tables. SLV wrote many parts of the non-parcellated connectome section. DW wrote parts of the section on the individualized connectome. MFG wrote the section on preprocessing and parts of the non-parcellated connectome section. All authors collaborated, reviewed, and commented extensively on the final manuscript and on the figure and tables.

Data and code availability statement

This review article does not include any relevant data or code

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References

Abbas, A., Belloy, M., Kashyap, A., Billings, J., Nezafati, M., Schumacher, E.H., Keilholz, S., 2019. Quasi-periodic patterns contribute to functional connectivity in the brain. Neuroimage 191, 193–204. doi:10.1016/j.neuroimage.2019.01.076.

Allen, E.A., Erhardt, E.B., Wei, Y., Eichele, T., Calhoun, V.D., 2012. Capturing inter-subject variability with group independent component analysis of fMRI data: a simulation study. Neuroimage 59, 4141–4159. doi:10.1016/j.neuroimage.2011.10.010.

Andersson, J.L., Hutton, C., Ashburner, J., Turner, R., Friston, K., 2001. Modeling geometric deformations in EPI time series. Neuroimage 13, 903–919. doi:10.1006/nimg.2001.0746.

Andersson, J.L.R., Graham, M.S., Drobnjak, I., Zhang, H., Campbell, J., 2018. Susceptibility-induced distortion that varies due to motion: correction in diffusion MR without acquiring additional data. Neuroimage 171, 277–295. doi:10.1016/j.neuroimage.2017.12.040.

Andersson, J.L.R., Graham, M.S., Drobnjak, I., Zhang, H., Filippini, N., Bastiani, M., 2017. Towards a comprehensive framework for movement and distortion correction of diffusion MR images: within volume movement. Neuroimage 152, 450–466. doi:10.1016/j.neuroimage.2017.02.085.

Assem, M., Glasser, M.F., Van Essen, D.C., Duncan, J., 2020. A domain-general cognitive core defined in multimodally parcellated human cortex. Cereb. Cortex 30, 4361–4380. doi:10.1093/cercor/bhaa023.

Assem, M., Shashidhara, S., Glasser, M.F., Duncan, J., 2021. Precise topology of adjacent domain-general and sensory-biased regions in the human brain. BioRxiv doi:10.1101/2021.02.21.431622.

Beckmann, C.F., Smith, S.M., 2004. Probabilistic independent component analysis for functional magnetic resonance imaging. IEEE Trans. Med. Imaging 23, 137–152. doi:10.1109/TMI.2003.822821.

Bentley, W.J., Li, J.M., Snyder, A.Z., Raichle, M.E., Snyder, L.H., 2016. Oxygen level and LFP in task-positive and task-negative areas: bridging BOLD fMRI and electrophysiology. Cereb. Cortex 26, 346–357. doi:10.1093/cercor/bhu260.

Betzel, R.F., Bassett, D.S., 2017. Multi-scale brain networks. Neuroimage 160, 73–83. doi:10.1016/j.neuroimage.2016.11.006.

Bijsterbosch, J.D., Beckmann, C.F., Woolrich, M.W., Smith, S.M., Harrison, S.J., 2019. The relationship between spatial configuration and functional connectivity of brain regions revisited. Elife 8. doi:10.7554/eLife.44890.

Bijsterbosch, J.D., Woolrich, M.W., Glasser, M.F., Robinson, E.C., Beckmann, C.F., Van Essen, D.C., Harrison, S.J., Smith, S.M., 2018. The relationship between spatial configuration and functional connectivity of brain regions. Elife 7 doi:10.7554/eLife.32992.

Bijsterbosch, J., Harrison, S., Duff, E., Alfaro-Almagro, F., Woolrich, M., Smith, S., 2017a. Investigations into within- and between-subject resting-state amplitude variations. Neuroimage 159, 57–69. doi:10.1016/j.neuroimage.2017.07.014.

Bijsterbosch, J., Harrison, S.J., Jbabdi, S., Woolrich, M., Beckmann, C., Smith, S., Duff, E.P., 2020. Challenges and future directions for representations of functional brain organization. Nat. Neurosci. 1–12. doi:10.1038/s41593-020-00726-z.

Bijsterbosch, J., Smith, S.M., Beckmann, C.F., 2017b. Introduction to Resting State FMRI Functional Connectivity, Oxford Neuroimaging Primers. Oxford University Press.

Biswal, B.B., 2012. Resting state fMRI: a personal history. Neuroimage 62, 938–944. doi:10.1016/j.neuroimage.2012.01.090.

Botvinik-Nezer, R., Holzmeister, F., Camerer, C.F., Dreber, A., Huber, J., Johannesson, M., Kirchler, M., Iwanir, R., Mumford, J.A., Adcock, R.A., Avesani, P., Baczkowski, B.M., Bajracharya, A., Bakst, L., Ball, S., Barilari, M., Bault, N., Beaton, D., Beitner, J., Benoit, R.G., Berkers, R.M.W.J., Bhanji, J.P., Biswal, B.B., Bobadilla-Suarez, S., Bortolini, T., Bottenhorn, K.L., Bowring, A., Braem, S., Brooks, H.R., Brudner, E.G., Calderon, C.B., Camilleri, J.A., Castrellon, J.J., Cecchetti, L., Cieslik, E.C., Cole, Z.J., Collignon, O., Cox, R.W., Cunningham, W.A., Czoschke, S., Dadi, K., Davis, C.P., Luca, A.D., Delgado, M.R., Demetriou, L., Dennison, J.B., Di, X., Dickie, E.W., Dobryakova, E., Donnat, C.L., Dukart, J., Duncan, N.W., Durnez, J., Eed, A., Eickhoff, S.B., Erhart, A., Fontanesi, L., Fricke, G.M., Fu, S., Galván, A., Gau, R., Genon, S., Glatard, T., Glerean, E., Goeman, J.J., Golowin, S.A.E., González-García, C., Gorgolewski, K.J., Grady, C.L., Green, M.A., Guassi Moreira, J.F., Guest, O., Hakimi, S., Hamilton, J.P., Hancock, R., Handjaras, G., Harry, B.B., Hawco, C., Herholz, P., Herman, G., Heunis, S., Hoffstaedter, F., Hogeveen, J., Holmes, S., Hu, C.-P., Huettel, S.A., Hughes, M.E., Iacovella, V., Iordan, A.D., Isager, P.M., Isik, A.I., Jahn, A., Johnson, M.R., Johnstone, T., Joseph, M.J.E., Juliano, A.C., Kable, J.W., Kassinopoulos, M., Koba, C., Kong, X.-Z., Koscik, T.R., Kucukboyaci, N.E., Kuhl, B.A., Kupek, S., Laird, A.R., Lamm, C., Langner, R., Lauharatanahirun, N., Lee, H., Lee, S., Leemans, A., Leo, A., Lesage, E., Li, F., Li, M.Y.C., Lim, P.C., Lintz, E.N., Liphardt, S.W., Losecaat Vermeer, A.B., Love, B.C., Mack, M.L., Malpica, N., Marins, T., Maumet, C., McDonald, K., McGuire, J.T., Melero, H., Méndez Leal, A.S., Meyer, B., Meyer, K.N., Mihai, G., Mitsis, G.D., Moll, J., Nielson, D.M., Nilsonne, G., Notter, M.P., Olivetti, E., Onicas, A.I., Papale, P., Patil, K.R., Peelle, J.E., Pérez, A., Pischedda, D., Poline, J.-B., Prystauka, Y., Ray, S., Reuter-Lorenz, P.A., Reynolds, R.C., Ricciardi, E., Rieck, J.R., Rodriguez-Thompson, A.M., Romyn, A., Salo, T., Samanez-Larkin, G.R., Sanz-Morales, E., Schlichting, M.L., Schultz, D.H., Shen, Q., Sheridan, M.A., Silvers, J.A., Skagerlund, K., Smith, A., Smith, D.V., Sokol-Hessner, P., Steinkamp, S.R., Tashjian, S.M., Thirion, B., Thorp, J.N., Tinghög, G., Tisdall, L., Tompson, S.H., Toro-Serey, C., Torre Tresols, J.J., Tozzi, L., Truong, V., Turella, L., van 't Veer, A.E., Verguts, T., Vettel, J.M., Vijayarajah, S., Vo, K., Wall, M.B., Weeda, W.D., Weis, S., White, D.J., Wisniewski, D., Xifra-Porxas, A., Yearling, E.A., Yoon, S., Yuan, R., Yuen, K.S.L., Zhang, L., Zhang, X., Zosky, J.E., Nichols, T.E., Poldrack, R.A., Schonberg, T., 2020. Variability in the analysis of a single neuroimaging dataset by many teams. Nature doi:10.1038/s41586-020-2314-9.

Braga, R.M., Buckner, R.L., 2017. Parallel interdigitated distributed networks within the individual estimated by intrinsic functional connectivity. Neuron 95, 457–471. doi:10.1016/j.neuron.2017.06.038, e5.

Brennan, B.P., Wang, D., Li, M., Perriello, C., Ren, J., Elias, J.A., Van Kirk, N.P., Krompinger, J.W., Pope Jr., H.G., Haber, S.N., Rauch, S.L., Baker, J.T., Liu, H., 2019. Use of an individual-level approach to identify cortical connectivity biomarkers in obsessive-compulsive disorder. Biol. Psychiatry Cogn. Neurosci. Neuroimag. 4, 27–38. doi:10.1016/j.bpsc.2018.07.014.

Brodmann, K., 1908. Beiträge Zur Histologischen Lokalisation der Großhirnrinde.

Burgess, G.C., Kandala, S., Nolan, D., Laumann, T.O., Power, J.D., Adeyemo, B., Harms, M.P., Petersen, S.E., Barch, D.M., 2016. Evaluation of denoising strategies to address motion-correlated artifacts in resting-state functional magnetic resonance imaging data from the human connectome project. Brain Connect. 6, 669–680. doi:10.1089/brain.2016.0435.

Burt, J.B., Demirtaş, M., Eckner, W.J., Navejar, N.M., Ji, J.L., Martin, W.J., Bernacchia, A., Anticevic, A., Murray, J.D., 2018. Hierarchy of transcriptomic specialization across human cortex captured by structural neuroimaging topography. Nat. Neurosci. 21, 1251–1259. doi:10.1038/s41593-018-0195-0.

Calhoun, V.D., Adali, T., Pearlson, G.D., Pekar, J.J., 2001. A method for making group inferences from functional MRI data using independent component analysis. Hum. Brain Mapp. 14, 140–151. doi:10.1002/hbm.1048.

Casey, B.J., Cannonier, T., Conley, M.I., Cohen, A.O., Barch, D.M., Heitzeg, M.M., Soules, M.E., Teslovich, T., Dellarco, D.V., Garavan, H., Orr, C.A., Wager, T.D., Banich, M.T., Speer, N.K., Sutherland, M.T., Riedel, M.C., Dick, A.S., Bjork, J.M., Thomas, K.M., Chaarani, B., Mejia, M.H., Hagler, D.J., Jr, Daniela, Cornejo, M., Sicat, C.S., Harms, M.P., Dosenbach, N.U.F., Rosenberg, M., Earl, E., Bartsch, H., Watts, R., Polimeni, J.R., Kuperman, J.M., Fair, D.A., Dale, A.M.ABCD Imaging Acquisition Workgroup, 2018. The Adolescent Brain Cognitive Development (ABCD) study: imaging acquisition across 21 sites. Dev. Cogn. Neurosci 32, 43–54. doi:10.1016/j.dcn.2018.03.001.

Catani, M., Thiebaut de Schotten, M., Slater, D., Dell'Acqua, F., 2013. Connectomic approaches before the connectome. Neuroimage 80, 2–13. doi:10.1016/j.neuroimage.2013.05.109.

Chandrasekaran, S., Bickel, S., Herrero, J.L., Kim, J.-W., Markowitz, N., Espinal, E., Bhagat, N.A., Ramdeo, R., Xu, J., Glasser, M.F., Bouton, C.E., Mehta, A.D., 2020. Evoking highly focal percepts in the fingertips through targeted stimulation of sulcal regions of the brain for sensory restoration. bioRxiv doi:10.1101/2020.11.06.20217372.

Ciric, R., Wolf, D.H., Power, J.D., Roalf, D.R., Baum, G.L., Ruparel, K., Shinohara, R.T., Elliott, M.A., Eickhoff, S.B., Davatzikos, C., Gur, R.C., Gur, R.E., Bassett, D.S., Satterthwaite, T.D., 2017. Benchmarking of participant-level confound regression strategies for the control of motion artifact in studies of functional connectivity. Neuroimage 154, 174–187. doi:10.1016/j.neuroimage.2017.03.020.

Coalson, T.S., Van Essen, D.C., Glasser, M.F., 2018. The impact of traditional neuroimaging methods on the spatial localization of cortical areas. Proc. Natl. Acad. Sci. U. S. A. 115, E6356–E6365. doi:10.1073/pnas.1801582115.

Craddock, R.C., James, G.A., Holtzheimer 3rd, P.E., Hu, X.P., Mayberg, H.S., 2012. A whole brain fMRI atlas generated via spatially constrained spectral clustering. Hum. Brain Mapp. 33, 1914–1928. doi:10.1002/hbm.21333.

Dadi, K., Rahim, M., Abraham, A., Chyzhyk, D., Milham, M., Thirion, B., Varoquaux, G.Alzheimer's Disease Neuroimaging Initiative, 2019. Benchmarking functional connectome-based predictive models for resting-state fMRI. Neuroimage 192, 115–134. doi:10.1016/j.neuroimage.2019.02.062.

Dohmatob, E., Richard, H., Pinho, A.L., Thirion, B., 2021. Brain topography beyond parcellations: local gradients of functional maps. Neuroimage 229, 117706. doi:10.1016/j.neuroimage.2020.117706.

Duff, E.P., Makin, T., Cottaar, M., Smith, S.M., Woolrich, M.W., 2018. Disambiguating brain functional connectivity. Neuroimage 173, 540–550. doi:10.1016/j.neuroimage.2018.01.053.

Duncan, J., 2010. The multiple-demand (MD) system of the primate brain: mental programs for intelligent behaviour. Trends Cogn. Sci. 14, 172–179. doi:10.1016/j.tics.2010.01.004.

Eickhoff, S.B., Yeo, B.T.T., Genon, S., 2018. Imaging-based parcellations of the human brain. Nat. Rev. Neurosci. 19, 672–686. doi:10.1038/s41583-018-0071-7.

Feilong, M., Swaroop Guntupalli, J., Haxby, J.V., 2020. The neural basis of intelligence in fine-grained cortical topographies. Cold Spring Harbor Lab. doi:10.1101/2020.06.06.138099.

Finn, E.S., Shen, X., Scheinost, D., Rosenberg, M.D., Huang, J., Chun, M.M., Papademetris, X., Constable, R.T., 2015. Functional connectome fingerprinting: identifying individuals using patterns of brain connectivity. Nat. Neurosci. 18, 1664–1671. doi:10.1038/nn.4135.

Fornito, A., Arnatkevičiūtė, A., Fulcher, B.D., 2019. Bridging the gap between connectome and transcriptome. Trends Cogn. Sci. 23, 34–50. doi:10.1016/j.tics.2018.10.005.
Friston, K., 2009. Causal modelling and brain connectivity in functional magnetic resonance imaging. PLoS Biol. doi:10.1371/journal.pbio.1000033.
Glasser, M.F., Coalson, T.S., Bijsterbosch, J.D., Harrison, S.J., Harms, M.P., Anticevic, A., Van Essen, D.C., Smith, S.M., 2019. Classification of temporal ICA components for separating global noise from fMRI data: reply to Power. Neuroimage 197, 435–438. doi:10.1016/j.neuroimage.2019.04.046.
Glasser, M.F., Coalson, T.S., Bijsterbosch, J.D., Harrison, S.J., Harms, M.P., Anticevic, A., Van Essen, D.C., Smith, S.M., 2018. Using temporal ICA to selectively remove global noise while preserving global signal in functional MRI data. Neuroimage 181, 692–717. doi:10.1016/j.neuroimage.2018.04.076.
Glasser, M.F., Coalson, T.S., Robinson, E.C., Hacker, C.D., Harwell, J., Yacoub, E., Ugurbil, K., Andersson, J., Beckmann, C.F., Jenkinson, M., Smith, S.M., Van Essen, D.C., 2016a. A multi-modal parcellation of human cerebral cortex. Nature 536, 171–178. doi:10.1038/nature18933.
Glasser, M.F., Smith, S.M., Marcus, D.S., Andersson, J.L.R., Auerbach, E.J., Behrens, T.E.J., Coalson, T.S., Harms, M.P., Jenkinson, M., Moeller, S., Robinson, E.C., Sotiropoulos, S.N., Xu, J., Yacoub, E., Ugurbil, K., Van Essen, D.C., 2016b. The Human Connectome Project's neuroimaging approach. Nat. Neurosci. 19, 1175–1187. doi:10.1038/nn.4361.
Glasser, M.F., Sotiropoulos, S.N., Wilson, J.A., Coalson, T.S., Fischl, B., Andersson, J.L., Xu, J., Jbabdi, S., Webster, M., Polimeni, J.R., Van Essen, D.C., Jenkinson, M., Consortium, WU-Minn HCP, 2013. The minimal preprocessing pipelines for the Human Connectome Project. Neuroimage 80, 105–124. doi:10.1016/j.neuroimage.2013.04.127.
Gordon, E.M., Laumann, T.O., Adeyemo, B., Huckins, J.F., Kelley, W.M., Petersen, S.E., 2016. Generation and evaluation of a cortical area parcellation from resting-state correlations. Cereb. Cortex 26, 288–303. doi:10.1093/cercor/bhu239.
Gordon, E.M., Laumann, T.O., Gilmore, A.W., Newbold, D.J., Greene, D.J., Berg, J.J., Ortega, M., Hoyt-Drazen, C., Gratton, C., Sun, H., Hampton, J.M., Coalson, R.S., Nguyen, A.L., McDermott, K.B., Shimony, J.S., Snyder, A.Z., Schlaggar, B.L., Petersen, S.E., Nelson, S.M., Dosenbach, N.U.F., 2017. Precision functional mapping of individual human brains. Neuron 95, 791–807. doi:10.1016/j.neuron.2017.07.011, e7.
Griffanti, L., Salimi-Khorshidi, G., Beckmann, C.F., Auerbach, E.J., Douaud, G., Sexton, C.E., Zsoldos, E., Ebmeier, K.P., Filippini, N., Mackay, C.E., Moeller, S., Xu, J., Yacoub, E., Baselli, G., Ugurbil, K., Miller, K.L., Smith, S.M., 2014. ICA-based artefact removal and accelerated fMRI acquisition for improved resting state network imaging. Neuroimage 95, 232–247. doi:10.1016/j.neuroimage.2014.03.034.
Haak, K.V., Beckmann, C.F., 2020. Understanding brain organisation in the face of functional heterogeneity and functional multiplicity. Neuroimage 220, 117061. doi:10.1016/j.neuroimage.2020.117061.
Haak, K.V., Marquand, A.F., Beckmann, C.F., 2018. Connectopic mapping with resting-state fMRI. Neuroimage 170, 83–94. doi:10.1016/j.neuroimage.2017.06.075.
Hacker, C.D., Laumann, T.O., Szrama, N.P., Baldassarre, A., Snyder, A.Z., Leuthardt, E.C., Corbetta, M., 2013. Resting state network estimation in individual subjects. Neuroimage 82, 616–633. doi:10.1016/j.neuroimage.2013.05.108.
Harms, M.P., Somerville, L.H., Ances, B.M., Andersson, J., Barch, D.M., Bastiani, M., Bookheimer, S.Y., Brown, T.B., Buckner, R.L., Burgess, G.C., Coalson, T.S., Chappell, M.A., Dapretto, M., Douaud, G., Fischl, B., Glasser, M.F., Greve, D.N., Hodge, C., Jamison, K.W., Jbabdi, S., Kandala, S., Li, X., Mair, R.W., Mangia, S., Marcus, D., Mascali, D., Moeller, S., Nichols, T.E., Robinson, E.C., Salat, D.H., Smith, S.M., Sotiropoulos, S.N., Terpstra, M., Thomas, K.M., Tisdall, M.D., Ugurbil, K., van der Kouwe, A., Woods, R.P., Zöllei, L., Van Essen, D.C., Yacoub, E., 2018. Extending the human connectome project across ages: imaging protocols for the lifespan development and aging projects. Neuroimage 183, 972–984. doi:10.1016/j.neuroimage.2018.09.060.
Harrison, S.J., Bijsterboch, J.D., Segerdahl, A.R., Fitzgibbon, S.P., Farahibozorg, S.-.R., Duff, E.P., Smith, S.M., Woolrich, M.W., 2020. Modelling subject variability in the spatial and temporal characteristics of functional modes. Neuroimage 117226. doi:10.1016/j.neuroimage.2020.117226.
Harrison, S.J., Woolrich, M.W., Robinson, E.C., Glasser, M.F., Beckmann, C.F., Jenkinson, M., Smith, S.M., 2015. Large-scale probabilistic functional modes from resting state fMRI. Neuroimage 109, 217–231. doi:10.1016/j.neuroimage.2015.01.013.
Haxby, J.V., Guntupalli, J.S., Nastase, S.A., Feilong, M., 2020. Hyperalignment: modeling shared information encoded in idiosyncratic cortical topographies. Elife 9. doi:10.7554/eLife.56601.
Hayashi, T., Hou, Y., Glasser, M.F., Autio, J.A., Knoblauch, K., Inoue-Murayama, M., Coalson, T., Yacoub, E., Smith, S., Kennedy, H., Van Essen, D.C., 2021. The non-human primate neuroimaging and neuroanatomy project. Neuroimage 229, 117726. doi:10.1016/j.neuroimage.2021.117726.
Honey, C.J., Sporns, O., Cammoun, L., Gigandet, X., Thiran, J.P., Meuli, R., Hagmann, P., 2009. Predicting human resting-state functional connectivity from structural connectivity. Proc. Natl. Acad. Sci. U. S. A. 106, 2035–2040. doi:10.1073/pnas.0811168106.
Hong, S.-J., Vos de Wael, R., Bethlehem, R.A.I., Lariviere, S., Paquola, C., Valk, S.L., Milham, M.P., Di Martino, A., Margulies, D.S., Smallwood, J., Bernhardt, B.C., 2019. Atypical functional connectome hierarchy in autism. Nat. Commun. 10, 1022. doi:10.1038/s41467-019-08944-1.
Hong, S.-J., Xu, T., Nikolaidis, A., Smallwood, J., Margulies, D.S., Bernhardt, B., Vogelstein, J., Milham, M.P., 2020. Toward a connectivity gradient-based framework for reproducible biomarker discovery. Neuroimage 223, 117322. doi:10.1016/j.neuroimage.2020.117322.
Huntenburg, J.M., Bazin, P.-.L., Margulies, D.S., 2018. Large-scale gradients in human cortical organization. Trends Cogn. Sci. 22, 21–31. doi:10.1016/j.tics.2017.11.002.
Huth, A.G., de Heer, W.A., Griffiths, T.L., Theunissen, F.E., Gallant, J.L., 2016. Natural speech reveals the semantic maps that tile human cerebral cortex. Nature 532, 453–458. doi:10.1038/nature17637.
Ioannidis, J.P.A., 2017. Acknowledging and overcoming nonreproducibility in basic and preclinical research. JAMA 317, 1019–1020. doi:10.1001/jama.2017.0549.
Kashyap, R., Kong, R., Bhattacharjee, S., Li, J., Zhou, J., Thomas Yeo, B.T., 2019. Individual-specific fMRI-Subspaces improve functional connectivity prediction of behavior. Neuroimage 189, 804–812. doi:10.1016/j.neuroimage.2019.01.069.
Kong, R., Li, J., Orban, C., Sabuncu, M.R., Liu, H., Schaefer, A., Sun, N., Zuo, X.-.N., Holmes, A.J., Eickhoff, S.B., Yeo, B.T.T., 2019. Spatial topography of individual-specific cortical networks predicts human cognition, personality, and emotion. Cereb. Cortex 29, 2533–2551. doi:10.1093/cercor/bhy123.
Laumann, T.O., Gordon, E.M., Adeyemo, B., Snyder, A.Z., Joo, S.J., Chen, M.-.Y., Gilmore, A.W., McDermott, K.B., Nelson, S.M., Dosenbach, N.U.F., Schlaggar, B.L., Mumford, J.A., Poldrack, R.A., Petersen, S.E., 2015. Functional system and areal organization of a highly sampled individual human brain. Neuron 87, 657–670. doi:10.1016/j.neuron.2015.06.037.
Lebois, L.A.M., Li, M., Baker, J.T., Wolff, J.D., Wang, D., Lambros, A.M., Grinspoon, E., Winternitz, S., Ren, J., Gönenç, A., Gruber, S.A., Ressler, K.J., Liu, H., Kaufman, M.L., 2021. Large-scale functional brain network architecture changes associated with trauma-related dissociation. Am. J. Psychiatry 178, 165–173. doi:10.1176/appi.ajp.2020.19060647.
Li, M., Wang, D., Ren, J., Langs, G., Stoecklein, S., Brennan, B.P., Lu, J., Chen, H., Liu, H., 2019. Performing group-level functional image analyses based on homologous functional regions mapped in individuals. PLoS Biol. 17, e2007032. doi:10.1371/journal.pbio.2007032.
Lindquist, M., 2021. The Role of Statistics in Large Complex Neuroimaging Studies.
Marek, S., Tervo-Clemmens, B., Calabro, F.J., Montez, D.F., Kay, B.P., Hatoum, A.S., Donohue, M.R., Foran, W., Miller, R.L., Feczko, E., Miranda-Dominguez, O., Graham, A.M., Earl, E.A., Perrone, A.J., Cordova, M., Doyle, O., Moore, L.A., Conan, G., Uriarte, J., Snider, K., Tam, A., Chen, J., Newbold, D.J., Zheng, A., Seider, N.A., Van, A.N., Laumann, T.O., Thompson, W.K., Greene, D.J., Petersen, S.E., Nichols, T.E., Thomas Yeo, B.T., Barch, D.M., Garavan, H., Luna, B., Fair, D.A., Dosenbach, N.U.F., 2020. Towards Reproducible Brain-Wide Association Studies (p. 2020.08.21.257758). https://doi.org/10.1101/2020.08.21.257758
Margulies, D.S., Ghosh, S.S., Goulas, A., Falkiewicz, M., Huntenburg, J.M., Langs, G., Bezgin, G., Eickhoff, S.B., Castellanos, F.X., Petrides, M., Jefferies, E., Smallwood, J., 2016. Situating the default-mode network along a principal gradient of macroscale cortical organization. Proc. Natl. Acad. Sci. U. S. A. 113, 12574–12579. doi:10.1073/pnas.1608282113.
Marquand, A.F., Haak, K.V., Beckmann, C.F., 2017. Functional corticostriatal connection topographies predict goal directed behaviour in humans. Nat. Hum. Behav. 1, 0146. doi:10.1038/s41562-017-0146.
Mesulam, M.M., 1998. From sensation to cognition. Brain 121 (Pt 6), 1013–1052. doi:10.1093/brain/121.6.1013.
Mesulam, M.-.M., Mufson, E.J., 1985. Association and Auditory Cortices. In: Peters, A., Jones, E.G. (Eds.), The Insula of Reil in Man and Monkey. Springer US, Boston, MA, pp. 179–226. doi:10.1007/978-1-4757-9619-3_5.
Miller, K.L., Alfaro-Almagro, F., Bangerter, N.K., Thomas, D.L., Yacoub, E., Xu, J., Bartsch, A.J., Jbabdi, S., Sotiropoulos, S.N., Andersson, J.L.R., Griffanti, L., Douaud, G., Okell, T.W., Weale, P., Dragonu, I., Garratt, S., Hudson, S., Collins, R., Jenkinson, M., Matthews, P.M., Smith, S.M., 2016. Multimodal population brain imaging in the UK Biobank prospective epidemiological study. Nat. Neurosci. 19, 1523–1536. doi:10.1038/nn.4393.
Montez, D.F., Van, A.N., Miller, R.L., Seider, N.A., Marek, S., Zheng, A., Newbold, D.J., Scheidter, K., Feczko, E., Perrone, A.J., Miranda-Dominguez, O., Earl, E.A., Kay, B.P., Jha, A.K., Sotiras, A., Laumann, T.O., Greene, D.J., Gordon, E.M., Dylan Tisdall, M., Van Der Kouwe, A., Fair, D.A., Dosenbach, N.U.F., 2021. Using synthetic MR images for field map-less distortion correction. bioRxiv doi:10.1101/2021.03.13.435270.
Mueller, S., Wang, D., Fox, M.D., Pan, R., Lu, J., Li, K., Sun, W., Buckner, R.L., Liu, H., 2015. Reliability correction for functional connectivity: theory and implementation. Hum. Brain Mapp. 36, 4664–4680. doi:10.1002/hbm.22947.
Mueller, S., Wang, D., Fox, M.D., Yeo, B.T.T., Sepulcre, J., Sabuncu, M.R., Shafee, R., Lu, J., Liu, H., 2013. Individual variability in functional connectivity architecture of the human brain. Neuron 77, 586–595. doi:10.1016/j.neuron.2012.12.028.
Mumford, J.A., Ramsey, J.D., 2014. Bayesian networks for fMRI: a primer. Neuroimage 86, 573–582. doi:10.1016/j.neuroimage.2013.10.020.
Murphy, A.C., Bertolero, M.A., Papadopoulos, L., Lydon-Staley, D.M., Bassett, D.S., 2020. Multimodal network dynamics underpinning working memory. Nat. Commun. 11, 3035. doi:10.1038/s41467-020-15541-0.
Murphy, K., Birn, R.M., Handwerker, D.A., Jones, T.B., Bandettini, P.A., 2009. The impact of global signal regression on resting state correlations: are anti-correlated networks introduced? Neuroimage 44, 893–905. doi:10.1016/j.neuroimage.2008.09.036.
Nickerson, L.D., Smith, S.M., Öngür, D., Beckmann, C.F., 2017. Using dual regression to investigate network shape and amplitude in functional connectivity analyses. Front. Neurosci. 11, 115. doi:10.3389/fnins.2017.00115.
Nieuwenhuys, R., 2013. The myeloarchitectonic studies on the human cerebral cortex of the Vogt-Vogt school, and their significance for the interpretation of functional neuroimaging data. Brain Struct. Funct. 218, 303–352. doi:10.1007/s00429-012-0460-z.
Paquola, C., Vos De Wael, R., Wagstyl, K., Bethlehem, R.A.I., Hong, S.-J., Seidlitz, J., Bullmore, E.T., Evans, A.C., Misic, B., Margulies, D.S., Smallwood, J., Bernhardt, B.C., 2019. Microstructural and functional gradients are increasingly dissociated in transmodal cortices. PLoS Biol. 17, e3000284. doi:10.1371/journal.pbio.3000284.
Park, H.-.J., Friston, K.J., Pae, C., Park, B., Razi, A., 2018. Dynamic effective connectivity in resting state fMRI. Neuroimage 180, 594–608. doi:10.1016/j.neuroimage.2017.11.033.
Pervaiz, U., Vidaurre, D., Woolrich, M.W., Smith, S.M., 2020. Optimising network modelling methods for fMRI. NeuroImage 211, 116–604. doi:10.1016/j.neuroimage.2020.116604.

Poldrack, R.A., Baker, C.I., Durnez, J., Gorgolewski, K.J., Matthews, P.M., Munafò, M.R., Nichols, T.E., Poline, J.-.B., Vul, E., Yarkoni, T., 2017. Scanning the horizon: towards transparent and reproducible neuroimaging research. Nat. Rev. Neurosci. 18, 115–126. doi:10.1038/nrn.2016.167.

Power, J.D., 2017. A simple but useful way to assess fMRI scan qualities. Neuroimage 154, 150–158. doi:10.1016/j.neuroimage.2016.08.009.

Power, J.D., Barnes, K.A., Snyder, A.Z., Schlaggar, B.L., Petersen, S.E., 2012. Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. Neuroimage 59, 2142–2154. doi:10.1016/j.neuroimage.2011.10.018.

Power, J.D., Cohen, A.L., Nelson, S.M., Wig, G.S., Barnes, K.A., Church, J.A., Vogel, A.C., Laumann, T.O., Miezin, F.M., Schlaggar, B.L., Petersen, S.E., 2011. Functional network organization of the human brain. Neuron 72, 665–678. doi:10.1016/j.neuron.2011.09.006.

Power, J.D., Lynch, C.J., Adeyemo, B., Petersen, S.E., 2020. A critical, event-related appraisal of denoising in resting-state fMRI studies. Cereb. Cortex. doi:10.1093/cercor/bhaa139.

Power, J.D., Mitra, A., Laumann, T.O., Snyder, A.Z., Schlaggar, B.L., Petersen, S.E., 2014. Methods to detect, characterize, and remove motion artifact in resting state fMRI. Neuroimage 84, 320–341. doi:10.1016/j.neuroimage.2013.08.048.

Power, J.D., Plitt, M., Gotts, S.J., Kundu, P., Voon, V., Bandettini, P.A., Martin, A., 2018. Ridding fMRI data of motion-related influences: removal of signals with distinct spatial and physical bases in multiecho data. Proc. Natl. Acad. Sci. U. S. A. 115, E2105–E2114. doi:10.1073/pnas.1720985115.

Power, J.D., Plitt, M., Laumann, T.O., Martin, A., 2017. Sources and implications of whole-brain fMRI signals in humans. Neuroimage 146, 609–625. doi:10.1016/j.neuroimage.2016.09.038.

Power, J.D., Schlaggar, B.L., Petersen, S.E., 2015. Recent progress and outstanding issues in motion correction in resting state fMRI. Neuroimage 105, 536–551. doi:10.1016/j.neuroimage.2014.10.044.

Power, J.D., Silver, B.M., Silverman, M.R., Ajodan, E.L., Bos, D.J., Jones, R.M., 2019. Customized head molds reduce motion during resting state fMRI scans. Neuroimage 189, 141–149. doi:10.1016/j.neuroimage.2019.01.016.

Raichle, M.E., MacLeod, A.M., Snyder, A.Z., Powers, W.J., Gusnard, D.A., Shulman, G.L., 2001. A default mode of brain function. Proc. Natl. Acad. Sci. U. S. A. 98, 676–682. doi:10.1073/pnas.98.2.676.

Reid, A.T., Headley, D.B., Mill, R.D., Sanchez-Romero, R., Uddin, L.Q., Marinazzo, D., Lurie, D.J., Valdés-Sosa, P.A., Hanson, S.J., Biswal, B.B., Calhoun, V., Poldrack, R.A., Cole, M.W., 2019. Advancing functional connectivity research from association to causation. Nat. Neurosci. doi:10.1038/s41593-019-0510-4.

Ren, J., Xu, T., Wang, D., Li, M., Lin, Y., Schoeppe, F., Ramirez, J.S.B., Han, Y., Luan, G., Li, L., Liu, H., Ahveninen, J., 2020. Individual variability in functional organization of the human and monkey auditory cortex. Cereb. Cortex. doi:10.1093/cercor/bhaa366.

Robinson, E.C., Garcia, K., Glasser, M.F., Chen, Z., Coalson, T.S., Makropoulos, A., Bozek, J., Wright, R., Schuh, A., Webster, M., Hutter, J., Price, A., Cordero Grande, L., Hughes, E., Tusor, N., Bayly, P.V., Van Essen, D.C., Smith, S.M., Edwards, A.D., Hajnal, J., Jenkinson, M., Glocker, B., Rueckert, D., 2018. Multimodal surface matching with higher-order smoothness constraints. Neuroimage 167, 453–465. doi:10.1016/j.neuroimage.2017.10.037.

Robinson, E.C., Jbabdi, S., Glasser, M.F., Andersson, J., Burgess, G.C., Harms, M.P., Smith, S.M., Van Essen, D.C., Jenkinson, M., 2014. MSM: a new flexible framework for multimodal surface matching. Neuroimage 100, 414–426. doi:10.1016/j.neuroimage.2014.05.069.

Salimi-Khorshidi, G., Douaud, G., Beckmann, C.F., Glasser, M.F., Griffanti, L., Smith, S.M., 2014. Automatic denoising of functional MRI data: combining independent component analysis and hierarchical fusion of classifiers. Neuroimage 90, 449–468. doi:10.1016/j.neuroimage.2013.11.046.

Satterthwaite, T.D., Wolf, D.H., Loughead, J., Ruparel, K., Elliott, M.A., Hakonarson, H., Gur, R.C., Gur, R.E., 2012. Impact of in-scanner head motion on multiple measures of functional connectivity: relevance for studies of neurodevelopment in youth. Neuroimage 60, 623–632. doi:10.1016/j.neuroimage.2011.12.063.

Schaefer, A., Kong, R., Gordon, E.M., Laumann, T.O., Zuo, X.-.N., Holmes, A.J., Eickhoff, S.B., Yeo, B.T.T., 2018. Local-global parcellation of the human cerebral cortex from intrinsic functional connectivity MRI. Cereb. Cortex 28, 3095–3114. doi:10.1093/cercor/bhx179.

Sereno, M.I., Dale, A.M., Reppas, J.B., Kwong, K.K., Belliveau, J.W., Brady, T.J., Rosen, B.R., Tootell, R.B., 1995. Borders of multiple visual areas in humans revealed by functional magnetic resonance imaging. Science 268, 889–893. doi:10.1126/science.7754376.

Shen, L., Jiang, C., Hubbard, C.S., Ren, J., He, C., Wang, D., Dahmani, L., Guo, Y., Liu, Y., Xu, S., Meng, F., Zhang, J., Liu, H., Li, L., 2020. Subthalamic nucleus deep brain stimulation modulates 2 distinct neurocircuits. Ann. Neurol. 88, 1178–1193. doi:10.1002/ana.25906.

Shen, X., Tokoglu, F., Papademetris, X., Constable, R.T., 2013. Groupwise whole-brain parcellation from resting-state fMRI data for network node identification. Neuroimage 82, 403–415. doi:10.1016/j.neuroimage.2013.05.081.

Shine, J.M., Breakspear, M., Bell, P.T., Ehgoetz Martens, K.A., Shine, R., Koyejo, O., Sporns, O., Poldrack, R.A., 2019. Human cognition involves the dynamic integration of neural activity and neuromodulatory systems. Nat. Neurosci. 22, 289–296. doi:10.1038/s41593-018-0312-0.

Siegel, J.S., Mitra, A., Laumann, T.O., Seitzman, B.A., Raichle, M., Corbetta, M., Snyder, A.Z., 2017. Data quality influences observed links between functional connectivity and behavior. Cereb. Cortex 27, 4492–4502. doi:10.1093/cercor/bhw253.

Smith, S.M., 2013. Introduction to the NeuroImage special issue "Mapping the connectome. Neuroimage 80, 1.

Smith, S.M., Fox, P.T., Miller, K.L., Glahn, D.C., Fox, P.M., Mackay, C.E., Filippini, N., Watkins, K.E., Toro, R., Laird, A.R., Beckmann, C.F., 2009. Correspondence of the brain's functional architecture during activation and rest. Proc. Natl. Acad. Sci. U. S. A. 106, 13040–13045. doi:10.1073/pnas.0905267106.

Smith, S.M., Miller, K.L., Salimi-Khorshidi, G., Webster, M., Beckmann, C.F., Nichols, T.E., Ramsey, J.D., Woolrich, M.W., 2011. Network modelling methods for FMRI. Neuroimage 54, 875–891. doi:10.1016/j.neuroimage.2010.08.063.

Smith, S.M., Nichols, T.E., 2018. Statistical challenges in "Big data" human neuroimaging. Neuron 97, 263–268. doi:10.1016/j.neuron.2017.12.018.

Smith, S.M., Nichols, T.E., Vidaurre, D., Winkler, A.M., Behrens, T.E.J., Glasser, M.F., Ugurbil, K., Barch, D.M., Van Essen, D.C., Miller, K.L., 2015. A positive-negative mode of population covariation links brain connectivity, demographics and behavior. Nat. Neurosci. 18, 1565–1567. doi:10.1038/nn.4125.

Smith, S.M., Vidaurre, D., Beckmann, C.F., Glasser, M.F., Jenkinson, M., Miller, K.L., Nichols, T.E., Robinson, E.C., Salimi-Khorshidi, G., Woolrich, M.W., Barch, D.M., Uğurbil, K., Van Essen, D.C., 2013. Functional connectomics from resting-state fMRI. Trends Cogn. Sci. 17, 666–682. doi:10.1016/j.tics.2013.09.016.

Snyder, A.Z., Raichle, M.E., 2012. A brief history of the resting state: the Washington University perspective. Neuroimage 62, 902–910. doi:10.1016/j.neuroimage.2012.01.044.

Spreng, R.N., Stevens, W.D., Chamberlain, J.P., Gilmore, A.W., Schacter, D.L., 2010. Default network activity, coupled with the frontoparietal control network, supports goal-directed cognition. Neuroimage 53, 303–317. doi:10.1016/j.neuroimage.2010.06.016.

Stoecklein, S., Hilgendorff, A., Li, M., Förster, K., Flemmer, A.W., Galiè, F., Wunderlich, S., Wang, D., Stein, S., Ehrhardt, H., Dietrich, O., Zou, Q., Zhou, S., Ertl-Wagner, B., Liu, H., 2020. Variable functional connectivity architecture of the preterm human brain: impact of developmental cortical expansion and maturation. Proc. Natl. Acad. Sci. U. S. A. 117, 1201–1206. doi:10.1073/pnas.1907892117.

Tavor, I., Parker Jones, O., Mars, R.B., Smith, S.M., Behrens, T.E., Jbabdi, S., 2016. Task-free MRI predicts individual differences in brain activity during task performance. Science 352, 216–220. doi:10.1126/science.aad8127.

Tozzi, L., Staveland, B., Holt-Gosselin, B., Chesnut, M., Chang, S.E., Choi, D., Shiner, M., Wu, H., Lerma-Usabiaga, G., Sporns, O., Barch, D.M., Gotlib, I.H., Hastie, T.J., Kerr, A.B., Poldrack, R.A., Wandell, B.A., Wintermark, M., Williams, L.M., 2020. The human connectome project for disordered emotional states: protocol and rationale for a research domain criteria study of brain connectivity in young adult anxiety and depression. Neuroimage 214, 116715. doi:10.1016/j.neuroimage.2020.116715.

Triarhou, L.C., 2007. The Economo-Koskinas atlas revisited: cytoarchitectonics and functional context. Stereotact. Funct. Neurosurg. 85, 195–203. doi:10.1159/000103258.

Uddin, L.Q., Yeo, B.T.T., Spreng, R.N., 2019. Towards a universal taxonomy of macro-scale functional human brain networks. Brain Topogr. doi:10.1007/s10548-019-00744-6.

Valk, S.L., Xu, T., Margulies, D.S., Masouleh, S.K., Paquola, C., Goulas, A., Kochunov, P., Smallwood, J., Thomas Yeo, B.T., Bernhardt, B.C., Eickhoff, S.B., 2020. Shaping brain structure: genetic and phylogenetic axes of macro scale organization of cortical thickness. bioRxiv doi:10.1101/2020.02.10.939561.

van den Heuvel, M.P., Sporns, O., 2019. A cross-disorder connectome landscape of brain dysconnectivity. Nat. Rev. Neurosci. 20, 435–446. doi:10.1038/s41583-019-0177-6.

van der Meer, D., Frei, O., Kaufmann, T., Chen, C.-.H., Thompson, W.K., O'Connell, K.S., Monereo Sánchez, J., Linden, D.E.J., Westlye, L.T., Dale, A.M., Andreassen, O.A., 2020. Quantifying the polygenic architecture of the human cerebral cortex: extensive genetic overlap between cortical thickness and surface area. Cereb. Cortex 30, 5597–5603. doi:10.1093/cercor/bhaa146.

Van Essen, D.C., Dierker, D.L., 2007. Surface-based and probabilistic atlases of primate cerebral cortex. Neuron 56, 209–225. doi:10.1016/j.neuron.2007.10.015.

Van Essen, D.C., Glasser, M.F., 2018. Parcellating cerebral cortex: how invasive animal studies inform noninvasive mapmaking in humans. Neuron 99, 640–663. doi:10.1016/j.neuron.2018.07.002.

Van Essen, D.C., Smith, S.M., Barch, D.M., Behrens, T.E.J., Yacoub, E., Ugurbil, K., Consortium, WU-Minn HCP, 2013. The WU-minn human connectome project: an overview. Neuroimage 80, 62–79. doi:10.1016/j.neuroimage.2013.05.041.

Vidaurre, D., Hunt, L.T., Quinn, A.J., Hunt, B.A.E., Brookes, M.J., Nobre, A.C., Woolrich, M.W., 2018. Spontaneous cortical activity transiently organises into frequency specific phase-coupling networks. Nat. Commun. 9, 2987. doi:10.1038/s41467-018-05316-z.

Vogel, J.W., La Joie, R., Grothe, M.J., Diaz-Papkovich, A., Doyle, A., Vachon-Presseau, E., Lepage, C., Vos de Wael, R., Thomas, R.A., Iturria-Medina, Y., Bernhardt, B., Rabinovici, G.D., Evans, A.C., 2020. A molecular gradient along the longitudinal axis of the human hippocampus informs large-scale behavioral systems. Nat. Commun. 11, 960. doi:10.1038/s41467-020-14518-3.

Vogt, O., Vogt, C., 1903. Zur anatomischen gliederung des cortex cerebri. J. Psychol. Neurol. 2, 160–180.

Von Bonin, G., Bailey, P., 1947. The neocortex of Macaca mulatta. (Illinois Monogr. Med. Sci. 5 (5), 163 No. 4.

Vos de Wael, R., Larivière, S., Caldairou, B., Hong, S.-.J., Margulies, D.S., Jefferies, E., Bernasconi, A., Smallwood, J., Bernasconi, N., Bernhardt, B.C., 2018. Anatomical and microstructural determinants of hippocampal subfield functional connectome embedding. Proc. Natl. Acad. Sci. U. S. A. 115, 10154–10159. doi:10.1073/pnas.1803667115.

Wang, D., Buckner, R.L., Fox, M.D., Holt, D.J., Holmes, A.J., Stoecklein, S., Langs, G., Pan, R., Qian, T., Li, K., Baker, J.T., Stufflebeam, S.M., Wang, K., Wang, X., Hong, B., Liu, H., 2015. Parcellating cortical functional networks in individuals. Nat. Neurosci. 18, 1853–1860. doi:10.1038/nn.4164.

Wang, D., Li, M., Wang, M., Schoeppe, F., Ren, J., Chen, H., Öngür, D., Brady Jr, R.O., Baker, J.T., Liu, H., 2020a. Individual-specific functional connectivity markers track dimensional and categorical features of psychotic illness. Mol. Psychiatry 25, 2119–2129. doi:10.1038/s41380-018-0276-1.

Wang, D., Tian, Y., Li, M., Dahmani, L., Wei, Q., Bai, T., Galiè, F., Ren, J., Farooq, R.K., Wang, K., Lu, J., Wang, K., Liu, H., 2020b. Functional connectivity underpinnings of electroconvulsive therapy-induced memory impairments in patients with depression. Neuropsychopharmacology 45, 1579–1587. doi:10.1038/s41386-020-0711-2.

Xu, T., Nenning, K.-H., Schwartz, E., Hong, S.-J., Vogelstein, J.T., Goulas, A., Fair, D.A., Schroeder, C.E., Margulies, D.S., Smallwood, J., Milham, M.P., Langs, G., 2020. Cross-species functional alignment reveals evolutionary hierarchy within the connectome. Neuroimage 223, 117346. doi:10.1016/j.neuroimage.2020.117346.

Yeo, B.T.T., Krienen, F.M., Sepulcre, J., Sabuncu, M.R., Lashkari, D., Hollinshead, M., Roffman, J.L., Smoller, J.W., Zöllei, L., Polimeni, J.R., Fischl, B., Liu, H., Buckner, R.L., 2011. The organization of the human cerebral cortex estimated by intrinsic functional connectivity. J. Neurophysiol. 106, 1125–1165. doi:10.1152/jn.00338.2011.

Zilles, K., Amunts, K., 2010. Centenary of Brodmann's map \quotesinglbaseÄî conception and fate. Nat. Rev. Neurosci. 11, 139–145.