A Common Space Approach to Comparative Neuroscience

Rogier B. Mars,[1,2] Saad Jbabdi,[1,*]
and Matthew F.S. Rushworth[3,*]

[1]Wellcome Centre for Integrative Neuroimaging, Centre for fMRI of the Brain (FMRIB), Nuffield Department of Clinical Neurosciences, John Radcliffe Hospital, University of Oxford, Oxford OX3 9DU, United Kingdom; email: rogier.mars@ndcn.ox.ac.uk

[2]Donders Institute for Brain, Cognition and Behaviour, Radboud University Nijmegen, 6525 HR Nijmegen, The Netherlands

[3]Wellcome Centre for Integrative Neuroimaging, Department of Experimental Psychology, University of Oxford, Oxford OX2 6GG, United Kingdom

*These authors contributed equally to this article

Keywords

translational neuroscience, mouse, macaque, connectivity, anatomy, model species

Abstract

Comparative neuroscience is entering the era of big data. New high-throughput methods and data-sharing initiatives have resulted in the availability of large, digital data sets containing many types of data from ever more species. Here, we present a framework for exploiting the new possibilities offered. The multimodality of the data allows vertical translations, which are comparisons of different aspects of brain organization within a single species and across scales. Horizontal translations compare particular aspects of brain organization across species, often by building abstract feature spaces. Combining vertical and horizontal translations allows for more sophisticated comparisons, including relating principles of brain organization across species by contrasting horizontal translations, and for making formal predictions of unobtainable data based on observed results in a model species.

Contents

INTRODUCTION

Evolution provided comparative neuroscience with a compelling natural experiment in brain diversity. But understanding how the organization of the brain of one species is similar and how it is different to those of other species is challenging. It requires the integration and synthesis of data from disparate fields, often lacking common references and terminologies. Neuroscientific data are difficult to obtain from outside of one's field and often require specialized training to interpret. By necessity, many researchers therefore focus on a particular data type in a particular model species, leaving interpretation of the usefulness of their data to understanding other species, including the human, to their colleagues. This has led to numerous confusions in the literature about anatomical translatability (van Heukelum et al. 2020) and even about the terminology used to describe behavioral tasks (Laubach et al. 2018). Alarmingly, these confusions might contribute to the failure of some clinical trials in neuropsychiatry (Hay et al. 2014).
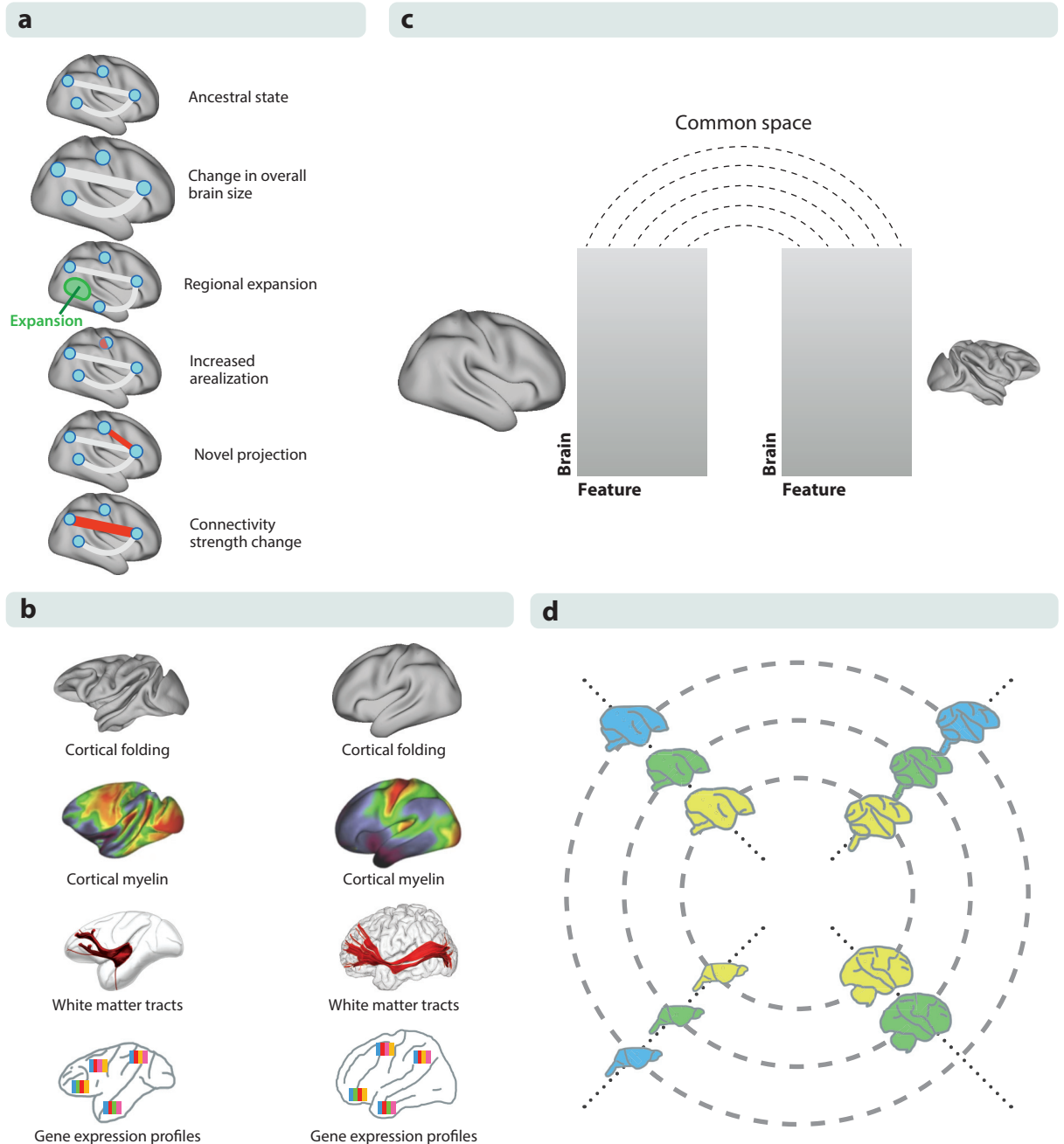
The emergence of various high-throughput methods for neuroscience has the potential to change this. Where previously various types of data were only available for parts of the brain, in a few species, and only to a few labs, high-quality data of various species' entire brains are now acquired and, crucially, made available to the community in a digital format. Multimodal high-quality human neuroimaging databases, including those of the Human Connectome Project (Van Essen et al. 2013) and UK Biobank Imaging (Miller et al. 2016), have set new standards for data availability. Now, for comparative neuroscience, MRI databases of nonhuman data are increasingly available thanks to initiatives such as the PRIMatE Data Exchange (Milham et al. 2018) and multicenter mouse MRI projects (Grandjean et al. 2020). Outside MRI data, transcriptomic databases from various species are becoming increasingly available (Keil et al. 2018), including the well-established Allen Institute databases for the human and mouse (Hawrylycz et al. 2012, Lein et al. 2007).

Comparing such data obtained from different species comes with challenges. A number of recent studies have focused on the issues of standardizing analysis pipelines and quality control, including comparisons of signal-to-noise ratios (Mandino et al. 2019, Milham et al. 2020, Xu et al. 2019). However, what has been largely absent is a framework to address the next stage in the analysis: the comparison of brain organization across scales and species. To make sense of brain differences, we need to be able to understand the data in the context of a shared frame of reference. Here, we synthesize the approaches presented in the literature into a coherent framework that allows just that.

THE COMMON SPACE APPROACH IN BRIEF

Brains can differ in many respects, including global or local size, the number and size of cortical fields, the connections between brain areas, and the cortical folding pattern (Krubitzer & Kaas

2005, Mars et al. 2018a) (**Figure 1***a*). These features interact. For instance, a change in size of the cortical sheet is often accompanied by an increase in the number of areas, which in turn can be accompanied by changes in areal connections. In fact, in anthropoid primates, brain diversity may be better characterized by brain reorganization than by changes in relative brain size (Smaers &

a

Ancestral state

Change in overall brain size

Regional expansion

Expansion

Increased arealization

Novel projection

Connectivity strength change

b

Cortical folding

Cortical myelin

White matter tracts

Gene expression profiles

Cortical folding

Cortical myelin

White matter tracts

Gene expression profiles

c

Common space

Brain

Feature

Brain

Feature

d

(Caption appears on following page)

The common space approach. (*a*) Brains can differ in many respects. Blue spheres indicate cortical regions, and gray lines represent connections. Brain changes compared to an ancestral or reference state (*top*) can include overall and local expansion, increased arealization, and changes in connectivity. (*b*) Many data types are now readily available across species, allowing vertical translations within species (columns) and horizontal translations across species (rows). Myelin map images adapted from Eichert et al. (2020); white matter tract images adapted from Thiebaut de Schotten et al. (2012) with permission from Elsevier. (*c*) By describing the brain in terms of a particular feature that has clearly defined homologs between species, it is possible to compare the brains in the same common space. (*d*) This framework can be generalized across multiple species and levels or data types (indicated by the different colors), even when not all data types are available in all species. For example, when we compare the human brain (*bottom right*) with the brains of other species, we might be able to compare data from some modalities directly (for example, resting state–based estimates of connectivity and diffusion-weighted imaging–based estimates of connectivity symbolized by *yellow* and *green* colors), but other data modalities, such as tract-tracing data (*blue*), might not be available for the human brain.

Soligo 2013). Any framework for comparative neuroscience has to be able to account for these considerations. We propose a common space approach that satisfies these requirements and can point the way to future advances. The proposed framework relies on three ingredients.

To visualize the issues the framework has to address, let us imagine we want to compare brain organization between two brains (**Figure 1b**). Identifying how the various aspects of brain organization that can differ between these brains manifest requires multiple types of information. Thus, rather than focusing on data of one particular modality in great detail, as was done by many of the great anatomists of the early twentieth century, the challenge for modern comparative neuroscience is to integrate information from multiple sources. This gives rise to the first ingredient, that of multimodality of the data.

The next question is at which scale the comparison should be made. By necessity, many large comparative neuroscience studies were previously done at the scale of whole brains or large sections of the brain. Although this practice has led to very fruitful insights (Barton 2007, Dunbar & Shultz 2007, Jerison 1973), it has also led to great controversies due to differences in regional definitions (Barton & Venditti 2013, Passingham & Smaers 2014). Moreover, local effects may be better reflections of the types of changes we outlined above. Thus, the second ingredient is local data, which are ideally of subregional resolution.

The final challenge is to provide a meaningful way to compare such local and multimodal information. This is particularly important when the brains under study are of vastly different size and morphology. Given that changes at one level, such as a local expansion of brain size, can have dramatic effects at other levels, such as the location of brain areas, it is essential to find a way in which similar features can be meaningfully compared across species. In other words, we need to ensure that we compare like with like. One way to solve this problem is to describe the local organization of brains in terms of an abstract feature space, rather than using physical x, y, and z coordinates. For instance, we previously showed that peak activations during functional tasks have seemingly arbitrary spatial arrangements in physical space but cluster together meaningfully when described in a space that encodes the similarity in their connectivity (Mars et al. 2018b). The connections, rather than spatial dimensions, form a common space in which activation peaks can be meaningfully compared (**Figure 1c**). The third ingredient is thus that of feature-based comparisons in a common space.

Armed with these three ingredients—multimodal, local, and feature-based—we can now address the question of how brains differ. First, using the multimodal data at each locality of the brain, one can investigate how the different aspects of brain organization relate to one another within a given species. We term this process vertical translation (i.e., comparing brains column-wise in **Figure 1b**). Second, one can investigate how a given modality differs between the species by using an abstraction into features of interest that allows meaningful comparisons. We term this

process horizontal translation (i.e., comparing row-wise in **Figure 1*b***). Finally, one can investigate how the relationship between different modalities differs between species by combining insights from both translations.

Figure 1*d* shows the generalized framework in four example species for which various types of data are available (or, in some cases, missing). Vertical translation within a species follows the dotted lines, and horizontal translation across species follows the dashed lines. One can compare species according to increasing phylogenetic distance by following the dashed lines from the human to the macaque, marmoset, and mouse brain, or make more direct comparisons, such as a translation from the mouse directly to the human. In what follows, we illustrate cases of these possible translations and discuss how thinking about comparisons within this framework provides structure and helps inspire novel questions.

VERTICAL TRANSLATION

One of the central tenets of neuroscience is that the brain is hierarchically organized: Cells form areas that form networks, which perform computations that produce behavior (Churchland & Sejnowski 1992, Mars 1987). Current high-throughput methods allow whole-brain measurements that span across all these scales (Lerch et al. 2017). Thus, vertical translation means not only integrating across different sources of information but also integrating across different scales. The traditional approach is to compare such measurements within specific parts of the brain. Early work looking at subdividing the brain into multiple functional areas mainly focused on cytoarchitectonic features. Differences in cytoarchitecture between adjacent cortical fields was taken to be an indication of a change in function. Later, these changes in cytoarchitecture were found to coincide with changes in the density of certain receptor types (Geyer et al. 1998) and changes in extrinsic connections (Passingham et al. 2002). More recently, multimodal MRI combining microstructure and functional measures allowed for the definition of areal borders in vivo and in individual brains (Glasser et al. 2016).

Alternative approaches to comparing features of areas within a given species have emerged in recent years. Importantly, the advantage of whole-brain data for these different modalities is that they allow us to move beyond lining up areal borders to investigate principles of organization across different levels. An impressive example of this is provided by Burt et al. (2018), who investigated whether the hierarchical organization of cortical areas, which was originally proposed based on laminar patterns of interareal connectivity (Barbas & Rempel-Clower 1997), is reflected at multiple levels of brain organization. As a proxy for anatomical hierarchy, they used an MRI-derived T1w/T2w map of the human cerebral cortex. This map is thought to reflect regional variation in gray matter myelin content, with high values in primary sensory areas and low values in association cortex (Glasser & Van Essen 2011). They then compared the T1w/T2w map to spatial maps reflecting the expression of layer-specific genes, showing a positive correlation of cortical hierarchy with supra- and infragranular layer genes and a negative correlation with granular layer 4 genes (**Figure 2*a***). Hierarchical gradients in gene expression were also reported for genes coding for specific neural cell types. Moreover, the authors found that the T1w/T2w map topography corresponds strongly with the first principal component of spatial gene expression profiles.

The study by Burt et al. (2018) demonstrates the use of the ingredients of the comparative approach that we outlined in the previous section. Using data from different high-throughput methods with high spatial resolution, in this case aggregating data from multiple subjects to create a group map, allowed them to compare the results from different modalities in a common space. As the brain under consideration is the same at each level, this common space can be a
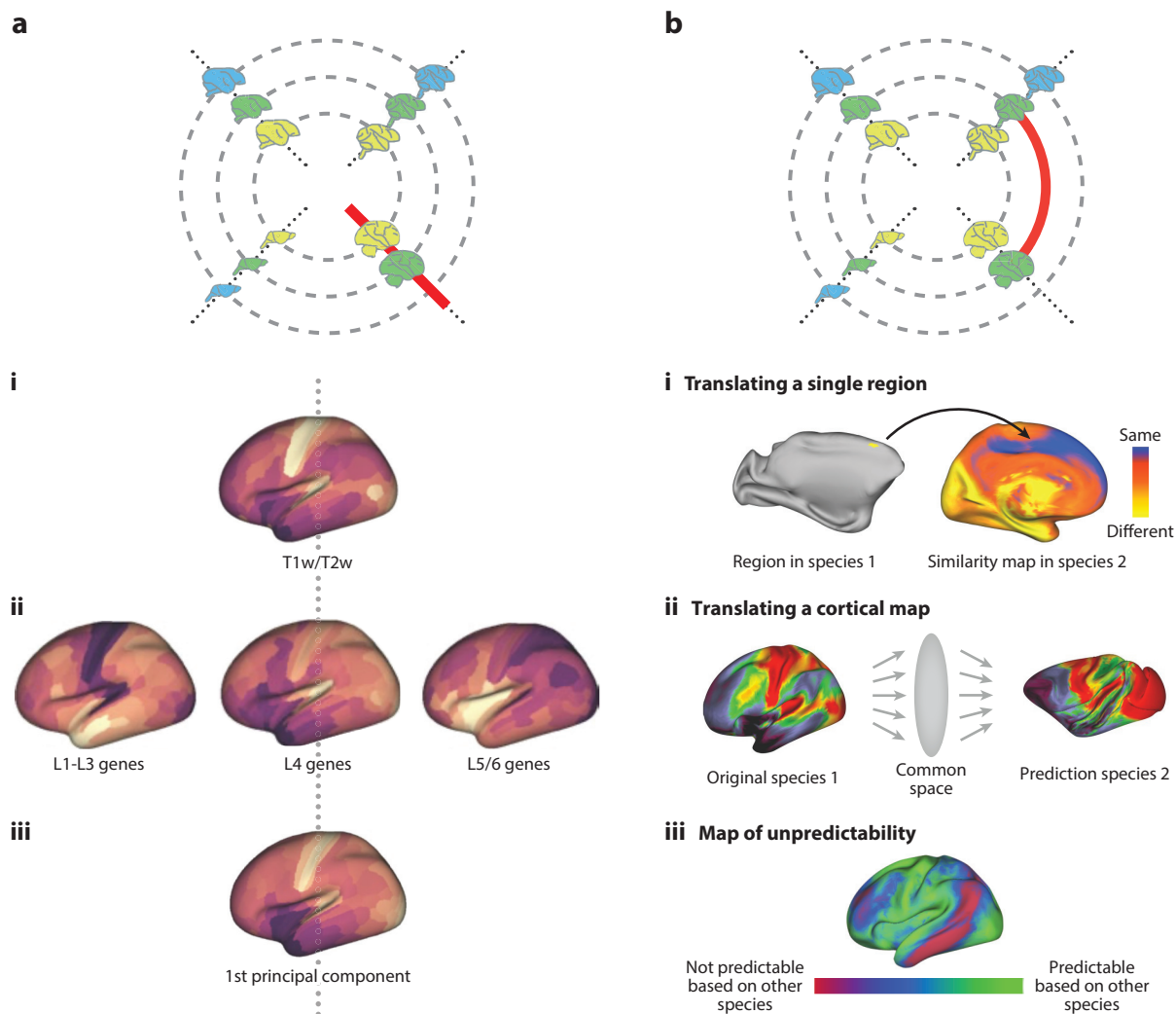
Figure 2

Vertical and horizontal translations. (*a*) Example of a vertical translation. A human T1w/T2w map shows high values in primary areas and low values in association cortex (*i*). This pattern is similar to that of the expression of layer (L)4 genes and the inverse of L1-L3 and L5/6 genes (*ii*). The first principal component of spatial gene expression also matches this pattern (*iii*). Panel *a* reproduced with permission from Springer Nature: *Nature Neuroscience*, Hierarchy of Transcriptomic Specialization Across Human Cortex Captured by Structural Neuroimaging Topography, Joshua B. Burt, Murat Demirtaş, William J. Eckner, Natasha M. Navejar, Jie Lisa Ji, William J. Martin, Alberto Bernacchia, Alan Anticevic, and John D. Murray, 2018. (*b*) Horizontal translations allow one to (*i*) quantify the similarity between a region in one species and areas across the entire brain of another, (*ii*) create whole-brain to whole-brain maps, and (*iii*) quantify which regions in any brain have the lowest similarity to the comparison brain. Panel *b* adapted from Mars et al. (2018c).

simple two-dimensional space representing the cortical sheet. However, their final analysis of performing, in effect, a spatial principal component analysis demonstrates how the topographic information can be effectively reduced to a lower-level space.

This idea of abstracting a complex spatial map to a low-dimensional space reflecting its essential features is present in numerous recent works looking at so-called cortical gradients (Blazquez

Freches et al. 2020, Haak et al. 2018, Vos de Wael et al. 2020). In addition to linear dimensionality reduction techniques such as principal components analysis, other techniques such as diffusion embedding translate relationships between data points—such as connectivity strengths between brain areas—into distances in an embedding space. In one prominent example of this approach, Margulies et al. (2016) used diffusion embedding to describe the human brain in terms of connectivity gradients. The first gradient runs from primary sensory and motor areas to the transmodal areas that together form the default mode network; the second gradient differentiates the different primary areas, thus dissociating different sensory modalities. The authors argue that the principal gradient provides an organizing spatial framework for large-scale cortical networks and suggest that it underlies the role of the default mode network in higher-level information processing that is unrelated to immediate sensory input.

The approach of lower-dimensional embedding to demonstrate principles of brain organization is well suited for comparisons across data modalities. Indeed, following the principle of vertical translation, Huntenburg et al. (2018) explore the idea that the principal primary-to-transmodal gradient is reflected in connectivity, tissue properties such as myelin, and function, referring to it as an intrinsic coordinate system for the cortex. Of course, vertical translations are also informative if the different levels do not line up. As a case in point, Paquola et al. (2019) showed that, although different modalities indeed display a similar hierarchy, they become increasingly dissociated in transmodal cortex.

HORIZONTAL TRANSLATION

The vertical translations discussed in the previous sections had the advantage that they all worked in the same brain space. This is clearly not true for horizontal translations, where brains can differ strongly in size and morphology. Before any comparison can be done, we must solve a correspondence problem and describe each part of the brain in terms of features that are shared between the different brains (**Figure 1c**).

A first solution to this problem is to describe homologous spatial landmarks that can be reliably identified on the brains of different species and to use these to guide a registration algorithm. An early version of this approach was pioneered by Van Essen and colleagues. As a prime example, Van Essen & Dierker (2007) defined a series of homologous locations, such as the primary sulci, on the cortical sheet of the macaque and human brain. These homologous features in effect formed the common feature space between the two brains. A surface-based registration algorithm was then used to find a spatial warping that best matched the locations of these landmarks, while interpolating between them. Once a transformation was found, they could then ask which parts of the cortical sheet had to be particularly distorted to allow alignment of the homologous landmarks. They found that the association cortex in lateral frontal, inferior parietal, and middle temporal cortex showed particularly strong distortions. Subsequent work showed similar effects in comparisons between marmosets, capuchins, and macaques (Chaplin et al. 2013). A more recent variant on this approach has been proposed by Auzias et al. (2013), who parameterized the cortical sheet in terms of a rectangular plane where different sulci run either mostly horizontally or vertically. Defining homologous sulci across species under this parameterization greatly simplifies the correspondence problem (Coulon et al. 2018).

An alternative approach to spatially matching cortical sulcal landmarks has emerged in recent years. The idea still relies on defining corresponding landmarks, but rather than matching their spatial location, the approach defines the landmarks to describe different brains in terms of a common connectivity space. This approach builds on the notion that brain areas have a unique connectivity fingerprint with the rest of the brain (Mars et al. 2018b, Passingham et al. 2002). For

example, subdivisions within premotor cortex may be more or less strongly connected with another given region, but what distinguishes them most clearly is the overall profile of connections that they have with other areas (Tomassini et al. 2007). The same is true in cingulate and parietal cortex (Beckmann et al. 2009, Mars et al. 2011). Thus, if one can identify a suitable number of homologous areas between two brains (landmarks), one can describe other areas in terms of their connectivity profiles with those landmark areas (Mars et al. 2016). The homologous areas form the dimensions of a connectivity space in which all areas of the brains under comparison can be described.

This connectivity fingerprint matching approach has been used to systematically compare most parts of human and macaque brain (Mars et al. 2013, Sallet et al. 2013, Xia et al. 2019). Importantly, it allows one not just to show whether a region is the same or different across species but to provide a more continuous assessment. For instance, Neubert et al. (2014, 2015) demonstrated that some areas of human anterior prefrontal cortex show a connectivity profile that is slightly different from any pattern found in the macaque. In a similar vein, Balsters et al. (2020) extended the approach to much more phylogenetically distant species by comparing striatal organization across mouse, macaque, and human and showed that parts of human striatum have no homolog in the other species.

The main determining factor for the validity of such a horizontal translation using a common space is whether a sufficient number of well-established homologous features can be defined. In the case of macaques and humans, many homologous areas are well defined, but as one moves outside of the common model species, the definition of homologous areas becomes more problematic. An alternative approach is to base the common space not on gray matter areas but on white matter tracts. For instance, a connectivity fingerprint of human medial and lateral frontal pole can be defined based on their differential connectivity with the frontal association tracts (Hartogsveld et al. 2017). This approach can be generalized by describing the entire cortical sheet in terms of its connectivity with each of the major white matter tracts, creating a cortex × white matter connectivity blueprint for each species in which the tracts form the common space (Mars et al. 2018c). This is an attractive approach since the bodies of many major white matter bundles can be identified reliably across different primate species, whereas the branching patterns of these tracts as they approach the cortex provide the key species differences. Thus, one can define automated and robust standardized protocols to reconstruct major tracts across species based on the tract bodies and then use tractography to investigate how each tract reaches the cortex in each brain. Protocols for all major white matter tracts have now been defined for the human, chimpanzee, and macaque (Bryant et al. 2020, Mars et al. 2018c, Warrington et al. 2020), and partial reconstructions are available for several additional species (e.g., Barrett et al. 2020, Roumazeilles et al. 2020, Schaeffer et al. 2017).

A full horizontal translation between two brains opens up a realm of possibilities (Mars et al. 2018c) (**Figure 2b**). One can investigate relative similarities on an area by area basis, but one can also take the connectivity fingerprint of a particular part of one brain and search for similarities across the entire brain of another species. This was done first to search for an area in macaque temporal cortex similar to the human temporoparietal junction area (Mars et al. 2013). Having established a whole-brain to whole-brain mapping, one can then use this to predict how a cortical map, such as a map of cortical myelin or a functional activation map, should look in another brain. For example, the white matter tract blueprint mentioned above was used by Mars et al. (2018c) to transform a human myelin map onto macaque brain geometry, and the resulting map showed strong resemblance to an empirical map based on macaque MRI. This approach arguably has great potential for comparative neuroscience, allowing one to make quantitative predictions about how a map should look in one brain based on knowledge of another. Finally, having established

cross-species similarity across entire brains, one can investigate which parts of the brain match least across species. For macaque–human comparisons, this approach shows areas in human lateral frontal and particularly some other parts of temporal association cortex that have a connectivity fingerprint that cannot be matched to any area in the macaque brain (Mars et al. 2018c). These areas in the human brain thus have access to a combination of information that no macaque brain area has.

As in the vertical translation, the common space can be used to create a low-dimensional embedding space where different species' brains can be concurrently projected. This approach was taken by Xu and colleagues (Xu et al. 2020) in a comparison of macaque–human connectivity. They defined a common space based on homologous areas, established the areas' connectivity fingerprints, and then used a gradient approach to define a low-dimensional joint embedding space. This joint space can then be used to describe each part of the two brains, showing how homologous areas occupy similar places and showing areas of low similarity in—again—frontal and temporoparietal association cortex as well as in parts of the default mode network on the medial wall of the hemispheres. Since the gradients are defined in the joint embedding space, their surface representation can be used to guide a surface-based registration between the two brains, simplifying the brain-to-brain translation.

The common spaces that we have described thus far have always been anatomical, based on known areal homologs, sulci, or gray or white matter connectivity. However, the common space can also be formed at a higher level of abstraction. For instance, in an approach that shares some similarities to the connectivity fingerprint–matching approach, Caspari et al. (2018) used a functional fingerprint–matching approach to investigate human/macaque similarities in areas involved in attentional processing. They required human subjects to perform various conditions of an attention-shifting paradigm and characterized the functional profiles of an area in the medial superior parietal lobule that shows activation when subjects shift their locus of attention. They then required macaque monkeys to do the same task and searched across the brain for voxels that matched the human functional profile, showing significant similarity in macaque areas V6 and V6a.

Another approach to defining an abstract common space is to describe brain areas in terms of neural representations. One particularly powerful example is given by representational similarity analysis. This method describes multivariate brain signals in terms of the geometry of the activity, i.e., how the collective multivariate response to different stimuli or conditions changes. Thus, it abstracts away not only spatial location but also the nature of the measured signal. This means that such methods can equally be applied to functional MRI signals or to electrophysiological recording, making it a powerful tool for cross-species comparisons (Barron et al. 2020) or even explicit comparisons between biological and artificial brains. As an example, Kriegeskorte et al. (2008) used a representational similarity approach to compare macaque extracellular recordings and human functional MRI. They found strikingly similar neuronal representations in inferior temporal cortex of the two species, suggesting a similar representational code in the two brains. Hunt et al. (2015) found similar single-trial indices of internal decision-making state in dorsolateral prefrontal cortex in local field potentials recorded from the macaque and magneto-encephalography recorded from the human.

COMPARING COMMON SPACES

Using a common space allows one to build a brain-to-brain translational mapping that in turn can be used to predict how any particular feature map from one brain might look in the other. If different modalities are used to construct the common spaces, an obvious question is whether the results obtained are consistent. As a case in point, Fulcher et al. (2019) were interested to see

whether the vertical relationship observed in primates between the cortical hierarchy evident in T1w/T2w maps and spatial gradients evident in other modalities is also present in the mouse. As one piece of evidence, they were able to show significant spatial correlations between the gene expression maps of a number of receptor subunit and cell type marker genes and the T1w/T2w map. They then focused on genes that have a known human ortholog and compared the gene–T1w/T2w correlation values between the mouse and the human. This resulted in a significant correlation of correlations, suggesting that the relationship between the modalities was preserved across species. In effect, whether one uses the T1w/T2w or the gene expression maps as a common space between the mouse and human brain, the results should show significant similarity.

Such a similarity between the T1w/T2w and gene expression maps as common spaces across the mouse and the human is comforting. The fact that the principle of organization—operationalized here as the relationship between different levels of the biological hierarchy—is comparable across the two species means that knowledge of multiple areas in the mouse can be used, in some cases, to make inferences about the nature of an area that is only found in humans and not in the mouse itself. However, it would be wrong to assume that horizontal translations using data from different modalities should always line up. Indeed, in discussions of homology in the context of the biological hierarchy, a number of authors have pointed out that homologous high-level characteristics can be due to low-level nonhomologies and vice versa (Sommer 2008, Striedter 2019). As an example of the former, Striedter & Northcutt (1991) discuss the example of the grasshopper *Calliptamus italicus*, which produces songs similar to those of other grasshoppers and in similar circumstances, but does so using a different part of the body. A parsimonious interpretation of grasshopper phylogenetic relations suggests that the behavior is homologous, but the way it is produced diverged. The so-called neural recycling hypothesis, which suggests that homologous anatomical regions contribute to highly species-specific behavior such as reading in the human brain (Dehaene & Cohen 2007), can be interpreted as an example of the opposite situation. The key message from these observations of homology at different levels of organization for the present framework is that in order to fully understand differences across brains, one needs to investigate how different horizontal translations line up. In fact, exploring differences between horizontal translations using different common spaces is a suitable way of investigating the types of changes that have occurred between brains.

Motivated by this line of thinking, Eichert et al. (2019, 2020) investigated whether various differences observed in the white matter organization of the human temporal lobe compared to that of other primates were all due to the same type of change. One of the hallmark results of primate comparative neuroscience using neuroimaging is the observation that the arcuate fascicle projects much more ventrally in the human temporal lobe than in the macaque and chimpanzee (Rilling et al. 2008). However, the horizontal translation based on homologous areas suggests that the temporal and inferior parietal territory close to the gray matter projection areas of the arcuate has vastly expanded in the human brain (Van Essen & Dierker 2007). This has, among other outcomes, led to area MT+ moving from a dorsal superior temporal sulcus location in the nonhuman primate to a much more ventral location in the human (Huk et al. 2002). This means that the ventral projections of the arcuate can be explained both by an expansion or relocation of its existing gray matter projections or, as suggested by Rilling et al. (2008), by invasion by the arcuate of new cortical territory (Mars et al. 2018a). Comparing horizontal translations based on multiple modalities can resolve this question.

In two studies, Eichert et al. (2019, 2020) used a common space based on one modality to determine the expansion and relocation of areas and then investigated whether the resulting horizontal translation could account for differences between species in the cortical projections of the arcuate fascicle. In the first study, they used the Van Essen & Dierker (2007) translation based

on cortical homologs and showed that this map could not predict changes in arcuate projections between macaques and humans (Eichert et al. 2019). In a second study, they used surface-based registration to align macaque, chimpanzee, and human T1w/T2w maps (Eichert et al. 2020). The resulting translations were able to account for some of the major relocations of cortical areas in occipitotemporal cortex, including the lateral-to-medial shift of primary visual cortex and the dorsal-to-ventral relocation of MT+ (**Figure 3***a*). When applied to projection maps of certain cortical tracts, including the ventral inferior fronto-occipital fascicle, these translations

a

i T1w/T2w

Predictions based on T1w/T2w

ii Arcuate fascicle projections

Predictions based on T1w/T2w

iii Comparison

Macaque predicted
Chimpanzee predicted
Human actual

b

i

Macaque tractography → Human tractography

Macaque tracer

ii

Macaque tractography → Human tractography

dlPFC 46 FEF Premotor
9/46 8B
9L 8A
9M 8/32 6 ProM
dmPFC 9/32
vlPFC 47O 45 6/32
OPAI 47L 44
OFC 11
OPro
13 14O 14A 10M 10L FP
25
vmPFC

Macaque tracer

(*Caption appears on following page*)

Figure 3 (*Figure appears on preceding page*)

Extending translations. (*a*) Comparing horizontal translations. One can use the T1w/T2w maps of the macaque, chimpanzee, and human brain (*i, top row*) to calculate a horizontal translation across the species. By creating the best possible registration from macaque to human and from chimpanzee to human (*i, bottom row*), it is possible to estimate how areas have relocated or expanded across species. These registrations can then be applied to other modalities such as maps of the projection of the arcuate fascicle (*ii*). The predicted projection maps based on the macaque to human (*iii, green*) and chimpanzee to human (*iii, blue*) projection maps can then be compared to the actual human map (*iii, red*). If they do not match, as is the case here, reorganization across levels has occurred between the brains. Panel *a* adapted from Eichert et al. (2020). (*b*) Combining translations allows one to make predictions for modalities that are not present in one of the species. For instance, a horizontal translation from macaque tracers to the human is not possible, as tracer data cannot be obtained in humans. Therefore, one can compare macaque tracers to macaque diffusion MRI tractography in a vertical translation and then compare tractography across species in a horizontal translation. Two example applications are (*i*) the amygdala-fugal tract that could be reconstructed using tractography only by using strong priors based on tracer data and (*ii*) the demonstration of a connectional hub in rostral anterior cingulate cortex across species. Panel *b* subpanel *i* macaque and human tractography adapted from Folloni et al. (2019) and tracer image reproduced with permission from Springer Nature: *Brain Structure and Function*, Connectivity Between the Central Nucleus of the Amygdala and the Bed Nucleus of the Stria Terminalis in the Non-Human Primate: Neuronal Tract Tracing and Developmental Neuroimaging Studies, Jonathan A. Oler, Do P.M. Tromp, Andrew S. Fox, Rothem Kovner, Richard J. Davidson, Andrew L. Alexander, Daniel R. McFarlin, Rasmus M. Birn, Benjamin E. Berg, Danielle M. deCampo, Ned H. Kalin, Julie L. Fudge, 2016; subpanel *ii* adapted from Tang et al. (2019).

could account for some between-species differences in cortical projections. However, this was not the case for the arcuate, whose ventral temporal projections far exceeded those predicted by the translations based on the T1w/T2w common space. Applying this approach to a range of temporal tracts showed a variety of degrees in which between-species differences in cortical projections were driven by cortical relocation or the expansion of projections.

Comparing common spaces thus allows one to investigate how the relationships between different levels of brain organization have diverged across species. This, in turn, allows a better understanding of the homology of features across species. An interesting example is the default mode network of the brain. This network was originally identified as a task-negative network of areas that tends to be more activated when the brain is not engaged in a specific task (Shulman et al. 1997), but it is now more generally interpreted as a network involved in generic high-level cognition through dynamic interactions with more task-related networks (Vatansever et al. 2015). As discussed above, Margulies et al. (2016) described the default mode network as situated at the extreme end of a gradient ranging from primary to transmodal cortices. A default mode–type network has now been reported in many different species, including in other primates such as the chimpanzee, macaque, and marmoset (Barks et al. 2015, Liu et al. 2019, Vincent et al. 2007) and also in carnivores and rodents (Lu et al. 2012, Szabó et al. 2019). At one level, one might interpret these networks as equivalent across the species, as they are suggested to fulfil the same role of dealing with the most abstract information a brain is capable of processing. On the other hand, at a lower level, the anatomical regions that form these networks need not be homologous. In the human, for instance, the default mode seems to involve regions in middle temporal cortex that might not have clear homologs in other species, especially outside the primate order (Bryant & Preuss 2018). Indeed, the default mode seems to have the connectivity fingerprints that differ the most between the human and macaque monkey (Xu et al. 2020). Therefore, the default mode network's function might be comparable across species, but the areas of which it is composed might not be.

COMBINING TRANSLATIONS

Arguably the greatest potential for comparative neuroscience lies in combining various translations. We already saw an example of this in the translation of cortical myelin maps in a common

space of white matter connections (Mars et al. 2018c) (**Figure 2b**). In essence, this corresponds to a vertical translation (myelin to connectivity space), followed by a horizontal translation (based on common connectivity space), which is then followed by another vertical translation (connectivity back to myelin). This type of explicit prediction of how a particular data type would look in one brain based on another is the true goal of comparative neuroscience.

Depending on what types of data are available for each species, we can dissociate two scenarios. In the first, the data from the species under investigation share at least one modality in common that can be used to build a common space for the horizontal translation, but other data modalities are only present in one of the species. Measurements of anatomical (axonal) connectivity are a good example. In animals, we can use neuroanatomical tracers to very accurately map the origin, termination, and sometimes the entire trajectory of axons. These techniques are not available in humans. Diffusion MRI tractography is a technique that can provide information about anatomical connections in humans, but it is a rather indirect probe of connectivity, and that makes it error prone. But diffusion MRI tractography is available for use in animals. Having this same technique in both humans and animals is a great opportunity for horizontal comparisons, as differences between the species cannot trivially be attributed to differences in measurement techniques.

Combined translational approaches of this type have been possible for some time. Croxson (2005) and colleagues, for instance, used diffusion-weighted imaging estimates of white matter pathways and their probabilities of interconnection with frontal cortical areas to compare humans and macaques. However, this approach has become increasingly refined. For example, Folloni et al. (2019) defined a protocol to reconstruct the amygdalofugal tract in the macaque monkey in a way that captured its course and projections as known from invasive tracers (vertical translation) and then used these protocols to study this tract in the human using tractography (horizontal translation) (**Figure 3b**). A similar approach has shown that it is possible to identify similar connectional hubs in anterior cingulate cortex based on tracers and tractography in the macaque and tractography in the human (Tang et al. 2019). By comparing tractography to tracers in the macaque monkey, we can also understand why some of the errors made by diffusion tractography algorithms occur (Jbabdi et al. 2013). We can then use this knowledge to predict or correct errors made in human tractography and obtain more anatomically faithful results despite the unavailability of neuroanatomical tracers in humans (Haber et al. 2020).

In the second scenario, all modalities might be present in both species, but we want to use one particular modality for the common space. This is the scenario discussed above in which the myelin map is translated based on a connectivity common space, but it can be extended to validate and improve the use of model animals to understand human brain function. An interesting example case is the use of rodents in the study of the neural basis of social behavior (Grimm et al. 2021). The rodent has a much less encephalized neocortex, many of whose subdivisions are implicated in social information processing in the human (Olsson et al. 2020, Rushworth et al. 2013). However, using a rodent model allows a much wider range of vertical translations, including the use of genetic mutants, optogenetics, and invasive tracers (Bicks et al. 2020, Velez et al. 2010). Horizontal translations based on connectivity or expression of orthologous genes can be used to first validate the model. For instance, one can predict brain morphological changes in individuals with particular genetic alleles based on changes observed in mutant mice models. If successful, the horizontal translations can then be used to predict effects that cannot be studied directly in the human, formalizing the link between preclinical and clinical research. Such a methodology would usher in a more quantitative approach to the use of model species, allowing finer predictions in the human, but also—using the reverse translation—by determining more carefully which model is appropriate to study any human condition or any particular aspect of the human brain. This could help refine the use and reduce the number of animals in research.

CONCLUSION

We have presented a framework for comparative neuroimaging. By exploiting multimodal data that provide local detail and constructing feature-based common spaces, we compare both across scales within a species through vertical translations and across species through horizontal translations. Importantly, this framework helps us to understand the different principles of brain organization across species through comparisons of horizontal translations and to make formal predictions, even when data are available in only a subset of species, by combining translations. Ultimately, such a formal framework benefits both translational neuroscience using model species and large-scale comparative neuroscience investigating diversity among large sections of the evolutionary tree.

DISCLOSURE STATEMENT

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

AUTHOR CONTRIBUTIONS

R.B.M. conceived of the idea and wrote the first draft, S.J. and M.F.S.R. edited the draft, and all authors approved the final manuscript.

LITERATURE CITED

Auzias G, Lefèvre J, Le Troter A, Fisher C, Perrot M, et al. 2013. Model-driven harmonic parameterization of the cortical surface: HIP-HOP. *IEEE Trans. Med. Imaging* 32:873–87

Balsters JH, Zerbi V, Sallet J, Wenderoth N, Mars RB. 2020. Primate homologs of mouse cortico-striatal circuits. *eLife* 9:e53680

Barbas H, Rempel-Clower N. 1997. Cortical structure predicts the pattern of corticocortical connections. *Cereb. Cortex* 7(7):635–46

Barks SK, Parr LA, Rilling JK. 2015. The default mode network in chimpanzees (*Pan troglodytes*) is similar to that of humans. *Cereb. Cortex* 25(2):538–44

Barrett RLC, Dawson M, Dyrby TB, Krug K, Ptito M, et al. 2020. Differences in frontal network anatomy across primate species. *J. Neurosci.* 40(10):2094–107

Barron HC, Mars RB, Dupret D, Lerch J, Sampaio-Baptista C. 2020. Cross-species neuroscience: closing the explanatory gap. *Phil Trans. R. Soc. B* 376:20190633

Barton RA. 2007. Evolutionary specialization in mammalian cortical structure. *J. Evol. Biol.* 20(4):1504–11

Barton RA, Venditti C. 2013. Human frontal lobes are not relatively large. *PNAS* 110(22):9001–6

Beckmann M, Johansen-Berg H, Rushworth MFS. 2009. Connectivity-based parcellation of human cingulate cortex and its relation to functional specialization. *J. Neurosci.* 29(4):1175–90

Bicks LK, Yamamuro K, Flanigan ME, Kim JM, Kato D, et al. 2020. Prefrontal parvalbumin interneurons require juvenile social experience to establish adult social behavior. *Nat. Commun.* 11(1):1003

Blazquez Freches G, Haak KV, Bryant KL, Schurz M, Beckmann CF, Mars RB. 2020. Principles of temporal association cortex organisation as revealed by connectivity gradients. *Brain Struct. Funct.* 225:1245–60

Bryant KL, Li L, Eichert N, Mars RB. 2020. A comprehensive atlas of white matter tracts in the chimpanzee. bioRxiv 2020.01.24.918516. **https://doi.org/10.1101/2020.01.24.918516**

Bryant KL, Preuss TM. 2018. A comparative perspective on the human temporal lobe. In *Digital Endocasts*, ed. E Bruner, N Ogihara, HC Tanabe, pp. 239–58. Tokyo: Springer Japan

Burt JB, Demirtaş M, Eckner WJ, Navejar NM, Ji JL, et al. 2018. Hierarchy of transcriptomic specialization across human cortex captured by structural neuroimaging topography. *Nat. Neurosci.* 21(9):1251–59

Caspari N, Arsenault JT, Vandenberghe R, Vanduffel W. 2018. Functional similarity of medial superior parietal areas for shift-selective attention signals in humans and monkeys. *Cereb. Cortex* 28(6):2085–99

Chaplin TA, Yu H-H, Soares JGM, Gattass R, Rosa MGP. 2013. A conserved pattern of differential expansion of cortical areas in simian primates. *J. Neurosci.* 33(38):15120–25

Churchland P, Sejnowski T. 1992. *The Computational Brain*. Cambridge, MA: MIT Press

Coulon O, Auzias G, Lemercier P, Hopkins WD. 2018. *Nested cortical organization models for human and non-human primate inter-species comparisons*. Paper presented at the Annual Meeting of the Organization for Human Brain Mapping, Singapore

Croxson PL. 2005. Quantitative investigation of connections of the prefrontal cortex in the human and macaque using probabilistic diffusion tractography. *J. Neurosci.* 25(39):8854–66

Dehaene S, Cohen L. 2007. Cultural recycling of cortical maps. *Neuron* 56(2):384–98

Dunbar RIM, Shultz S. 2007. Evolution in the social brain. *Science* 317(5843):1344–47

Eichert N, Robinson EC, Bryant KL, Jbabdi S, Jenkinson M, et al. 2020. Cross-species cortical alignment identifies different types of anatomical reorganization in the primate temporal lobe. *eLife* 9:e53232

Eichert N, Verhagen L, Folloni D, Jbabdi S, Khrapitchev AA, et al. 2019. What is special about the human arcuate fasciculus? Lateralization, projections, and expansion. *Cortex* 118:107–15

Folloni D, Sallet J, Khrapitchev AA, Sibson N, Verhagen L, Mars RB. 2019. Dichotomous organization of amygdala/temporal-prefrontal bundles in both humans and monkeys. *eLife* 8:e47175

Fulcher BD, Murray JD, Zerbi V, Wang X-J. 2019. Multimodal gradients across mouse cortex. *PNAS* 116(10):4689–95

Geyer S, Matelli M, Luppino G, Schleicher A, Jansen Y, et al. 1998. Receptor autoradiographic mapping of the mesial motor and premotor cortex of the macaque monkey. *J. Comp. Neurol.* 397(2):231–50

Glasser MF, Coalson TS, Robinson EC, Hacker CD, Harwell J, et al. 2016. A multi-modal parcellation of human cerebral cortex. *Nature* 536:171–78

Glasser MF, Van Essen DC. 2011. Mapping human cortical areas in vivo based on myelin content as revealed by T1- and T2-weighted MRI. *J. Neurosci.* 31(32):11597–616

Grandjean J, Canella C, Anckaerts C, Ayrancı G, Bougacha S, et al. 2020. Common functional networks in the mouse brain revealed by multi-centre resting-state fMRI analysis. *NeuroImage* 205:116278

Grimm C, Balsters JH, Zerbi V. 2021. Shedding light on social reward circuitry: (un)common blueprints in humans and rodents. *Neuroscientist* 27(2):159–83

Haak KV, Marquand AF, Beckmann CF. 2018. Connectopic mapping with resting-state fMRI. *NeuroImage* 170:83–94

Haber SN, Tang W, Choi EY, Yendiki A, Liu H, et al. 2020. Circuits, networks, and neuropsychiatric disease: transitioning from anatomy to imaging. *Biol. Psychiatry* 87(4):318–27

Hartogsveld B, Bramson B, Vijayakumar S, van Campen AD, Marques JP, et al. 2017. Lateral frontal pole and relational processing: activation patterns and connectivity profile. *Behav. Brain Res.* 355:2–11

Hawrylycz MJ, Lein ES, Guillozet-Bongaarts AL, Shen EH, Ng L, et al. 2012. An anatomically comprehensive atlas of the adult human brain transcriptome. *Nature* 489(7416):391–99

Hay M, Thomas DW, Craighead JL, Economides C, Rosenthal J. 2014. Clinical development success rates for investigational drugs. *Nat. Biotechnol.* 32(1):40–51

Huk AC, Dougherty RF, Heeger DJ. 2002. Retinotopy and functional subdivision of human areas MT and MST. *J. Neurosci.* 22:7195–205

Hunt LT, Behrens TEJ, Hosokawa T, Wallis JD, Kennerley SW. 2015. Capturing the temporal evolution of choice across prefrontal cortex. *eLife* 4:e11945

Huntenburg JM, Bazin P-L, Margulies DS. 2018. Large-scale gradients in human cortical organization. *Trends Cogn. Sci.* 22(1):21–31

Jbabdi S, Lehman JF, Haber SN, Behrens TE. 2013. Human and monkey ventral prefrontal fibers use the same organizational principles to reach their targets: tracing versus tractography. *J. Neurosci.* 33(7):3190–201

Jerison HJ. 1973. *Evolution of Brain and Intelligence*. New York: Academic

Keil JM, Qalieh A, Kwan KY. 2018. Brain transcriptome databases: a user's guide. *J. Neurosci.* 38(10):2399–412

Kriegeskorte N, Mur M, Ruff DA, Kiani R, Bodurka J, et al. 2008. Matching categorical object representations in inferior temporal cortex of man and monkey. *Neuron* 60(6):1126–41

Krubitzer L, Kaas J. 2005. The evolution of the neocortex in mammals: How is phenotypic diversity generated? *Curr. Opin. Neurobiol.* 15(4):444–53

Laubach M, Amarante LM, Swanson K, White SR. 2018. What, if anything, is rodent prefrontal cortex? *eNeuro* 5(5):ENEURO0315-18.2018

Lein ES, Hawrylycz MJ, Ao N, Ayres M, Bensinger A, et al. 2007. Genome-wide atlas of gene expression in the adult mouse brain. *Nature* 445(7124):168–76

Lerch JP, van der Kouwe AJW, Raznahan A, Paus T, Johansen-Berg H, et al. 2017. Studying neuroanatomy using MRI. *Nat. Neurosci.* 20(3):314–26

Liu C, Yen CC-C, Szczupak D, Ye FQ, Leopold DA, Silva AC. 2019. Anatomical and functional investigation of the marmoset default mode network. *Nat. Commun.* 10(1):1975

Lu H, Zou Q, Gu H, Raichle ME, Stein EA, Yang Y. 2012. Rat brains also have a default mode network. *PNAS* 109(10):3979–84

Mandino F, Cerri DH, Garin CM, Straathof M, van Tilborg GAF, et al. 2019. Animal functional magnetic resonance imaging: trends and path toward standardization. *Front. Neuroinform.* 13:78

Margulies DS, Ghosh SS, Goulas A, Falkiewicz M, Huntenburg JM, et al. 2016. Situating the default-mode network along a principal gradient of macroscale cortical organization. *PNAS* 113(44):12574–79

Mars NJI. 1987. *Onderzoek van Niveau: Kennistechnologie in Wording. Inaugural Lecture University of Twente*. Enschede, Neth.: Univ. Twente

Mars RB, Eichert N, Jbabdi S, Verhagen L, Rushworth MFS. 2018a. Connectivity and the search for specializations in the language-capable brain. *Curr. Opin. Behav. Sci.* 21:19–26

Mars RB, Jbabdi S, Sallet J, O'Reilly JX, Croxson PL, et al. 2011. Diffusion-weighted imaging tractography-based parcellation of the human parietal cortex and comparison with human and macaque resting-state functional connectivity. *J. Neurosci.* 31(11):4087–100

Mars RB, Passingham RE, Jbabdi S. 2018b. Connectivity fingerprints: from areal descriptions to abstract spaces. *Trends Cogn. Sci.* 22(11):1026–37

Mars RB, Sallet J, Neubert F-X, Rushworth MFS. 2013. Connectivity profiles reveal the relationship between brain areas for social cognition in human and monkey temporoparietal cortex. *PNAS* 110(26):10806–11

Mars RB, Sotiropoulos SN, Passingham RE, Sallet J, Verhagen L, et al. 2018c. Whole brain comparative anatomy using connectivity blueprints. *eLife* 7:e35237

Mars RB, Verhagen L, Gladwin TE, Neubert F-X, Sallet J, Rushworth MFS. 2016. Comparing brains by matching connectivity profiles. *Neurosci. Biobehav. Rev.* 60:90–97

Milham M, Petkov CI, Margulies DS, Schroeder CE, Basso MA, et al. 2020. Accelerating the evolution of nonhuman primate neuroimaging. *Neuron* 105(4):600–3

Milham MP, Ai L, Koo B, Xu T, Amiez C, et al. 2018. An open resource for non-human primate imaging. *Neuron* 100(1):61–74.e2

Miller KL, Alfaro-Almagro F, Bangerter NK, Thomas DL, Yacoub E, et al. 2016. Multimodal population brain imaging in the UK Biobank prospective epidemiological study. *Nat. Neurosci.* 19(11):1523–36

Neubert F-X, Mars RB, Sallet J, Rushworth MFS. 2015. Connectivity reveals relationship of brain areas for reward-guided learning and decision making in human and monkey frontal cortex. *PNAS* 112(20):E2695–704

Neubert F-X, Mars RB, Thomas AG, Sallet J, Rushworth MFS. 2014. Comparison of human ventral frontal cortex areas for cognitive control and language with areas in monkey frontal cortex. *Neuron* 81(3):700–13

Olsson A, Knapska E, Lindström B. 2020. The neural and computational systems of social learning. *Nat. Rev. Neurosci.* 21(4):197–212

Paquola C, Wael RVD, Wagstyl K, Bethlehem RAI, Hong S-J, et al. 2019. Microstructural and functional gradients are increasingly dissociated in transmodal cortices. *PLOS Biol.* 17(5):e3000284

Passingham RE, Smaers JB. 2014. Is the prefrontal cortex especially enlarged in the human brain? Allometric relations and remapping factors. *Brain Behav. Evol.* 84(2):156–66

Passingham RE, Stephan KE, Kötter R. 2002. The anatomical basis of functional localization in the cortex. *Nat. Rev. Neurosci.* 3(8):606–16

Rilling JK, Glasser MF, Preuss TM, Ma X, Zhao T, et al. 2008. The evolution of the arcuate fasciculus revealed with comparative DTI. *Nat. Neurosci.* 11(4):426–28

Roumazeilles L, Eichert N, Bryant KL, Folloni D, Sallet J, et al. 2020. Longitudinal connections and the organization of the temporal cortex in macaques, great apes, and humans. *PLOS Biol.* 18(7):e3000810

Rushworth MFS, Mars RB, Sallet J. 2013. Are there specialized circuits for social cognition and are they unique to humans? *Curr. Opin. Neurobiol.* 23(3):436–42

Sallet J, Mars RB, Noonan MP, Neubert F-X, Jbabdi S, et al. 2013. The organization of dorsal frontal cortex in humans and macaques. *J. Neurosci.* 33(30):12255–74

Schaeffer DJ, Adam R, Gilbert KM, Gati JS, Li AX, et al. 2017. Diffusion-weighted tractography in the common marmoset monkey at 9.4T. *J. Neurophysiol.* 118(2):1344–54

Shulman GL, Fiez JA, Corbetta M, Buckner RL, Miezin FM, et al. 1997. Common blood flow changes across visual tasks: II. Decreases in cerebral cortex. *J. Cogn. Neurosci.* 9(5):648–63

Smaers JB, Soligo C. 2013. Brain reorganization, not relative brain size, primarily characterizes anthropoid brain evolution. *Proc. R. Soc. B* 280(1759):20130269

Sommer RJ. 2008. Homology and the hierarchy of biological systems. *Bioessays* 30(7):653–58

Striedter GF. 2019. Variation across species and levels: implications for model species research. *Brain Behav. Evol.* 93(2–3):57–69

Striedter GF, Northcutt RG. 1991. Biological hierarchies and the concept of homology. *Brain Behav. Evol.* 38(4–5):177–89

Szabó D, Czeibert K, Kettinger Á, Gácsi M, Andics A, et al. 2019. Resting-state fMRI data of awake dogs (*Canis familiaris*) via group-level independent component analysis reveal multiple, spatially distributed resting-state networks. *Sci. Rep.* 9(1):15270

Tang W, Jbabdi S, Zhu Z, Cottaar M, Grisot G, et al. 2019. A connectional hub in the rostral anterior cingulate cortex links areas of emotion and cognitive control. *eLife* 8:e43761

Thiebaut de Schotten M, Dell'Acqua F, Valabregue R, Catani M. 2012. Monkey to human comparative anatomy of the frontal lobe association tracts. *Cortex* 48(1):82–96

Tomassini V, Jbabdi S, Klein JC, Behrens TE, Pozzilli C, et al. 2007. Diffusion-weighted imaging tractography-based parcellation of the human lateral premotor cortex identifies dorsal and ventral subregions with anatomical and functional specializations. *J. Neurosci.* 27(38):10259–69

Van Essen DC, Dierker DL. 2007. Surface-based and probabilistic atlases of primate cerebral cortex. *Neuron* 56(2):209–25

Van Essen DC, Smith SM, Barch DM, Behrens TEJ, Yacoub E, Ugurbil K. 2013. The WU-Minn Human Connectome Project: an overview. *NeuroImage* 80:62–79

van Heukelum S, Mars RB, Guthrie M, Buitelaar JK, Beckmann CF, et al. 2020. Where is cingulate cortex? A cross-species view. *Trends Neurosci.* 43:285–99

Vatansever D, Menon DK, Manktelow AE, Sahakian BJ, Stamatakis EA. 2015. Default mode dynamics for global functional integration. *J. Neurosci.* 35(46):15254–62

Velez L, Sokoloff G, Miczek KA, Palmer AA, Dulawa SC. 2010. Differences in aggressive behavior and DNA copy number variants between BALB/cJ and BALB/cByJ substrains. *Behav. Genet.* 40(2):201–10

Vincent JL, Patel GH, Fox MD, Snyder AZ, Baker JT, et al. 2007. Intrinsic functional architecture in the anaesthetized monkey brain. *Nature* 447(7140):83–86

Vos de Wael R, Benkarim O, Paquola C, Lariviere S, Royer J, et al. 2020. BrainSpace: a toolbox for the analysis of macroscale gradients in neuroimaging and connectomics datasets. *Commun. Biol.* 3(1):103

Warrington S, Bryant KL, Khrapitchev AA, Sallet J, Charquero-Ballester M, et al. 2020. XTRACT—Standardised protocols for automated tractography in the human and macaque brain. *NeuroImage* 217:116923

Xia X, Fan L, Cheng C, Yao R, Deng H, et al. 2019. Interspecies differences in the connectivity of ventral striatal components between humans and macaques. *Front. Neurosci.* 13:623

Xu T, Nenning K-H, Schwartz E, Hong S-J, Vogelstein JT, et al. 2020. Cross-species functional alignment reveals evolutionary hierarchy within the connectome. *Neuroimage* 223:117346

Xu T, Sturgeon D, Ramirez JSB, Froudist-Walsh S, Margulies DS, et al. 2019. Interindividual variability of functional connectivity in awake and anesthetized rhesus macaque monkeys. *Biol. Psychiatry Cogn. Neurosci. Neuroimaging* 4(6):543–53