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# Situating the default-mode network in a principal gradient of macroscale cortical organization

Daniel S. Margulies<sup>a,1</sup>, Satrajit S. Ghosh<sup>b,c</sup>, Alexandros Goulas<sup>d</sup>, Marcel Falkiewicz<sup>a</sup>, Julia M. Huntenburg<sup>a,e</sup>, Georg Langs<sup>f</sup>, Gleb Bezgin<sup>g</sup>, Simon Eickhoff<sup>h,i</sup>, F. Xavier Castellanos<sup>j</sup>, Michael Petrides<sup>k</sup>, Elizabeth Jefferies<sup>l</sup>, and Jonathan Smallwood<sup>l</sup>

<sup>a</sup>Max Planck Research Group for Neuroanatomy & Connectivity, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, 04103, Germany; <sup>b</sup>McGovern Institute for Brain Research, MIT, Cambridge, MA, 02139, USA; <sup>c</sup>Department of Otolaryngology, Harvard Medical School, MA, 02115, USA; <sup>d</sup>Department of Computational Neuroscience, University Medical Center Hamburg-Eppendorf, Hamburg, 20246, Germany; <sup>e</sup>Neurocomputation and Neuroimaging Unit, Department of Education and Psychology, Free University of Berlin, 14195, Berlin, Germany; <sup>f</sup>Department of Biomedical Imaging and Image-guided Therapy, CIR Lab, Medical University of Vienna, Vienna, A-1090, Austria; <sup>g</sup>Cognitive Neuroscience Unit, Montreal Neurological Institute, McGill University, Montreal, H3A 2B4, Canada; <sup>h</sup>Institute for Neuroscience and Medicine (INM-1), Research Center Jülich, Jülich, 52428, Germany; <sup>i</sup>Institute of Clinical Neuroscience and Medical Psychology, Heinrich-Heine University, Düsseldorf, 40225, Germany; <sup>j</sup>Child Study Center, Department of Child and Adolescent Psychiatry, NYU Langone Medical Center, NY, 10016, USA; <sup>k</sup>McConnell Brain Imaging Centre, Montreal Neurological Institute, McGill University, Montreal, H3A 2B4, Canada; <sup>l</sup>Department of Psychology and York Neuroimaging Centre, University of York, York, YO10 5DD, United Kingdom

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**Understanding how the structure of cognition arises from the topographical organization of the cortex is a primary goal in neuroscience. Previous work has described local functional gradients extending from perceptual and motor regions to cortical areas representing more abstract functions, yet an overarching framework for the association between structure and function is still lacking. Here we show that the principal gradient revealed by the decomposition of connectivity data in humans and the macaque monkey is anchored, at one end, by regions serving primary sensory/motor functions and, at the other, by transmodal regions that, in humans, are known as the default-mode network (DMN). These DMN regions exhibit the greatest geodesic distance along the cortical surface — and are precisely equidistant — from primary sensory/motor morphological landmarks. The principal gradient also provides an organizing spatial framework for multiple large-scale networks and characterizes a spectrum from unimodal to heteromodal activity in a functional meta-analysis. Together these observations provide a novel characterization of the topographical organization of cortex and indicate that the role of the DMN in cognition might arise from its position at one extreme of a hierarchy, allowing it to process transmodal information that is unrelated to immediate sensory input.**

topography | connectivity | cortical organization | default-mode network

**A** key assumption in neuroscience is that the topographical structure of the cerebral cortex provides an organizing principle that constrains its cognitive processes. Recent advances in the field of human connectomics have revealed multiple large-scale networks [e.g., 1–3], each characterized by distinct functional profiles [4]. Some are related to basic primary functions, such as moving or perceiving sounds and images; some serve well-documented, domain-general functions, such as attention or cognitive control [5–8]; and some have functional characteristics that remain less well understood, such as the default-mode network (DMN) [9, 10]. Although the topography of these distinct distributed networks has been described using multiple methods [e.g., 1–3], the reason for their particular spatial relationship and how this constrains their function remains unclear.

Advances in mapping local processing streams have revealed spatial gradients that support increasingly abstract levels of representation, often extending along adjacent cortical regions in a stepwise manner [11]. In the visual domain, for example, the ventral occipito-temporal object stream transforms simple visual features, coded by neurons in primary visual cortex,

into more complex visual descriptions of objects in anterior inferior temporal cortical regions, and ultimately contributes to multimodal semantic representations in the middle temporal cortex and the most anterior temporal cortex that capture the meaning of what we see, hear and do [12–15]. Similarly, in the prefrontal cortex, a rostral-caudal gradient has been proposed whereby goals become increasingly abstract in anterior areas more distant from motor cortex, as they are increasingly removed from selection processes that operate on specific motor representations [5, 16–19]. Much like the function–structure correspondence elucidated by topographic maps within sensory and motor areas [20, 21], these processing gradients provide a systematic mapping between spatial position and a functional spectrum of increasingly abstract representation [22].

Processing gradients have proven useful for understanding the relation between specific regions and function in separate domains; Mesulam observed that the emergence of more abstract functional classes of cortex may follow a similar trajectory, hypothesizing that abstract categories emerge from the convergence of information across modalities [23, and see Figure 1C]. This notion has recently been extended by Buckner and Krienen [24], who proposed the ‘tethering hypothesis’, arguing that association cortex gains its functional attributes

## Significance Statement

We describe an overarching organization of large-scale connectivity that situates the default-mode network at the opposite end of a spectrum from primary sensory and motor regions. This topography, based on the differentiation of connectivity patterns, is also embedded in the spatial distance along the cortical surface between these respective systems. In addition, this connectivity gradient accounts for the respective positions of canonical networks and captures a functional spectrum from perception and action to more abstract cognitive functions. These results suggest that the default-mode network consists of regions at the top of a representational hierarchy that describe the current cognitive landscape in the most abstract terms.

DSM, MP, EJ, JS, Conception and design, Analysis and interpretation of data, Drafting or revising the article; SSG, AG, MF, JMH, GL, SE, FXC, Analysis and interpretation of data, Drafting or revising the article; GB, Contributed unpublished, essential data, or reagents.

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<sup>1</sup>To whom correspondence should be addressed. E-mail: margulies@cbs.mpg.de

125 through its increasing spatial distance from the constraints  
126 that determine the functional specialization of primary cortex.  
127 These viewpoints suggest that there may be macroscale gradi-  
128 ents that integrate information across multiple domains into  
129 progressively more abstract representations, in which local  
130 gradients within specific cortical systems could be situated  
131 and understood.

132 One large-scale cortical system whose function remains  
133 unclear is the DMN. Initially identified through its tendency  
134 to deactivate during externally-oriented tasks [25], the DMN  
135 has since been shown to activate in tasks that depend on  
136 information retrieved from memory such as remembering the  
137 past or thinking about the future, or considering the men-  
138 tal states of others (for reviews, see [10, 26]). The DMN is  
139 also known to play a role in states that are less related to  
140 ongoing environmental events, such as daydreaming and mind-  
141 wandering [27–30], and contributes to lapses in the integrity  
142 of external processing [31]. A consensus view on the role of  
143 the DMN in human cognition is still lacking, however, because  
144 of the increasing number of cognitive domains in which it has  
145 been implicated. As well as playing an active role during states  
146 such as autobiographical memory retrieval, social cognition,  
147 and future thinking, the DMN has recently been shown to  
148 operate in concert with regions implicated in cognitive control  
149 during complex working memory tasks [32–36]. This emerging  
150 evidence illustrates that the DMN is not tied to a specific form  
151 of informational content, leading to suggestions that it acts as  
152 a hub that integrates representational information across the  
153 cortex [30, 37].

154 To understand the topographic organization of the cerebral  
155 cortex at the macroscale [38], we explore how the principal  
156 variance in cortical connectivity relates to the topography of  
157 structure and function by addressing four key questions: (a) Is  
158 there a macroscale gradient of connectivity in the human brain  
159 that reflects the systematic integration across modalities in a  
160 hierarchical fashion? (b) Does this macroscale organization  
161 relate to the geometric structure of the cortex? (c) Does the  
162 organization captured by the principal gradient account for the  
163 spatial distribution of large-scale networks and the associated  
164 functions across the cortex? (d) Do these observations provide  
165 a framework for understanding the functional role of the DMN  
166 in cognition?

## 168 Results

169 We began our analysis by characterizing the components de-  
170 scribing the maximum variance in functional connectivity  
171 patterns — the extent to which nodes agree in the spatial dis-  
172 tribution of correlations — across the human cerebral cortex  
173 (Figures 1 & S2). The functional connectivity matrix con-  
174 sisted of 91282 cortical and subcortical ‘grayordinates’ with a  
175 resolution of 2 mm from the preprocessed dense connectome  
176 S900 release of the Human Connectome Project (HCP) [39].  
177 These data were based on one hour of resting-state fMRI  
178 data acquired from 820 healthy adult individuals. No further  
179 processing of the connectivity matrices beyond those already  
180 implemented by the HCP, which included minimal spatial  
181 smoothing of 2 mm FWHM [40], were conducted.

182 Rather than delineating discrete network parcellations, we  
183 implemented a method that captures gradients in connectivity  
184 patterns over space — a cortical feature, termed ‘connec-  
185 topies’ [41]. This method, known as diffusion embedding [42],

187 allows local and long distance connections to be projected into  
188 a common space more effectively than approaches that use  
189 linear dimensionality reduction, such as principal component  
190 analysis (see Supporting Information (SI)). The resultant com-  
191 ponents, which we describe here as ‘gradients’, are unitless,  
192 and identify the position of nodes along the respective em-  
193 bedding axis that encodes the dominant differences in nodes’  
194 connectivity patterns.

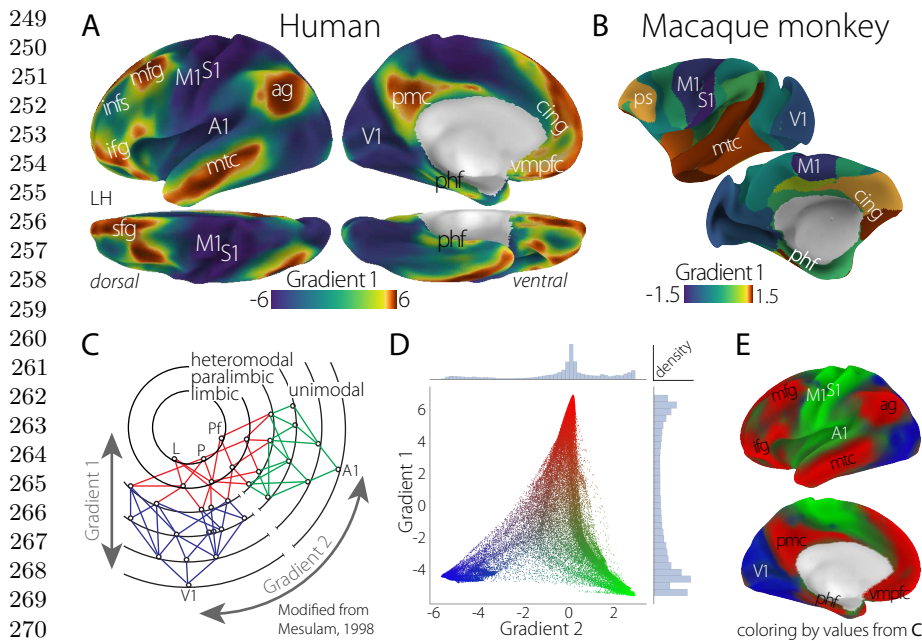
## The principal gradient in humans and macaque monkeys.

196 The principal gradient (Figure 1A), which accounts for the  
197 greatest variance in connectivity in the human brain (see Fig-  
198 ure S1), is anchored at one end by the primary and unimodal  
199 visual, somatosensory/motor, and auditory regions. At the  
200 other end are regions including the angular gyrus, rostral an-  
201 terior cingulate, posteromedial cortex, middle temporal gyrus,  
202 and middle and superior frontal gyri — regions that in humans  
203 are collectively described as the default-mode network (DMN).  
204 Regions situated between the two extreme ends of the principal  
205 gradient include the inferior frontal sulcus, intraparietal sulcus,  
206 and the inferior temporal sulcus, constituting heteromodal  
207 integration and higher-order cognitive regions.

208 The initial proposal of Mesulam was motivated by tract-  
209 tracing studies conducted in the macaque monkey. To deter-  
210 mine whether our method would generalize to this form of  
211 data, we performed the same embedding analysis on a publicly  
212 available database of tract-tracing studies conducted in the  
213 macaque monkey. The principal gradient of the macaque mon-  
214 key cerebral cortex is presented in Figure 1B, and, similar to  
215 the human functional connectivity-based results, is anchored at  
216 one end by visual and somatosensory/motor regions and at the  
217 other by higher-order transmodal regions in the temporal lobe  
218 and the medial and lateral prefrontal cortex. The cross-species  
219 correspondence of the principal gradient suggests this axis of  
220 connectivity variation is phylogenetically conserved, and may  
221 represent a primary dimension of cortical expansion [43].

222 The topography of the principal gradient in both the hu-  
223 man and macaque monkey is consistent with the claim that  
224 cortical connectivity is organized along a dimension spanning  
225 primary/unimodal and transmodal regions — a hypothesis  
226 that is summarized schematically along the ‘Gradient 1’ di-  
227 mension in Figure 1C. However, for this spectrum to indi-  
228 cate hierarchical integration across distinct modalities, the  
229 following connectivity component should distinguish between  
230 primary modalities, as indicated by the dimension ‘Gradient  
231 2’ in Figure 1C.

232 Consistent with Mesulam’s hypothesis [23, and Figure 1C],  
233 the component accounting for the second-most variance in  
234 connectivity in the human brain differentiates regions solely  
235 within the unimodal-end of the principal gradient (Figure 1D).  
236 One end of the spectrum is characterized by regions of the  
237 occipital cortex implicated in processing of visual input, while  
238 the opposite end includes the somatosensory and motor re-  
239 gions surrounding the central sulcus as well as the auditory  
240 regions of the temporal perisylvian region (Figure 1E). The  
241 convergence described by the first two connectivity gradients  
242 across sensory/motor modalities, and towards a singular set of  
243 nodes within transmodal cortex, is consistent with the claim  
244 that the principal gradient is organized along a dimension  
245 that integrates unimodal regions in a hierarchical manner (Fig-  
246 ure 1C). Moreover, the principal gradient, anchored at one end  
247 by the DMN, contains within it several local processing gra-  
248



**Fig. 1.** The principal gradient of connectivity in both the human (A) and macaque monkey (B) cortices demonstrates a spectrum between unimodal regions (dark blue) and transmodal regions (sienna), which in the human cortex peaks in regions corresponding to the default-mode network. The proximity of colors can be interpreted as greater similarity of connectivity patterns. (C) The illustration of connectivity organization suggested by Mesulam [23] proposes a hierarchy of processing from distinct unimodal areas to integrative transmodal areas. Labels 'Gradient 1/2', which were not included in the original figure, correspond to the results in (D). (D) A scatter plot of the first two connectivity embedding gradients. Gradient 1 extends between primary sensorimotor and transmodal regions (red). Gradient 2 separates somatomotor and auditory cortex (green) from visual cortex (blue). Histograms depicting the distribution of values are presented on the respective axes. (E) Colors from the scatter plot are presented on the cortical surface for anatomical orientation. V1/A1/M1/S1, primary visual/auditory/motor/somatosensory; ag, angular gyrus; mfg/ifg/sfg, middle/inferior/superior frontal gyrus; infs, intermediate frontal sulcus; pmc, posteromedial cortex; phf, parahippocampal formation; cing, anterior cingulate cortex; vmprc, ventromedial prefrontal cortex; mtg, middle temporal cortex, L, limbic; P, parietal; Pf, prefrontal.

dients that have already been described within the temporal and frontal lobes [12–15, 17–19]. Further gradients describing progressively less connectivity variance are available in Figure S2.

**DMN peaks of the principal gradient are equidistant from primary areas.** Having characterized the topography of a principal gradient in connectivity, we next investigated whether it is related to the intrinsic geometry of the cortex. To do so, we examined whether regions at the extreme of the DMN-end occupy spatial locations that are maximally distant along the cortical surface from unimodal regions. We selected 7 peak cortical nodes across the DMN clusters of the principal gradient, and calculated the minimum geodesic distance from all other nodes to any of these 'seed' nodes (see SI for further description of methods).

Figure 2 demonstrates that cortical distance reproduces many features of the spatial embedding of the principal gradient. Four of the peak DMN nodes are equidistant from the central sulcus, which is the topographical landmark of primary somatosensory/motor cortex. Likewise, we observe a similar correspondence with the calcarine sulcus, marking the location of primary visual cortex. More generally, distance clearly increases with lower principal gradient values, with an especially rapid transition in the connectivity gradient between 25–40 mm and plateaus at the extremes (Figure 2B). This relationship is nevertheless captured by a linear fit ( $R^2 = 0.55$ ). It is noteworthy that beyond a distance of 40 mm from DMN peaks, the cortex exclusively consists of unimodal regions. In similar analyses of macaque monkey cortical distance (Figure S3), we observed a comparable distance threshold for unimodal regions. In sum, this analysis demonstrates that the principal connectivity gradient reflects macrostructural features of cortical organization: the nodes corresponding to one extreme end of the gradient — core regions of the DMN — are maximally distant from regions that directly govern perception and action.

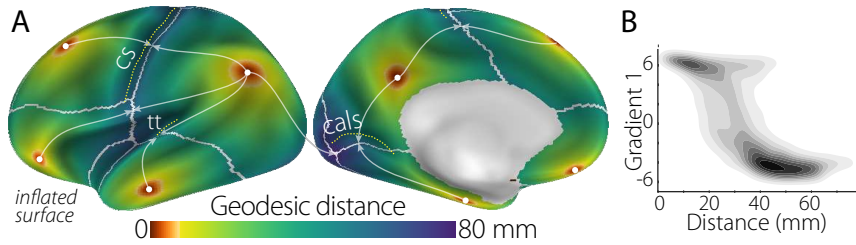
**The principal gradient captures the spatial layout of large-scale networks.** We next examined the extent to which the principal gradient captures the macroscale layout of intrinsic functional connectivity networks. Despite the high reproducibility of large-scale resting-state networks [1, 44–46], there is no clear over-arching spatial schema to explain the transition of one network to another. We examined the widely-used 7-network parcellation from Yeo et al. [2] with respect to the position of each network along the principal gradient (Figure 3A). (Results using the 17-network parcellation from [2] are presented in Figure S5.)

Figure 3 demonstrates that networks are not randomly distributed along this dimension: instead, as demonstrated in the box plots of Figure 3B, cortical nodes from the same network tend to cluster at similar positions. Importantly, the DMN identified in this parcellation (red) occupies one extreme position along the principal gradient and is maximally separated from visual (purple) and motor (blue) networks, which lie at the other extreme. One exception is the limbic network (beige), which captures an extensive range of values. However, the spatial distribution of this network may be accounted for by low signal-to-noise within the original data used for parcellation [2], and it may thus not accurately reflect the connectivity of its constituent regions.

This analysis therefore demonstrates that the principal gradient of connectivity provides a framework for the spatial ordering of large-scale networks. In addition, the principal gradient captures similar, repeating transitions between these networks, which occur across cortical lobes (Figure 3C). We represent this consistent arrangement as a schematic illustration in Figure 3D. Notably, outlier gradient values for each network are located predominantly at their boundaries (Figure S4), suggesting that in some cases the principal gradient describes gradual connectivity transitions that are obscured by discrete network parcellation.

**Distribution of functions along the principal gradient.** Our final analysis explored whether the regions located at the DMN-

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**Fig. 2.** (A) The minimum geodesic distance (in mm) from each point on the cortical surface to 7 seed nodes located in the positive peak of the principal gradient. Morphological landmarks of primary areas, denoted by white dotted lines, such as the central sulcus (*cs*; somatosensory/motor), calcarine sulcus (*cals*; visual), and transverse temporal gyrus (*tt*, auditory) are equidistant from the surrounding DMN peaks (illustrated by arrows). Gray lines mark the calculated equidistant line. (B) The contour scatter plot demonstrates the negative relationship between geodesic distance from the 7 positive peak locations and the principal gradient ( $R^2 = 0.55$ ).

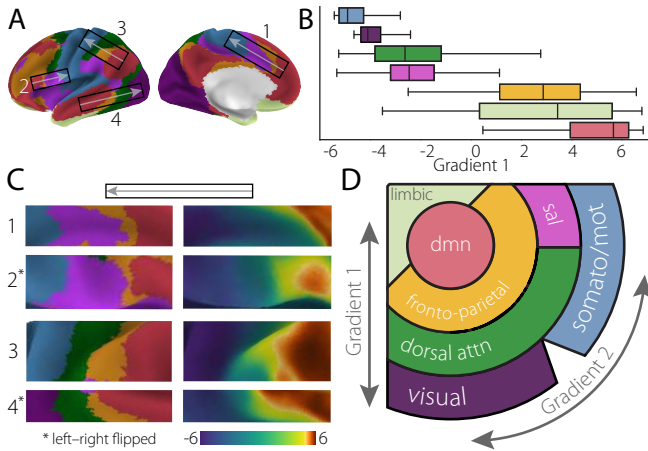
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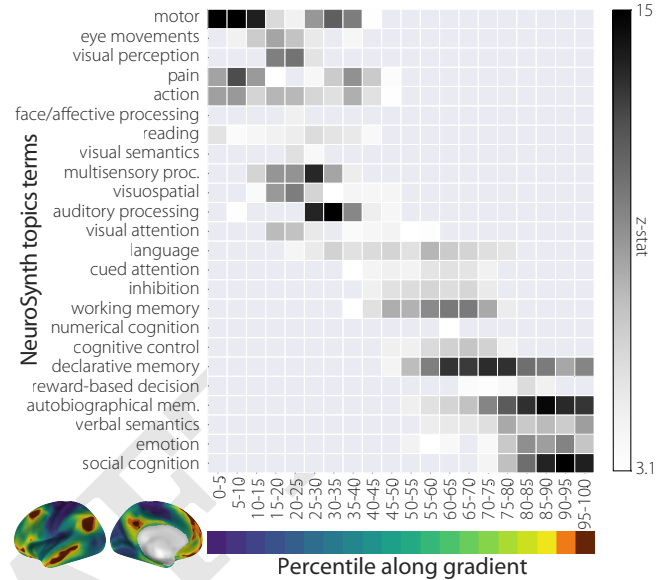


**Fig. 3.** (A) The principal gradient values from each of 7-networks [2] are presented as (B) box plots ordered by the mean value. (C) Illustrative cutouts taken from (A) to demonstrate the repeated patterns of network spatial adjacency captured by the principal gradient. Arrows in (A) indicate the corresponding orientation of the cutouts. (D) A schematic of the spatial relationships of canonical resting-state networks [2] applying the schema suggested by [23] presented in Figure 1C. dmn, default-mode network; sal, salience network; dorsal attn, dorsal attention network, somato/mot, somatosensory/motor network.

extreme of the gradient serve functions that are abstracted from perception and action. We conducted a meta-analysis using the NeuroSynth database [47] (see Figure S6 & S7 for corresponding analysis using the BrainMap database [48]), and examined the association between a list of topic terms with regions-of-interest created from 5-percentile bins of the principal gradient. Topic terms were sorted by their weighted average position along the gradient, revealing a systematic shift in function. Figure 4 demonstrates that the unimodal-end is characterized by terms depicting acting and perceiving, such as ‘motor’, ‘visual perception’, ‘multisensory processing’, and ‘auditory processing’, while the end characterized by the DMN emphasizes terms such as ‘social cognition’, ‘verbal semantics’, and ‘autobiographical memory’ — tasks which rely on complex representations abstracted away from specific sensory and motor processes. Between the extremes we observe domain-general functions such as ‘cued attention’, ‘inhibition’, and ‘working memory’ in regions corresponding to the dorsal attention and salience networks above (Figure 3D).

## Discussion

Our analysis characterized a principal gradient of cortical organization in the human connectome, which is anchored at one end by systems implicated in perceiving and acting, and at the other, by transmodal association regions, corresponding in



**Fig. 4.** NeuroSynth meta-analysis of regions-of-interest along the principal gradient using 24 topic terms. Terms are ordered by the weighted mean of their location along the gradient. Sensory processing terms are located at the top, followed by domain-general cognitive functions, and then by higher-order abstract cognitive and memory-related processes. Similar results using the BrainMap database are available in SI.

humans to the default-mode network (DMN; Figure 1). A comparative analysis using tract-tracing data from studies in the macaque monkey found a corresponding gradient, providing initial evidence that this axis of connectivity variation may be phylogenetically conserved. The observation that the principal gradient corresponds to the intrinsic geometry of the cortex — regions in the DMN have the greatest geodesic distance along the cortical surface from primary sensory-motor areas — further indicates this axis may provide a crucial blueprint for cortical organization (Figure 2). We additionally found that large-scale networks are arranged along this axis, with the same transitions between consistently adjacent networks occurring throughout the cortex (Figure 3). Finally, a task-based meta-analysis characterizing the functional attributes of this gradient showed a spectrum of increasing abstraction that follows the transition from unimodal cortex to the extreme end of the gradient in the DMN (Figure 4).

The location of the DMN at one extreme end of the principal gradient provides an organizing principle for understanding its role in cognition. First, these findings provide anatomical support for why the DMN has been associated with processes that are unrelated to immediate stimulus input, such

497 as daydreaming or mind-wandering [27, 28, 30]. The DMN is  
 498 at a maximal distance from systems involved in perception  
 499 and action in both functional connectivity and anatomical  
 500 space, indicating that the neural activity in these regions is  
 501 likely to be comparably insulated from direct environmental  
 502 input [49, 50]. Second, the location of the DMN as equidistant  
 503 from all sensory/motor systems is aligned with its broad  
 504 range of functions that require integration between multiple  
 505 sensory systems, including episodic [51] and semantic mem-  
 506 ory [52–54], social cognition [55, 56], goal-directed working  
 507 memory tasks [26, 32, 33, 35] and reward-guided decision mak-  
 508 ing [57, 58]. The two cardinal features of the DMN related  
 509 to abstraction — stimulus independence and content hetero-  
 510 geneity — can be accounted for by its position at the end of  
 511 a topographical hierarchy that is equidistant from unimodal  
 512 systems, thus acting as a hub of integration across multiple  
 513 sensory modalities [37] (Figure 3D).

514 The principal gradient illustrates a broader topographic  
 515 organization of large-scale connectivity [38] that accounts for  
 516 the spatial arrangement of local processing streams through-  
 517 out the cerebral cortex. Gradients in both the temporal and  
 518 prefrontal cortex are apparent in Figure 1, demonstrating that  
 519 these hierarchies are not isolated local phenomena; they emerge  
 520 as elements of a spectrum that begins within input–output  
 521 systems and ends with the DMN. Notably, our results are  
 522 consistent with a recent modification of the rostral–caudal pro-  
 523 cessing gradient described within lateral frontal cortex [59, 60].  
 524 Rather than the more rostral areas being further along in  
 525 the processing hierarchy [18, 19], two distinct hierarchical gra-  
 526 dients of temporal- and feature-related abstraction converge  
 527 in middle lateral prefrontal cortex [60]. The consistency be-  
 528 tween the principal gradient and this revised lateral prefrontal  
 529 hierarchy suggests it may provide a source for future studies  
 530 investigating the detailed topography of local processing  
 531 streams.

532 In addition to incorporating local processing streams within  
 533 a global framework, the principal gradient situates discrete  
 534 large-scale connectivity networks along a continuous spectrum.  
 535 With recent landmark advances in multimodal cortical parcel-  
 536 lation [61], the current approach provides a complementary  
 537 means to describe the gestalt of the cortical mosaic. Future  
 538 studies are needed to better characterize the types of tran-  
 539 sitions between different patterns of large-scale connectivity,  
 540 and to identify where processing occurs in a step-wise [11] or  
 541 ‘gradiential’ manner [22].

542 It is now widely accepted that the DMN is important be-  
 543 cause it permits cognitive processing that is independent of  
 544 the here and now. This capacity is adaptive because it per-  
 545 mits flexibility: more abstract representations of a stimulus  
 546 enable the generation of alternative behaviors, allowing origi-  
 547 nal and creative thoughts to emerge [62]. Along those lines, a  
 548 ‘positive-negative’ axis of brain-behavior covariation describes  
 549 a similar connectivity spectrum, distinguishing the DMN from  
 550 sensory/motor regions [63]. As Mesulam stated, however, the  
 551 capacity for abstraction is a double-edged sword. Beyond sup-  
 552 porting states of creativity and planning [64, 65], the DMN has  
 553 also been implicated in almost all psychiatric conditions [66],  
 554 indicating that there are costs, as well as benefits that accrue  
 555 from the capacity to apprehend the world as it might be rather  
 556 than seeing it as it is right now.

## Materials and Methods

All MRI data used in this study were publicly available and  
 anonymized. Participant recruitment procedures and informed  
 consent forms, including consent to share de-identified data, were  
 previously approved by the Washington University institutional  
 review board as part of the Human Connectome Project [39].

All software used in this study is openly available at:  
[neuroanatomyandconnectivity.github.io/gradient\\_analysis/](https://neuroanatomyandconnectivity.github.io/gradient_analysis/)

Further information regarding methods and Supporting Figures  
 are available in the Supporting Information.

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