

Evidence of Brain Modularity



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Synonyms

Brain community structure

Definition

Evidence of brain modularity is the empirical body of findings that demonstrates that the brain is organized into semiautonomous groups of neurons and brain regions that interact with one another through relatively sparse and long-distance pathways in the brain.

Introduction

Before there were brains, there was modularity. Modularity describes the extent to which a system has components that connect to or interact with other components, each of which is independent and functionally specialized. An example of a modular system is an electric circuit board made of

connected electric components. Each component of the circuit board is an autonomous module with a specific independent function, connected to other modules with similar or different functions. Biological modularity, like artificial modularity, provides the organism with robust and specialized functions. These functions can independently evolve, develop, and respond to change. From this perspective, it is unsurprising that modularity is ubiquitous across biological systems (Scholsser and Wagner 2004).

The human body comprises various modular systems such as the cardiovascular system, the respiratory system, the digestive and excretory system, the visual system, the auditory system, and the nervous system. Each system has organs that constitute system modules that work together to support the smooth functioning of the system and organism in its entirety. In the human nervous system, the visual system's main organs, the eyes, communicate with the brain to interpret light waves as images. The inner and outer ear in the auditory system communicate via the brain to help us hear sounds of varying frequencies, such as a high-pitched sound of a chalk screeching on the blackboard or a low-pitched sound of distant thunder. More generally, the nervous system is composed of the central nervous system (brain and spinal cord) and the peripheral nervous system. Within the central nervous system, the spinal cord of vertebrates is a modular system with many ganglia. The brain is the "master ganglion" in vertebrates, and within the brain, there are numerous modularized systems.

Modularity in the Brain

A new branch of neuroscience called “network neuroscience” (Bassett and Sporns 2017) uses computational approaches based in graph theory to describe the organization of anatomical and functional brain networks at different spatial and temporal resolution scales (Betzel and Bassett 2016). A brain network can be depicted mathematically as a graph $G = \{N, E\}$, where N is a set of nodes (such as neurons or brain regions) and E is a set of edges (such as dendritic or axonal connections) connecting pairs of nodes. Statistics developed in graph theory allow us to compute network properties over G to make statements about the organization and roles of nodes, edges, or indeed the entire network.

The edges (region-region relationships) in a brain network are typically defined by three types of connectivity: anatomical connectivity, functional connectivity, or effective connectivity (Park and Friston 2013). Anatomical connectivity refers to anatomical connections among regions or neurons in the brain. At a low level of organization, anatomical connectivity can be detected using labeled tracer injections (Gamanut et al. 2017). In humans, anatomical connectivity can be computed from diffusion imaging data that represents white-matter pathways among regions in the brain. In contrast, functional connectivity at a high level of organization is often computed from the pairwise relationships between nodes via signals of BOLD-fMRI or electroencephalography (EEG)/magnetoencephalography (MEG). BOLD-fMRI signal can be obtained by scanning in the MRI scanner. The EEG/MEG signals can be recorded via multichannel recording using a group of electrodes centered over distinct regions of the brain. At a high level of organization, entire functional and anatomical networks can be mapped in the human brain, forming human “connectomes” (Sporns et al. 2005).

Functional networks are assembled from estimates of statistical dependencies between neuronal or regional time series data. Specifically, functional connectivity is often defined by the correlation, coherence, mutual information, or other measures of associations between time

series across nodes. Functional connectivity does not give information about causality or directionality. In contrast, effective connectivity is estimated from the lagged relationships between nodal activity in BOLD-fMRI and EEG/MEG signals. It is sometimes interpreted to represent the potential influence one neural system exerts over another at the synaptic or cortical level. Effective connectivity can evaluate directed relationships between regions as it is estimated with models with lagged parameters (e.g., vector autoregression, Granger causality, structural equation modeling, or unified structural equation modeling) or with a model of physiological dynamics (e.g., dynamic causal modeling).

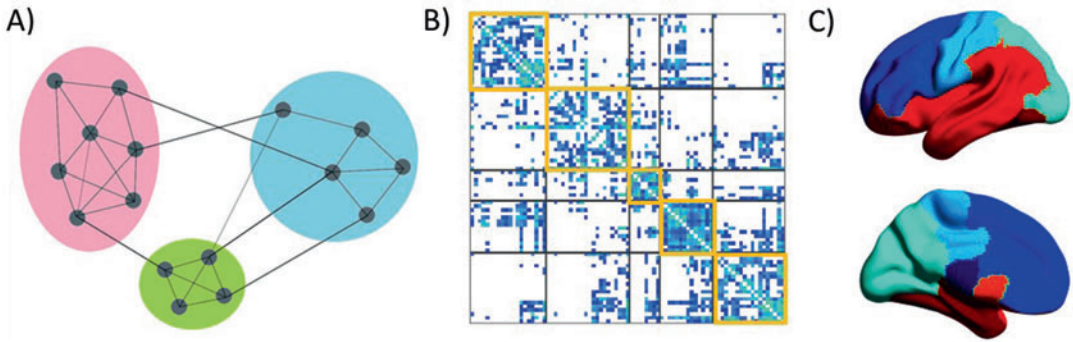
Once a graph is constructed that represents a network, statistical diagnostics can be used to describe the organization of functional or anatomical connections in the brain from local to global scales (Rubinov and Sporns 2010). “Mesoscale” diagnostics are those that describe the organization of the network in between these two scales. Modularity is a mesoscale property of a network: modularity describes the organization of nodes into groups based on their connection to one another within the brain. A network is modular when sets of nodes form densely interconnected groups with sparser connectivity between groups relative to a null expectation (Newman 2006) (Fig. 1).

While specific definitions of modularity vary, one popular mathematical expression is defined by Newman and Girvan (2004). Consider an undirected graph with adjacency matrix A_{ij} and a partition of this graph into clusters or modules defined by $\{c_i\}$, where c_i describes which module node i belongs to; Newman and Girvan’s modularity Q is defined as:

$$Q = \frac{1}{2m} \sum_{i,j} \left(A_{ij} - \frac{k_i k_j}{2m} \right) \delta(c_i, c_j).$$

where $k_i = \sum_j A_{ij}$ is the degree of each node, $m = \frac{1}{2} \sum_i k_i = \frac{1}{2} \sum_{ij} A_{ij}$ is the total number of edges, and $\delta(c_i, c_j)$ is defined as- $\delta(c_i, c_j) = 1$; if nodes i and j belong to the same module,

$\delta(c_i, c_j) = 0$; otherwise.



Evidence of Brain Modularity, Fig. 1 What does modularity look like? (a) In principle, modularity is the extent to which nodes (gray circles) are grouped into discrete communities (nodes grouped into communities schematically represented by different colored backgrounds) based on the pattern of connections among nodes. Communities may have different sizes and configurations of within- and between-module connectivity. (b) An example connectivity matrix (“graph”) constructed from anatomical diffusion imaging data from one healthy individual. Each row and

column represents an “edge” – here, the number of estimated white-matter connections between a pair of regions. The highlighted squares along the matrix diagonal are those identified to be a module using a *community detection* algorithm. The off-diagonal rectangles are therefore the connections between modules. (c) These modules can be mapped back into a brain volume. Here, different communities are represented in different colors on a brain surface

Conceptually, Newman’s modularity compares the fraction of within-module edges in the graph to the expected fraction of within-module edges in a random graph with the same degree sequence as given by the configuration model. The randomization of edges is done to preserve the degree of each node for use as a null model that defines the expectation for Q under a random network of the same degree as the original network.

The value of Q is normalized such that it always lies in the interval $(-1, 1)$. The value of Q depends on the partition resulting from a stochastic algorithm. Different methods for community detection have been developed to search for the partition of the graph that will maximize Q . Regardless of the specific algorithm, Q is a property of the partitioned graph and is considered a measure of modularity.

The notion of a “hub” is a key concept to understand the links within and between modules. Highly connected nodes in the brain may form links to multiple communities and are called connector hubs, which are more likely to be in the medial portions of the brain (Sporns et al. 2007). Connectors play important roles in intermodular communication. Regions that maintain relatively high connections within their own community form

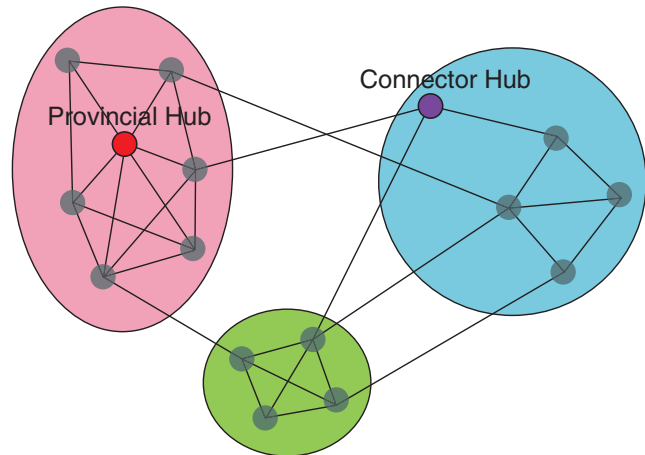
provincial hubs (Sporns et al. 2007; See Fig. 2). Hubs are thought to serve key roles governing organization within and between brain network modules by regulating intra- and intermodular information flow (Van den Heuvel and Sporns 2013).

Evidence of Brain Modularity (Functional and Anatomical Connections)

Evidence of brain modularity is widely observed both in anatomical and functional brain networks. Modules can allow rapid and efficient sharing of information among brain regions that tend to contribute to a common set of tasks or responses while promoting their functional specialization by creating boundaries that restrict the spread of information across the entire network. Anatomical networks are more stable on shorter timescales relative to functional networks. Functional networks can be highly variable, exhibiting spontaneous dynamic changes during rest as well as characteristic modulations in different task conditions (Eickhoff et al. 2011). Some major common findings have emerged regarding anatomical and functional brain modularity.

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Fig. 2 Schematic of hubs. A “provincial” hub (red) is a node with high connectivity with other nodes within a module. A “connector” hub (purple) is a node that connects multiple modules to one another



Anatomical Brain Networks

Modular organization at the anatomical level has been studied in both animal studies and human studies. In animal studies of the cat and the macaque, whole-brain anatomical connectivity has been obtained in tracer studies (Hilgetag et al. 2000). A network partition procedure identified four subnetworks, classified as the visual, auditory, somatosensorimotor, and frontolimbic systems (Hilgetag et al. 2000). This was an early example that the general notion of modularity recovers some of the basic assumptions within functional neurology and neuroanatomy. Another study that uncovered the modularity in mouse, rat, macaque, and human connectomes showed that most communities are assortative, while others form core-periphery and disassortative structures (Betz et al. 2017). Assortative communities are those composed of nodes with similar features (e.g., numbers of connections or “degree”). Core-peripheral communities are those with a densely intra-connected set of nodes with typically fewer peripherally connected nodes. Disassortative communities are those where nodes with quite different nodal features are associated with one another. Thus, within major networks in the brain, diverse roles in regulating information within communities can be observed, forming different putative roles in cognitive processes that are associated with variations in human performance (Betz et al. 2017).

In human in vivo neuroimaging studies, modularity has been examined in anatomical networks constructed from diffusion tractography used to

estimate cortical and subcortical connectivity. Examining anatomical network organization also helps us understand the functional networks commonly observed using functional neuroimaging techniques.

Modularity in anatomical brain networks can be observed early during brain development (Fan et al. 2011). The anatomical networks of early developing brains have small-world topology and nonrandom modular organization like that of adult brain networks. The so-called default-mode network is one of several major brain networks that emerges during the developmental phase from infancy and matures during brain development from adolescence to adulthood. The network activates “by default” even when a person is not involved in a task. Anatomically, the default-mode network consists of the dorsal medial subsystem and the medial temporal lobe subsystem. Like all brain networks, the default-mode network is a large-scale brain network of interacting brain regions known to have activity highly correlated with one other and distinct from other networks in the brain.

The density of connections in the brain increases from early development to adulthood, but reduces during the rest of the life-span, leading to sparsity in the module connections (Betz et al. 2014). The brain starts developing into modules at early development, and it continues through adolescent years. As an adult, the brain is developed into modules with functional relevant roles with dense connections between modules. As we

age, through the rest of the life-span, the brain experiences age-related changes leading to sparsity in the connections between the modules, potentially reducing intermodular communication and cognitive flexible performance (Song et al. 2014; Monge et al. 2017).

Modularity in anatomical networks also differs across the sexes. One study that involved a connection-wise analysis showed that male brains are structured to facilitate intra-hemispheric cortical connectivity, in the entire brain, except in the cerebellum (Ingalhalikar et al. 2014). Male brains have enhanced local, short range within-lobe connectivity. Networks in the male brain are more transitive, modular, and discrete to facilitate the within-lobe and within-hemispheric connectivity. Transitivity is characterized by the connectivity of a region to its neighbors. Male brains have higher transitivity than female brains which indicate that their brains have a greater disposition of nodes to form numerous strongly connected communities. Female brains are structured to facilitate higher interhemispheric connectivity. The connection-wise analysis was also used to examine gender differences during development. The connectivity profiles showed that adolescent and young adult males had higher intra-hemispheric connectivity and same-aged females had higher interhemispheric connectivity. This confirms that modularity in the brain networks begins from early development helping to form functionally independent modules in adult brains.

Anatomical network partitions exhibit a community structure that reproduces some functionally specialized networks, such as visual, auditory/language, somatosensorimotor, and superior parietal systems (Meunier et al. 2010). Moreover, anatomical network modularity shapes much, but not all, of the activity observed in functional modular networks (Honey et al. 2009; Hermundstad et al. 2013; Medaglia et al. 2017; Real et al. 2017; Sethi et al. 2017). However, modularity in some functional brain networks exceeds what can be interpreted from anatomy alone; thus, we need behavioral and cognitive manipulations linked to the connectivity to better understand the modularity in the brain.

Functional Brain Networks

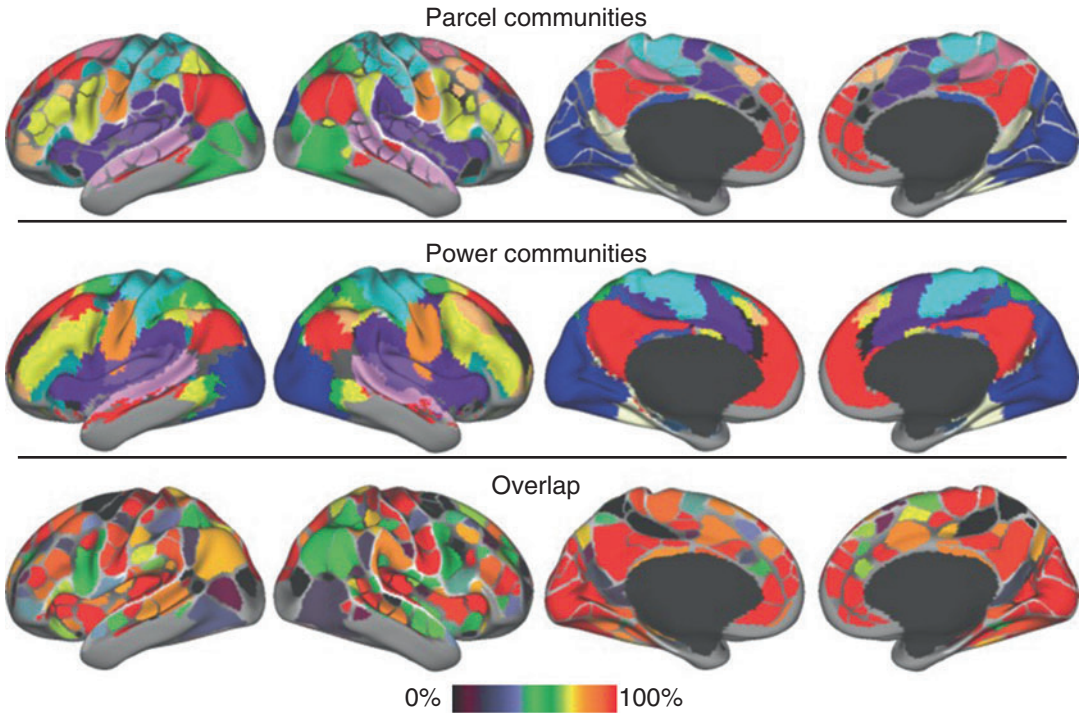
As anatomical brain networks help us understand the stable connections in the brain that facilitate communication among regions, functional brain networks help us understand the neurophysiological dynamics of the brain. Modularity in functional brain networks can be inferred from neural measurements such as those acquired during BOLD-fMRI imaging or from electrophysiological recording (EEG/MEG).

Functional MRI (fMRI)

The functional modules that are observed during rest using functional MRI form identifiable resting networks that organize task-related activity. This phenomenon has been observed in a few studies (Fig. 3).

Certain brain networks such as the frontal-parietal brain network are widely recruited in a variety of cognitively demanding tasks. The dorsolateral prefrontal cortex (DLPFC) is the area in the prefrontal cortex of the brain which is involved in executive functions such as working memory, cognitive flexibility, decision-making, inhibition, and abstract reasoning. An example of the behavioral task is the combined A-not-B/delayed response task, in which the subject finds a hidden object after a certain delay. This task requires holding information in mind, that is, using the working memory, which is one of the functions of DLPFC. Thus, the frontal-parietal brain networks are highly flexible and variably connected in the brain, which allows the frontal-parietal brain networks to use multiple networks when performing a task (Cole et al. 2013).

In another study, a region-to-region information mapping procedure was applied to real fMRI data to test its ability to infer cognitive information transfer in the human brain (Cole et al. 2016). Using a novel experimental task design meant to manipulate cognitive complexity, the brain network analysis utilized within-region vertex-level activation patterns along with vertex-to-vertex resting-state functional connectivity between regions to predict information content in each region – a measure of “flow” across the network. A region-to-region information transfer matrix was computed that represented the region-



Evidence of Brain Modularity, Fig. 3 Module organization example from fMRI. (a) Parcel communities: Communities identified with a community detection algorithm using the boundary map-derived parcels as network nodes. (b) Network structure of the brain calculated using every

voxel as a network node. (c) Spatial overlap of the voxel-wise and parcel wise community assignments. (Figure and caption reproduced with permission from Gordon et al. 2016)

to-region information transfers at the network level. Significant region-to-region information transfers were detected in all tasks suggesting that resting-state functional connectivity is relevant to cognitive task activations due to its role in shaping task-evoked activity flow among brain regions. Thus, resting-state functional connectivity topology describes the channels of information transfer across multiple functional networks and across multiple task content domains.

Another finding by Cole et al. (2016) was that regions within the frontoparietal network collectively act as flexible hub networks to communicate task-based demands in different cognitive domains. Individual differences in intrinsic network activity flow helped explain individual differences in cognitive task activations. In addition, the reconfiguration efficiency of the functional connectivity between specific networks and the rest of the brain is significantly correlated with

performance. The efficiency of some networks was related to performance on specific tasks (language task, reasoning task, and a working memory task), whereas other networks were associated with performance across multiple tasks. Efficiency in the salience network may reflect the ability to integrate and process multimodal information important for guiding behavior across a variety of task demands.

Another study showed that the cognitive control networks are global hubs, allowing for efficient information transfer across the brain. Functional and anatomical connectivity analyses illustrate that the default-mode network regions are the strongest global hubs. Using novel statistical methods with resting-state fMRI, high connectivity was demonstrated in both the cognitive control network regions and the default mode network regions. This within-module network connectivity changes can be one hallmark of

cognitively relevant brain activity (Sridharan et al. 2008; Ito et al. 2017; Medaglia et al. 2018).

Brain modularity varies across people, suggesting that the amount of information segregation and integration across the entire brain varies among people. Modular variability is related to the level of difference in the cognitive performance across individuals (Bassett et al. 2013; Yue et al. 2017). Cognitive performance is measured during cognitive processes that support sequential, goal-directed behavior.

A graph theoretic measure called the participation coefficient considers how a region's links are distributed across modules. When network links for regions are distributed across different modules (participation coefficients close to one), they help regulate intermodular communication between individual brain regions. Regions with low participation coefficients (close to zero) play a greater role in effecting communication patterns within their own module. Regions with high participant coefficients are considered parts of the default mode, salience, control, and attention networks suggesting that higher-order cognitive systems might owe parts of their functionality to the fact that their components span multiple modules and can efficiently integrate information from those sources (Betz et al. 2016).

Electrophysiological Techniques

Electrophysiological techniques are another way to measure the functional connectivity and modularity in brain networks. EEG and MEG have high temporal resolution but low spatial resolution, forming a natural complement to BOLD fMRI. Modularity in brain networks can also be observed using electrophysiological techniques. In one study, MEG electrodes were used to measure levels of synchronization in the delta to gamma frequency bands in a resting-state task in healthy individuals. Undirected unweighted graphs obtained by thresholding matrices of synchronization likelihood values showed that in the delta, theta, and gamma (>30 Hz) frequency bands, functional networks exhibited the property of “small-world networks.” This showed that the brain might be organized for efficient information processing, connecting different brain areas (modules) by

connections in the brain (Stam 2004). In another MEG study analyzing the connectivity structure in normal brains, brains of healthy individuals exhibited sparse connections between modules (Chavez et al. 2010). These results suggest that modularity plays a key role in the functional organization of brain areas, maintaining relative specialization of individual modules.

EEG studies have also identified the presence of small-world networks (Micheloyannis et al. 2006). The small-world nature of the EEG networks is negatively correlated with the level of intellectual functioning. The small-world character of EEG networks is also decreased in students (aged 21–26 years) compared to children (8–12 years) in the beta and gamma bands. Thus, the “small-world” network organization is observed in this study as well from early development to adulthood (Micheloyannis et al. 2009).

Modules and the Mind

In a cognitive context, Machery suggested a “massive modularity hypothesis” (Machery 2007). The massive modularity hypothesis proposes that the human mind consists of many innate, domain-specific modules. These modules have putatively evolved due to natural selection and are functionally distinct. Many cognitive competences such as choosing one's food habits, spatial navigation, seeing, and face recognition are supported by the modules. However, the routing and domain-integration demands in certain cognitive tasks have caused many commentators to challenge this pure modularity of the mind. For example, there are some cognitive tasks such as reading which could use many modules together or support “domain-general” and integrative processes in cognition (Carruthers 2006). Moreover, the shared variance among cognitive domains across individuals has been argued to suggest that domain-general mechanisms must exist or alternatively that the parts that compose one domain's function contribute to multiple domains (Rabaglia et al. 2011). While these debates are ongoing, a fundamental issue remains whether and how cognitive modules map to empirically detected brain modules. However, there are several potential evolutionary

advantages to brain modularity in general even if their precise cognitive relevance has not been fully clarified.

Evolutionary Origins and Selection of Brain Modularity

Brain modularity may directly or indirectly provide an organism with survival and reproductive advantages. Specifically, as described above, modularity balances specialized and integrated processing. Modular networks can engage in specialized information processing, perform focal functions, and support complex neural dynamics. In addition, modularity provides functional robustness and may in principle make the brain more naturally adaptable. Aging and disease lead to a decrease in brain modularity which reduces the ability of these systems to respond to external stress. Modular brain systems are more robust because the effect of harmful perturbations can be isolated to specific modules. In addition, if one module fails, the rest of the brain may be left relatively unaffected by having other modules perform the lost function. Thus, the brain is neuroplastic. Once a neural system evolves a basic modular architecture, it can facilitate further evolutionary adaptation. Components of modular systems can evolve semi-independently because different parts of system can be optimized separately without drastically interfering with the functioning of other parts. Moreover, different modules can be combined to create new functions. Within a modular system, information can be stored in pieces or swapped in large chunks from one module to another (Lorenz et al. 2011).

A key constraint on brain evolution concerns the energy costs and geometric constraints associated with specific brain network configurations. The wiring cost of the brain network is a fundamental trait that contributes to the brain's modular organization (Betz et al. 2016). The brain's restricted energy resources form a constraint on connection lengths, which becomes skewed in favor of low-cost connections. Some features of brain modularity suggest that evolution has provided an economical wiring solution that

optimizes modularity under this constraint. Brain networks favor short-range connections that densely connect nearby areas, which contribute on key aspect to the modular clustering observed in “small-world” brain networks, facilitating local processing. However, the brain still has a small number of long-range connections which have been preserved over the course of evolution. These connections are a result of the trade-off between the formation of connections that reduce the network's wiring cost and those that improve its functionality. Long-distance connections are extremely important for brain function, because they improve the efficacy of interregional communication and information transfer by reducing the average number of processing steps in the network, mediating communication through many hubs in the brain. This means that they are highly involved in the shortest paths across brain networks. Long-distance connections are also disproportionately observed along the brain's longest axis, facilitating communication all the way from the anterior frontal cortex to the visual cortex. Thus, evolutionary selection has favored economical, modular brain networks that facilitate robust, flexible, and adaptive processing throughout the organism's life-span and over evolutionary time.

Conclusion

Like many biological organisms and systems, the human brain exhibits modularity from early development to adulthood. In adulthood, the modules become refined and perform tasks under diverse demands to achieve goals. Brain modularity potentially provides evolutionary fitness by providing specialized, modifiable, and robust bases for cognitive functions. Thus, modularity in the human brain is a pervasive, dynamic, and essential phenomenon throughout the life-span.

Cross-References

- [Adaptation and Natural Selection](#)
- [Adaptations Designed to Deliver Benefits](#)
- [Adaptations: Product of Evolution](#)

- Adaptive Plasticity
- All Psychology is Evolutionary Psychology
- Brain Development
- Brain Growth Throughout Adolescence
- Brain Size and Complexity
- Carruthers on Massive Modularity
- Evidence for Modularity
- Modularity
- Modularity of Mind
- Relative Brain Size, Encephalization Quotient
- Sex Differences in Cognitive Development
- Theory of Mind and Evidence of Brain Modularity

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