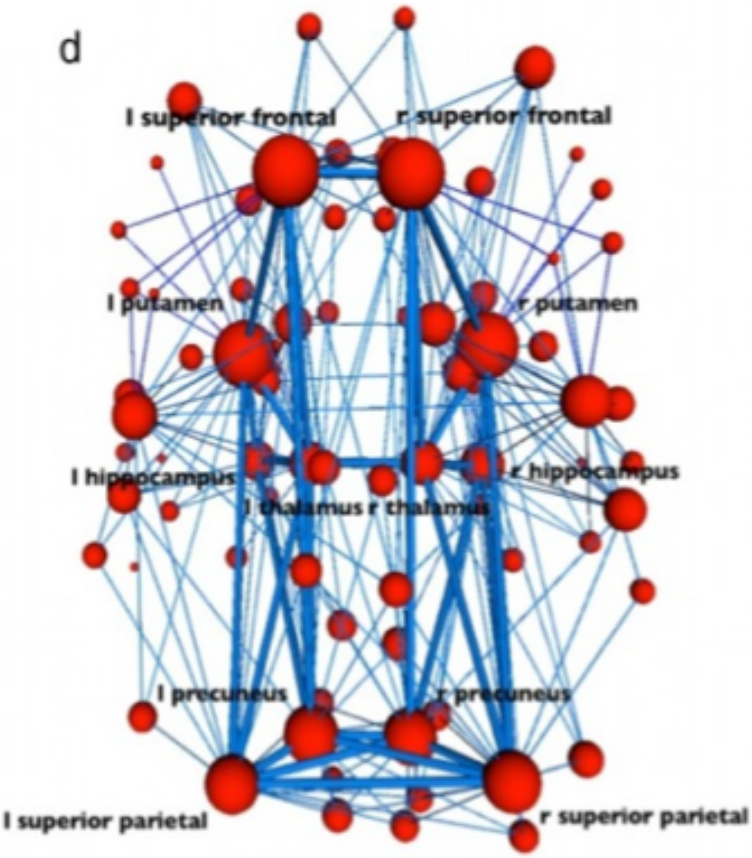
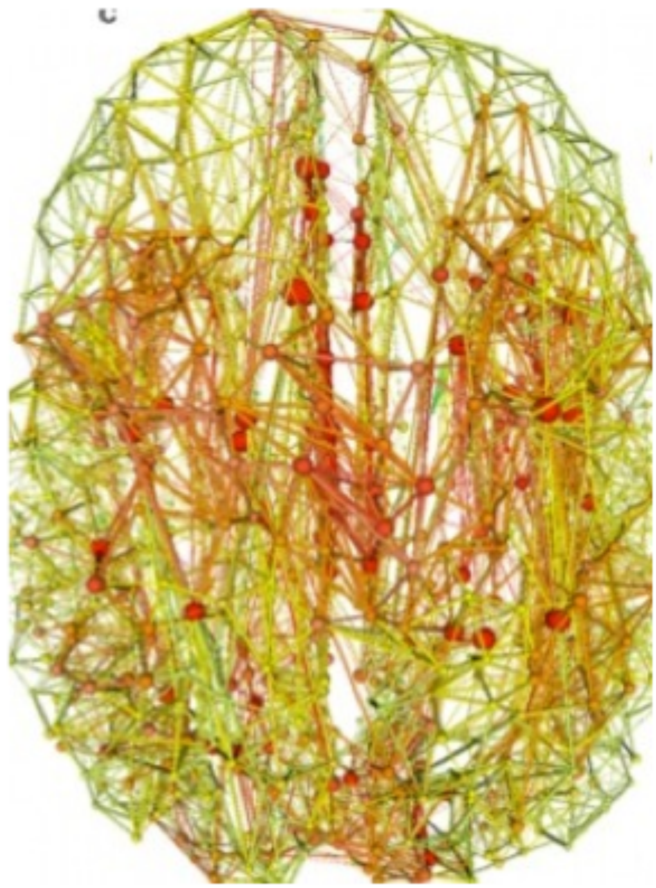
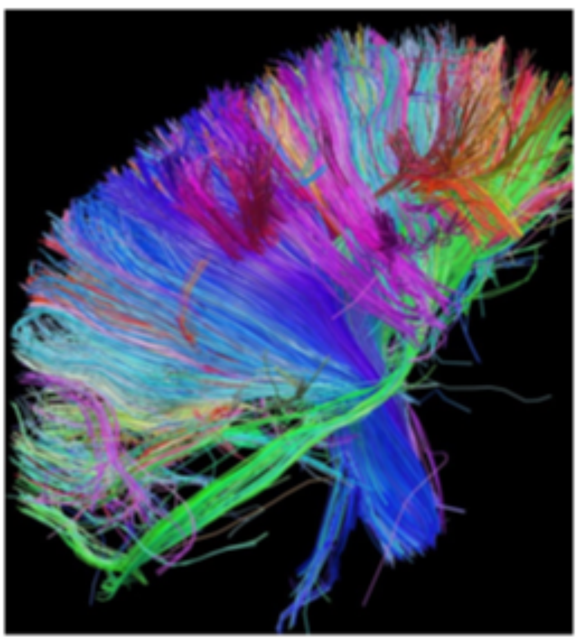
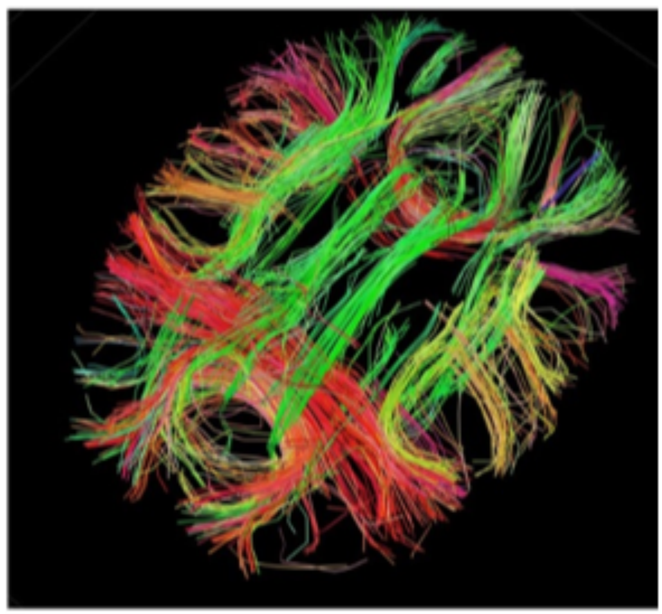
Your brain is a network: The Human Connectome and brain network research notebook (Dr. Kevin McGrew: 8-8-12







White Matter Fibers, Brainstem and above



White Matter Fibers, connecting gyri and hemispheres

THE CREATIVITY POST
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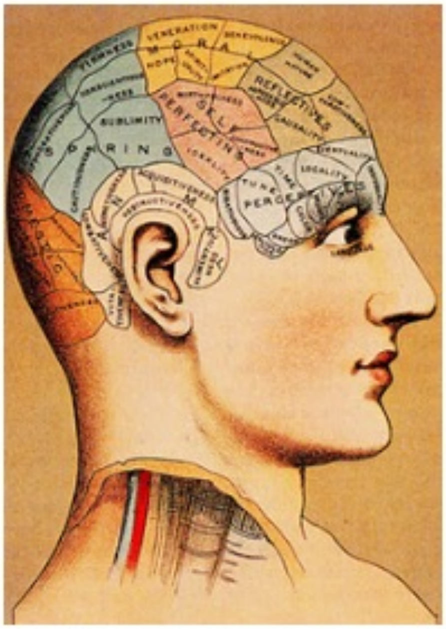
The Brain as a Network: Focusing Your Network

By Dr. Kevin McGrew | Dec 22, 2011

Synopsis

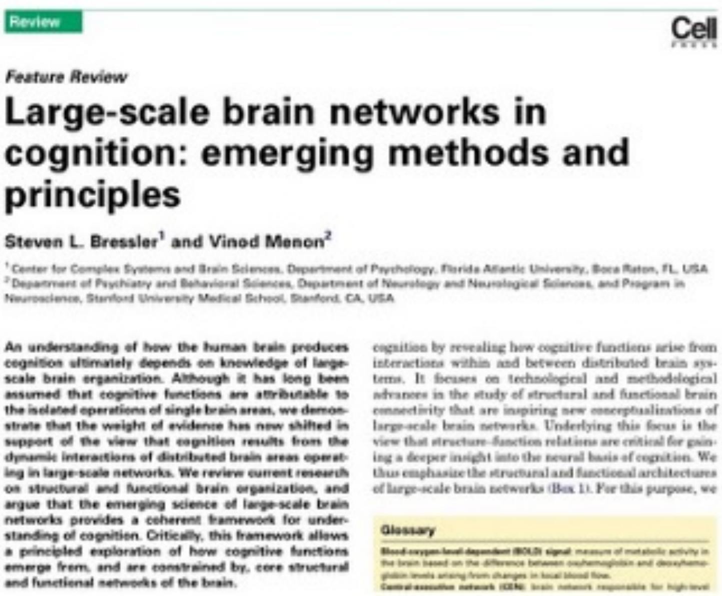
Contemporary neuroscience research suggests that cognition is the result of a number of large scale brain networks that require efficient brain rhythm or synchronization.

Man has always known that the brain is the center of human behavior. Early attempts at understanding which locations in the brain controlled different functions were non-scientific and included such practices as phrenology. This pseudoscience believed that by feeling the bumps of a persons head it was possible to draw conclusions about specific brain functions and traits of the person.



Eventually brain science revealed that different regions of the brain where specialized for different specific cognitive processes (but it was not related to the phrenological brain bump maps). This has been called the modular or functional specialization view of the brain, which is grounded in the conclusion that different brain areas acted more-or-less as independent mechanisms for completing specific cognitive functions.

One of the most exciting developments in contemporary neuroscience is the recognition that the human brain processes information via different *brain circuits or loop*s which at a higher level can be studied as *large scale brain networks.* Although the modular view still provides important brain insights, the accumulating evidence suggests that it has serious limitations and might in fact be misleading (Bresslor and Menon, 2010). One of the best summaries of this cutting edge research is that by Bresslor and Menon.



Review

Cell

Feature Review

Large-scale brain networks in cognition: emerging methods and principles

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An understanding of how the human brain produces cognition ultimately depends on knowledge of large-scale brain organization. Although it has long been assumed that cognitive functions are attributable to the isolated operations of single brain areas, we demonstrate that the weight of evidence has now shifted in support of the view that cognition results from the dynamic interactions of distributed brain areas operating in large-scale networks. We review current research on structural and functional brain organization, and argue that the emerging science of large-scale brain networks provides a coherent framework for understanding of cognition. Critically, this framework allows a principled exploration of how cognitive functions emerge from, and are constrained by, core structural and functional networks of the brain.

cognition by revealing how cognitive functions arise from interactions within and between distributed brain systems. It focuses on technological and methodological advances in the study of structural and functional brain connectivity that are inspiring new conceptualizations of large-scale brain networks. Underlying this focus is the view that structure–function relations are critical for gaining a deeper insight into the neural basis of cognition. We thus emphasize the structural and functional architectures of large-scale brain networks (Box 1). For this purpose, we

Glossary

Blood-oxygen-level-dependent (BOLD) signal: measure of metabolic activity in the brain based on the difference between oxyhemoglobin and deoxyhemoglobin levels arising from changes in local blood flow.
Central-executive network (CEN): brain network responsible for high-level

Large scale brain network research suggests that congitive functioning is the result of interactions or *communication between different brain systems distributed throughout the brai*n. That is, when performing a particular task, just one isolated brain area is not working alone. Instead, different areas of the brain, often far apart from each other within the geogrpahic space of the brain, are communicating through a fast-paced sychronized set of brain signals. These networks can be considered *preferred pathway*s for sending signals back and forth to perform a specific set of cognitive or motor behaviors.

To understand preferred neural pathways, think of walking on a college campus where there are paved sidewalks connecting different buildings that house specialized knowledge and activities. If you have spent anytime on a college campus, one typically finds foot-worn short cuts in the grass that are the preferred (and more efficient) means by which most people move between building A and B. The combined set of frequently used paved and unpaved pathways are the most efficient or preferred pathways for moving efficiently between buildings. The human brain has developed preferred communication pathays that link together different brain circuits or loops in order to quickly and efficiently complete specific tasks.

According to Bresslor and Menon (2010), "*a large-scale functional network can therefore be defined as a collection of interconnected brain areas that interact to perform circumscribed functions.*" More importantly, component brain areas in these large-scale brain networks perform different roles. Some act as *controllers or task switchers* that coordinate, direct and synchronize the involvement of other brain networks. Other brain networks handle the flow of sensory or motor information and engage in concious manipulation of the information in the form of "thinking."

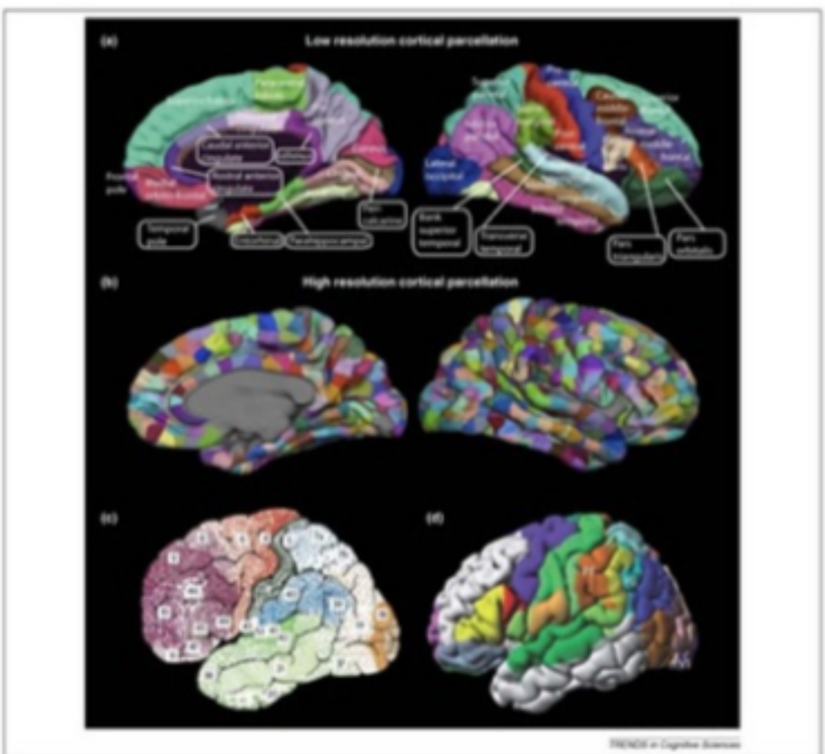
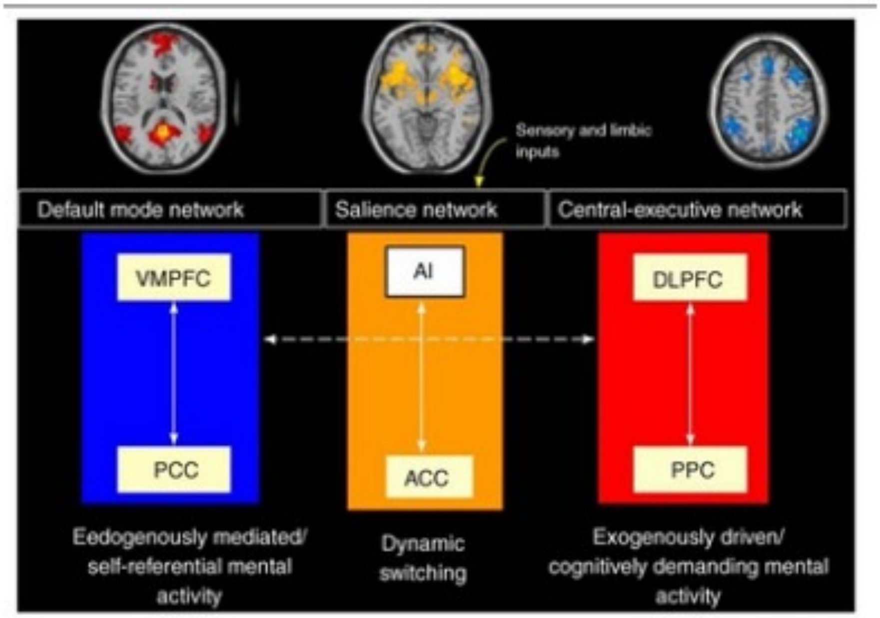


Figure 1. Identification of large-scale structural network nodes in the human brain by four methods currently in use. **(a)** Automated parcellation of a single subject's structural MR image into nodes based on the geometry of large sulcal landmarks. **(b)** High-resolution parcellation with arbitrary granularity. (Reproduced with permission from [36].) **(c)** Classical Brodmann atlas based on cytoarchitectonic features. **(d)** The Jülich-Düsseldorf cytoarchitectonic probabilistic brain atlas, based on observer-independent mapping of cortical areas in ten post-mortem brains. (Not all brain areas are currently covered in this schema.) (Reproduced with permission from [160].)

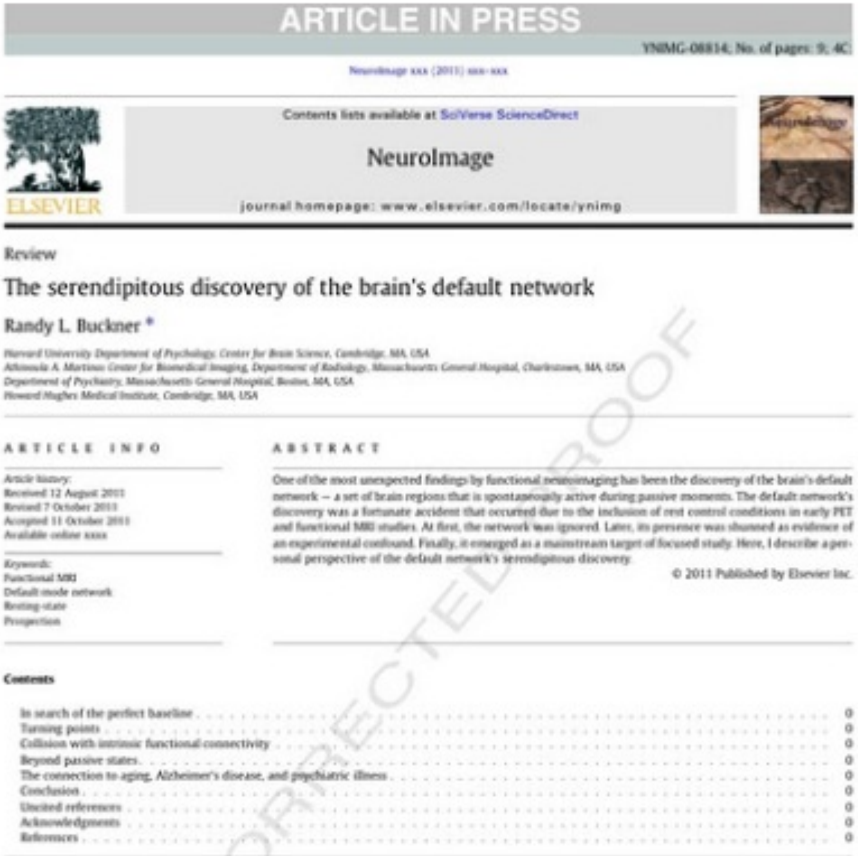
As illustrated in the figure above, neuroscientists have identified a number of core brain network nodes or circuits. The important new insight is that these various nodes or circuits are integrated together into a grander set of higher-level core functional brain networks. Three important core networks are receiving considerable attention in explaining human beavhior.

Major functional brain networks



TRENDS in Cognitive Sciences

The *default mode (DMN) or default brain network* (shown in blue) is what your brain does when not engaged in specific tasks. It is the busy or active part of your brain when you are mentally passive. According to Bresslor and Brennon the "*DMN is seen to collectively comprise an integrated system for autobiographical, self-monitoring and social cognitive functions*." It has also been characterized as responsible for *REST* (rapid episodic spontaneous thinking). In other words, this is the spontaneous mind wandering and internal self-talk and thinking we engage in when not working on a specific task or, when completing a task that is so automatized (e.g., driving a car) that our mind starts to wander and generate spontaneous thoughts. As I have discussed previously at the Interactive Metronome-HOME blog, the default network is responsible for the *unquiet or noisy mind*. And, it is likely that people differ in amount of spontaneous mind wandering (which can be both positive creative thinking or distracting thoughts), with some having a very unquiet mind that is hard to turn off, while others can turn off the inner thought generation and self-talk and display tremendous self-focus or controlled attention to perform a cognitively or motorically demanding task. A very interesting discussion of the serendipitous discovery and explanation of the default brain network is in the following soon to be published scientific article.



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Review

The serendipitous discovery of the brain's default network

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ABSTRACT

One of the most unexpected findings by functional neuroimaging has been the discovery of the brain's default network — a set of brain regions that is spontaneously active during passive moments. The default network's discovery was a fortunate accident that occurred due to the inclusion of rest control conditions in early PET and functional MRI studies. At first, the network was ignored. Later, its presence was shunned as evidence of an experimental confound. Finally, it emerged as a mainstream target of focused study. Here, I describe a personal perspective of the default network's serendipitous discovery.

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The *salience network* (shown in yellow) is a controllor or network switcher. It monitors information from within (internal input) and from the external world arounding us, which is constantly bombarding us with information. Think of the salience network as the air traffic controllor of the brain. Its job is to scan all information bombarding us from the outside world and also that from within our own brains. This controller decides which information is most urgent, task relevant, and which should receive priority in the que of sending brain signals to areas of the brain for processing. This controlling network must suppress either the default or executive networks depending on the task at hand. It must supress one, and activiate the other. Needless to say, this decision making and distribution of information must require exquisite and efficienct *neural timing as regulated by the brain clock(s*).

Finally, the *central-executive network* (CEN; shown in red) "*is engaged in higher-order cognitive and attentional control.*" In other words, when you must engage your concious brain to work on a problem, place information in your working memory as you think, focus your attention on a task or problem, etc., you are "thinking" and must focus your controlled attention. As I understand this research, the salience or controller network is a multi-switching mechanism that is constantly initiating dynamic switching between the *REST* (sponatenous and often creative unquie mind wandering) and thinking networks to best match the current demands you are facing.

According to Bresslor and Melon, not only is this large scale brain network helping us better understand normal cognitive and motor behavior, it is providing insights into clinical disorders of the brain. Poor synchronization between the three major brain networks has been implicated in Alzheimer's, schizophrenia, autism, the manic phase of biploar and Parkinson's (Bresslor and Melon, 2010), disorders that have all been linked to a brain or neural timing (i.e, the brain clock or clocks). I also believe that ADHD would be implicated. If the synchronized milli-second based communicaiton between and within these large networks is compromised, and if the network traffic controller (the salience network) is disrupted in particular, efficient and normal cognition or motor behavior can be compromised.

I find this emerging research fascinating. I believe it provides a viable working hypothesis to explain why different brain fitness or training neurotechnologies have shown promise in improving cognitive function in working memory, ADHD, and other clinical disorders. It is my current hypothesis that various brain training technologies may focus on different psychological constructs (e.g., working memory; planning; focus or controlled attention), but their effectiveness may all be directly or indirectly facilitating the sychronization between the major brain networks. More specifically, by strengthing the ability to invoke the salience or controller network, a person can learn to supress, inhibit or silence the *REST*-producing default brain network more efficiently, long enough to exert more controlled attention or focus when invoking the thinking central executive network. Collectively these brain fitness techonologies may all improving the use of those abilities called executive function, or what I have called the *personal brain manager*. Those technologies that focus on rhythm or brain timing are those I find most fascinating. For example, the recent example of the use of melodic intonation therapy with Congresswoman Gabby Giffords (she suffered serious brain trauma due to a gun shot) demonstrates how rhythm-based brain timing therapies may help repair destroyed preferred and efficient neural pathways or, develop new pathways, much like the development of a new foot worn pathway in the grass on a college campus if a preferred pathway is disrupted by a new building, temporary work or rennovation, or some other destruction of a preferred and efficient network of movement path.

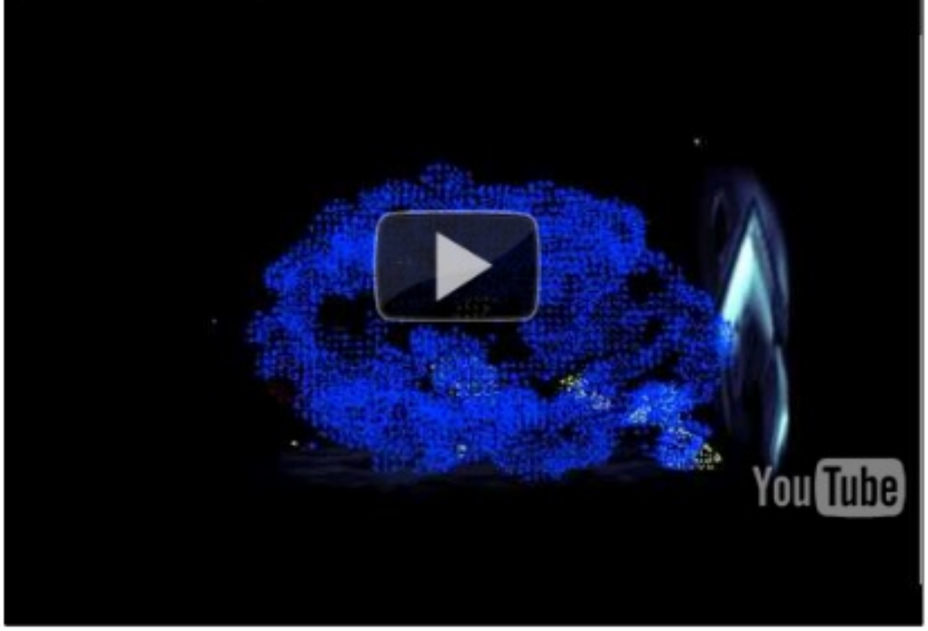
To understand the beauty of the synchronized brain, it is best to see the patterns of brain network connections in action. Below is a video called the "Meditating Mind." I urge you to view the video for a number of reasons.

A number of observations should be clear. First, during the first part of the video the brain is seen as active even during a resting state. This is visual evidence of the silent private dialouge (*REST*) of the default mode or network of the brain. Next, the video mentions the rhythm of increased and decreased neural activation as the brain responds to no visual information or presentation of a video. The changes in color and sound demonstrate the rich rhthymic sychronization of large and different parts of the brain, depending on whether the brain is engaged in a passive or active cognitive task. The beauty of the rapidly changing and spreading communication should make it obvious that efficient rhythmic synchronization of timing of brain signals to and from different networks or ciruits is critical to efficient brain functioning.

Finally, the contrast between the same brain under normal conditions and when engaged in a form of meditation is striking. Clearly when this person's brain is mediating, the brain is responding with a change in rates and frequency of brain network activation and synchrony. As I described in my personal IM-HOME based experience post, mastering Interactive Metronome (IM) therapy requires *"becoming one with the tone*"...which sounds similar to the language of those who engage in various forms of meditation. Could it be that the rhythmic demans of IM, which require an individual to "lock on" to the auditory tone and stay in that synchronized, rhythmic and repetitive state for as long as possible, might be similar to the underlying mechanics of some forms of meditation, which also seek to suppress irrelevant and distracting thoughts and eventually "let the mind go"---posibbly to follow a specific train of thought with complete and distraction free focus.

Yes...this is speculation. I am trying to connect research-based and personal experience dots. It is exciting. My IM-HOME based induce personal focus experience makes sense from the perspective of the function and interaction between the three major large scale brain networks.

The meditating brain



Brain Researchers Start Mapping the Human 'Connectome'

ScienceDaily (July 2, 2012) — A research effort called the Human Connectome Project is seeking to explore, define, and map the functional connections of the human brain. An update on progress in and upcoming plans for the Human Connectome Project appears in the July issue of *Neurosurgery*, official journal of the Congress of Neurological Surgeons.

The journal is published by Lippincott Williams & Wilkins, a part of Wolters Kluwer Health.

Analogous to the Human Genome Project -- which mapped the human genetic code -- the Human Connectome Project seeks to map "the complete, point-to-point spatial connectivity of neural pathways in the brain," according to Arthur W. Toga, PhD, and colleagues of David Geffen School of Medicine, University of California Los Angeles. They write, "For neuroscientists and the lay public alike, the ability to assess, measure, and explore this wealth of layered information concerning how the brain is wired is a much sought after prize."

'Connectome' Mapping to Understand Brain Functional Networks

The 100 billion neurons of the human nervous system interconnect to form a relatively small number of "functional neural networks" responsible for behavior and thought. However, even after more than a century of research, there is no comprehensive map of the connections of the human brain.

Historically, studies of the human brain function have employed a "modular" view -- for example, "region X is responsible for function Y." However, a more appropriate approach is to consider which network of two or more "connected or interacting" regions is involved in a given function. Until recently, it was not possible to view networks in the living brain.

But newer magnetic resonance imaging (MRI) methods sensitive to water diffusion have made it possible to create detailed maps of the underlying white matter connections between different areas of the brain. This opens the way to new approaches to mapping the structural connectivity of the brain, and showing it in ways that correspond to the brain anatomy.

Researchers are working out ways to analyze these data using sophisticated modeling approaches to represent the "nodes and connections" that make up the functional networks of the brain. Such efforts are in their infancy, but these network models are capturing not only the connectedness of brain networks, but also their capacity to process information.

Data Will Lend Insights into Alzheimer's, Autism and Other Diseases

Preliminary studies have yielded tantalizing findings, such as a link between more efficient cortical networks and increased intelligence and differences in connectedness between the right and left hemispheres of the brain. "The HCP has recently generated considerable interest because of its potential to explore connectivity and its relationship with genetics and behavior," Dr. Toga and coauthors write.

The project has far-reaching implications for a wide range of neurological and psychiatric diseases, such as autism, schizophrenia, and Alzheimer's disease. "The similarities and differences that mark normal diversity will help us to understand variation among people and set the stage to chart genetic influences on typical brain development and decline in human disease," according to the authors.

Dr. Toga and colleagues are making their data available for download and analysis by other researchers on the project website, http://www.humanconnectomeproject.org/. In the future, the data will be openly available for exploration by the public. Meanwhile, a gallery of beautiful and fascinating images illustrating the various modeling techniques and preliminary findings on brain connectivity can be viewed at http://www.humanconnectomeproject.org/gallery/.

Story Source:

The above story is reprinted from materials provided by **Wolters Kluwer Health: Lippincott Williams & Wilkins**.

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Journal Reference:

1. Arthur W. Toga, Kristi A. Clark, Paul M. Thompson, David W. Shattuck, John Darrell Van Horn. **Mapping the Human Connectome**. *Neurosurgery*, 2012; 71 (1): 1 DOI: 10.1227/NEU.0b013e318258e9ff

Note: If no author is given, the source is cited instead.

Mapping the Human Connectome

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The human nervous system consists of on the order of 100 billion neurons that are interconnected to form a relatively small number of functional neural networks that underlie behavior and cognition. The elemental beauty of this system was elegantly described in the work of Ramón y Cajal and others well over a century ago. Since that time, despite the intense effort that has gone into elucidating the structure and function of neural systems, we do not currently have a comprehensive map of the complete network connectivity structure of the brain of any species, with the notable exception of a worm, *Caenorhabditis elegans*.[1] In humans, our basic understanding of network connectivity is largely based on painstaking neuroanatomical efforts conducted at a microscopic scale.[2,3] These maps are derived histologically, and are sparsely observed and incomplete.

The connection matrix of the human brain, ie, the human "connectome," represents an indispensable foundation for basic and applied neurobiological research. The axon of a neuron in one region of the brain extends to another region following a particular anatomic course or trajectory. The ensemble over all brain neurons of axonal origin, termination, and trajectory relative to other structures defines the connectome, at least from an anatomic point of view.

Functional networks are certainly served by these anatomic substrates but may involve multiple overlapping systems carrying quantifiably different forms of information to other parts of the brain for integration, further processing, and resulting behavioral action. Brain function depends on the communication among neurons organized within local as well as widely distributed circuits, leading to a vast and extraordinarily complicated set of interconnected brain systems. Human connectomics explores the structural and functional organization and properties of these neural connections to define the architecture of the brain.

For the foreseeable future, a comprehensive description of the complete connectome of even a single human brain might be viewed as unattainable. But the science of connectomics is devoted to filling in the gaps, with a variety of imaging and other modalities. Building on traditional neuroscience techniques, the *Human Connectome Project (HCP)* (http://www.humanconnectomeproject.org/) uses novel imaging technologies and mathematical analysis methods and databases to organize, relate, and share the derived information. With support from the NIH Blueprint program (http://neuroscienceblueprint.nih.gov/), researchers at multiple institutions are rapidly performing the physical, data processing, informatics, and inferential challenges of conducting human connectomics research. This multi-site effort, in concert with similar efforts elsewhere, seeks to obtain connectomic data sets and make them openly available for the expert and lay public to explore and examine using conventional web browsers, or to study them in greater detail using more advanced interactive tools.

A MAP OF THE HUMAN CONNECTOME

The connectome may be defined as the complete, point-to-point spatial connectivity of neural pathways in the brain.[4] This detailed, multiscaled, and multivariate matrix is defined computationally and statistically using sophisticated in vivo neuroimaging data, electrical recordings, and postmortem tissue samples to provide a detailed framework to understand the anatomically based interactions of functional regions of the brain. The connectome gives rise to population-level atlases of distributed connectivity and makes it possible to assess disruptions of connectivity in clinical samples. Demographic, genomic, and cognitive/behavioral data can be superimposed on the connectome to permit inferences concerning genetic and other influences on connectedness.[5,6] Information concerning connectivity is essential for understanding fundamental cognitive operations, systems-level brain activity, conditional structure-function models of brain, and debilitating brain diseases.

Mapping the functional and structural connectivity of the brain using the latest neuroimaging methods must be accompanied by the tools needed to explore those data and to appreciate their richness. The expectation is that HCP will

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Brain wiring a no-brainer?

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No tangles! The human brain's connections turn out to be a an orderly 3D grid structure with no diagonals. 2D sheets of parallel fibers cross at right angles -- " like the warp and weft of a fabric." The first pictures from the most powerful brain scanner of its kind reveal an "astonishingly simple architecture." This diffusion spectrum image of a whole human brain came from the new Connectom scanner, part of the NIH's Human Connectome Project. See full story at www.nimh.nih.gov *This video has NO audio.* Source: Van Wedeen, MD, Martinos Center and Dept. of Radiology, Massachusetts General Hospital and Harvard University Medical School

category: Education

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Behavioral/Systems/Cognitive

Rich-Club Organization of the Human Connectome

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The human brain is a complex network of interlinked regions. Recent studies have demonstrated the existence of a number of highly connected and highly central neocortical hub regions, regions that play a key role in global information integration between different parts of the network. The potential functional importance of these "brain hubs" is underscored by recent studies showing that disturbances of their structural and functional connectivity profile are linked to neuropathology. This study aims to map out both the subcortical and neocortical hubs of the brain and examine their mutual relationship, particularly their structural linkages. Here, we demonstrate that brain hubs form a so-called "rich club," characterized by a tendency for high-degree nodes to be more densely connected among themselves than nodes of a lower degree, providing important information on the higher-level topology of the brain network. Whole-brain structural networks of 21 subjects were reconstructed using diffusion tensor imaging data. Examining the connectivity profile of these networks revealed a group of 12 strongly interconnected bihemispheric hub regions, comprising the precuneus, superior frontal and superior parietal cortex, as well as the subcortical hippocampus, putamen, and thalamus. Importantly, these hub regions were found to be more densely interconnected than would be expected based solely on their degree, together forming a rich club. We discuss the potential functional implications of the rich-club organization of the human connectome, particularly in light of its role in information integration and in conferring robustness to its structural core.

Neuron
Article

Functional Network Organization of the Human Brain

Jonathan D. Power,[1,*] Alexander L. Cohen,[1] Steven M. Nelson,[2] Gagan S. Wig,[1] Kelly Anne Barnes,[1] Jessica A. Church,[1] Alecia C. Vogel,[1] Timothy O. Laumann,[1] Fran M. Miezin,[1,3] Bradley L. Schlaggar,[1,3,4,5] and Steven E. Petersen[1,2,3,5,6,7]
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DOI 10.1016/j.neuron.2011.09.006

SUMMARY

Real-world complex systems may be mathematically modeled as graphs, revealing properties of the system. Here we study graphs of functional brain organization in healthy adults using resting state functional connectivity MRI. We propose two novel brain-wide graphs, one of 264 putative functional areas, the other a modification of voxelwise networks that eliminates potentially artificial short-distance relationships. These graphs contain many subgraphs in good agreement with known functional brain systems. Other subgraphs lack established functional identities; we suggest possible functional characteristics for these subgraphs. Further, graph measures of the areal network indicate that the default mode subgraph shares network properties with sensory and motor subgraphs: it is internally integrated but isolated from other subgraphs, much like a "processing" system. The modified voxelwise graph also reveals spatial motifs in the patterning of systems across the cortex.

mental interest to neuroscientists because they offer the first opportunity to comprehensively and noninvasively explore the functional network structure of the human brain (Bullmore and Sporns, 2009).

Although a variety of methods may be used to study rs-fcMRI data, one of the most powerful and flexible approaches is the graph theoretic approach (Bullmore and Sporns, 2009; Rubinov and Sporns, 2010). Within this framework, a complex system is formalized as a mathematical object consisting of a set of items and a set of pairwise relationships between the items. Items are called nodes, relationships are called ties, and collections of these nodes with their ties are called graphs or networks. A short and incomplete list of established topics in graph theory includes quantifying hierarchy and substructure within a graph, identifying hubs and critical nodes, determining how easily traffic flows in different portions and at different scales of a network, and estimating the controllability of a system (Liu et al., 2011; Newman, 2010). Because graph theoretic analyses can model properties at the level of the entire graph, subgraphs, or individual nodes, and because the brain itself is a complex network, graph theoretic approaches are a natural and attractive choice for rs-fcMRI analysis.

A current obstacle to the graph-based study of functional brain organization is that it very difficult to define the individual nodes that make up a brain network. On first principles, treating a graph as a model of a real system, if the nodes of the graph

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Feature Review

Large-scale brain networks in cognition: emerging methods and principles

Steven L. Bressler[1] and Vinod Menon[2]

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An understanding of how the human brain produces cognition ultimately depends on knowledge of large-scale brain organization. Although it has long been assumed that cognitive functions are attributable to the isolated operations of single brain areas, we demonstrate that the weight of evidence has now shifted in support of the view that cognition results from the dynamic interactions of distributed brain areas operating in large-scale networks. We review current research on structural and functional brain organization, and argue that the emerging science of large-scale brain networks provides a coherent framework for understanding of cognition. Critically, this framework allows a principled exploration of how cognitive functions emerge from, and are constrained by, core structural and functional networks of the brain.

cognition by revealing how cognitive functions arise from interactions within and between distributed brain systems. It focuses on technological and methodological advances in the study of structural and functional brain connectivity that are inspiring new conceptualizations of large-scale brain networks. Underlying this focus is the view that structure–function relations are critical for gaining a deeper insight into the neural basis of cognition. We thus emphasize the structural and functional architectures of large-scale brain networks (Box 1). For this purpose, we

Glossary

Blood-oxygen-level-dependent (BOLD) signal: measure of metabolic activity in the brain based on the difference between oxyhemoglobin and deoxyhemoglobin levels arising from changes in local blood flow.

Central-executive network (CEN): brain network responsible for high-level cognitive functions, notably the control of attention and working memory.

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Glossary

Blood-oxygen-level-dependent (BOLD) signal: measure of metabolic activity in the brain based on the difference between oxyhemoglobin and deoxyhemoglobin levels arising from changes in local blood flow.

Central-executive network (CEN): brain network responsible for high-level cognitive functions, notably the control of attention and working memory.

Default-mode network (DMN): large-scale network of brain areas that form an integrated system for self-related cognitive activity, including autobiographical, self-monitoring and social functions.

Diffusion-based tractography: class of noninvasive magnetic resonance imaging techniques that trace fiber bundles (white matter tracts) in the human brain *in vivo* based on properties of water molecule diffusion in the local tissue microstructure.

Dynamic causal modeling: statistical analysis technique based on bilinear dynamic models for making inferences about the effects of experimental manipulations on inter-regional interactions in latent neuronal signals.

Functional interdependence: statistical inter-relation of variables representing temporal changes in different network nodes.

Granger causality analysis (GCA): statistical method that, when applied to the brain, measures the degree of predictability of temporal changes in one brain area that can be attributed to those in another area.

Independent component analysis (ICA): computational technique that separates a multivariate signal into additive components based on the assumption that the components arise from statistically independent non-Gaussian sources.

Intrinsic connectivity network (ICN): large-scale network of interdependent brain areas observed at rest.

Large-scale: term referring to neural systems that are distributed across the entire extent of the brain.

Local field potential (LFP): electric potential generated in a volume of neural tissue by a local population of neurons. LFPs result from the flow of current in the extracellular space generated by electromotive forces operating across the cell membranes of neurons, principally at synapses.

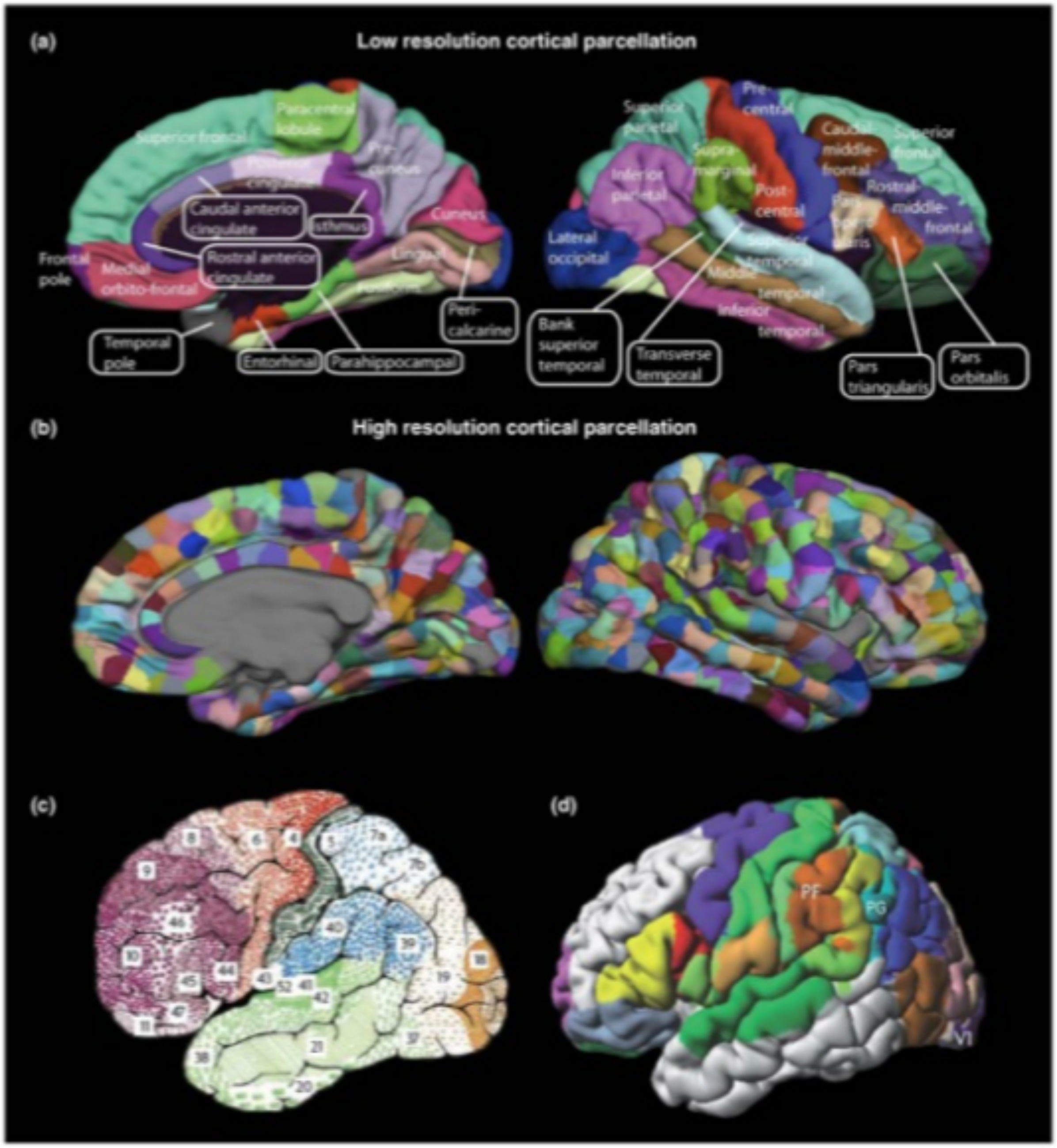
Functional magnetic resonance imaging (fMRI): noninvasive neuroimaging method that measures BOLD signals in the brain *in vivo*.

Network: physical system that can be represented by a graph consisting of nodes and edges.

Network edge: component of networks that links nodes.

Network node: component of networks linked by edges.

Phase synchrony: tendency for two time series to exhibit temporal locking, or a constant relative phase relation, usually in a narrow frequency range.



TRENDS in Cognitive Sciences

Figure 1. Identification of large-scale structural network nodes in the human brain by four methods currently in use. **(a)** Automated parcellation of a single subject's structural MR image into nodes based on the geometry of large sulcal landmarks. **(b)** High-resolution parcellation with arbitrary granularity. (Reproduced with permission from [35].) **(c)** Classical Brodmann atlas based on cytoarchitectonic features. **(d)** The Jülich–Düsseldorf cytoarchitectonic probabilistic brain atlas, based on observer-independent mapping of cortical areas in ten post-mortem brains. (Not all brain areas are currently covered in this scheme.) (Reproduced with permission from [160].)

lower-order visual network [105,107]. This technique has allowed intrinsic (Figure 5), as well as task-related (Figure 6), fMRI activation patterns to be used for identification of distinct functionally coupled systems, including a central-executive network (CEN) anchored in dorsolateral prefrontal cortex (DLPFC) and posterior parietal cortex (PPC), and a salience network anchored in anterior insula (AI) and anterior cingulate cortex (ACC) [107].

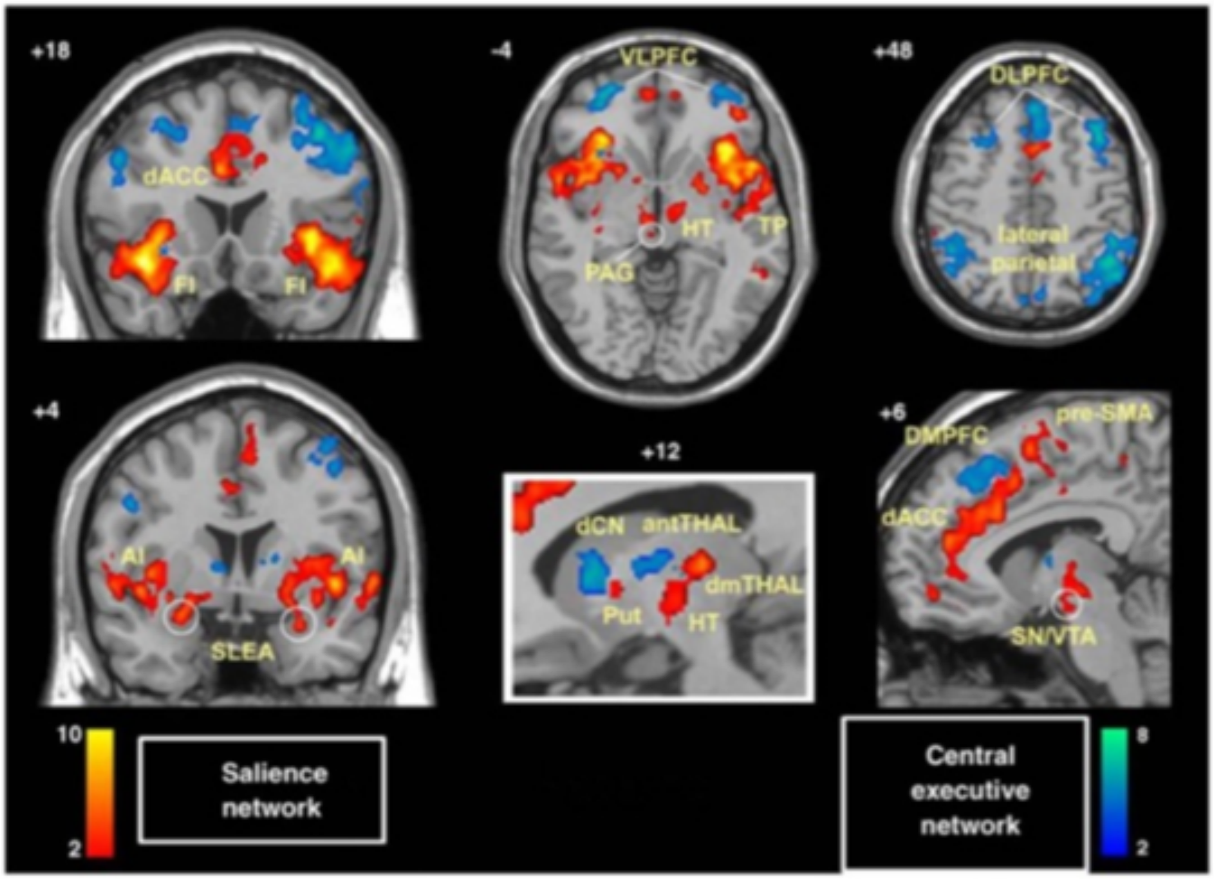


Figure 5. Two core brain networks identified using intrinsic physiological coupling in resting-state fMRI data. The salience network (shown in red) is important for monitoring the salience of external inputs and internal brain events, and the central-executive network (shown in blue) is engaged in higher-order cognitive and attentional control. The salience network is anchored in anterior insular (AI) and dorsal anterior cingulate cortices (dACC), and features extensive connectivity with subcortical and limbic structures involved in reward and motivation. The central-executive network links the dorsolateral prefrontal and posterior parietal cortices, and has subcortical coupling that is distinct from that of the salience network. (Reproduced with permission from [107].)

Large-scale functional brain networks

The primate brain has evolved to provide survival value to primate species by allowing individual species members to behave in ways that accommodate a wide variety of environmental contingencies, performing different behaviors under different sets of conditions. At each moment, a specific set of conditions must be analyzed by the perceptual apparatus of the brain and sets of percepts must be combined with learned concepts to create a 'solution' to the immediate problem of understanding the environment and acting appropriately. It is reasonable to assume that collections of interconnected brain areas act in concert to produce these solutions, as well as corresponding behaviors, and that they interact dynamically to achieve concerted action [49]. A large-scale functional network can therefore be defined as a collection of interconnected brain areas that interact to perform circumscribed functions.

Structural networks provide a complex architecture that promotes the dynamic interactions between nodes that give rise to functional networks. The connectivity patterns of structural networks, which vary with species [50], determine the functional networks that can emerge. Some functional networks, such as for language, depend on species-specific structural specializations [51], whereas others are common across species. The topological form of functional networks (which nodes are connected to which other nodes) changes throughout an individual's lifespan and is uniquely shaped by maturational and learning processes within the large-scale neuroanatomical connectivity matrix for each individual [52].

Large-scale functional networks in the brain exert coordinated effects on effector organs, subcortical brain structures and distributed cortical areas during a host of different cognitive functions. Component brain areas of large-scale functional networks perform different roles, some acting as controllers that direct the engagement of other areas [53] and others contributing specific sensory or conceptual content to network operations. For instance, coordinated prefrontal and posterior parietal control areas channel the flow of activity among sensory and motor areas in preparation for, and during, perceptuomotor processing [54–57].

medial PFC in social cognitive processes related to self and others [122], the MTL in episodic memory [123], and the angular gyrus in semantic processing [124]. These studies suggest that the functions of the DMN nodes are very different. However, when considered as a core brain network, the DMN is seen to collectively comprise an integrated system for autobiographical, self-monitoring and social cognitive functions [125], even though a unique

ways in which it interacts with other networks. We use the salience network to illustrate this point. As described above, it has been suggested that this network mediates attention to the external and internal worlds [130]. To determine whether this network indeed specifically performs this function will require testing and validation of a sequence of putative network mechanisms that includes: (i) bottom-up detection of salient events; (ii) switching

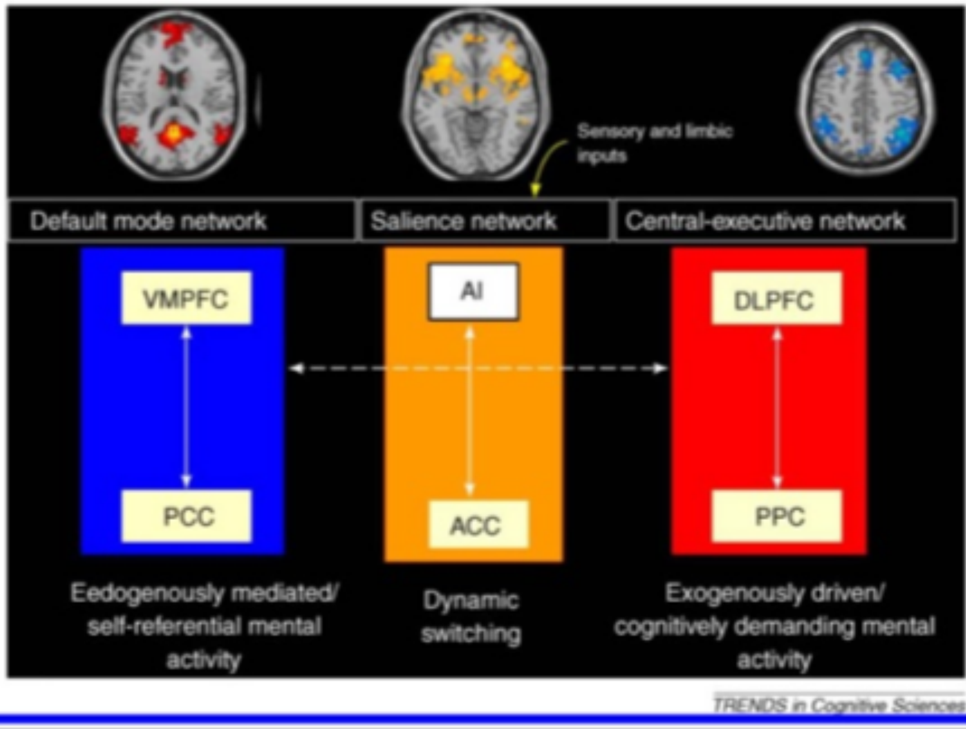


Figure 7. Multi-network switching initiated by the salience network. It is hypothesized that the salience network initiates dynamic switching between the central-executive and default-mode networks, and mediates between attention to endogenous and exogenous events. In this model, sensory and limbic inputs are processed by the AI, which detects salient events and initiates appropriate control signals to regulate behavior via the ACC and homeostatic state via the mid and posterior insular cortex. Key nodes of the salience network include the AI and ACC; the default-mode network includes the VMPFC and PCC; the central-executive network includes the DLPFC and PPC. (Based on [129] and [130].)

Functional brain networks and psychopathology

The systematic exploration of large-scale functional brain networks is yielding not only parsimonious accounts of normal cognitive processes, but also novel insights into psychiatric and neurological disorders [131–133]. Abnormalities in intrinsic functional connectivity have been identified within the DMN in Alzheimer's disease [134,135] and in major depression [131], albeit in different network nodes. Abnormalities have been observed in the phase synchrony of oscillatory neuronal population activity [136] in relation to Alzheimer's disease [137], schizophrenia [138–140], autism [141–143], the manic phase of bipolar disorder [144] and Parkinson's disease [145]. Thus, impairment of functional network interactions might be common in psychiatric and neurological disorders, and observable by functional interdependence analysis of both oscillatory neuronal population and fMRI activity.

A particularly striking example of this new view of psychopathology comes from the finding, discussed above, that the AI is a critical node for initiation of network switching. This key insight reveals the potential for profound deficits in cognitive functioning should AI integrity or connectivity be compromised. AI hyperactivity has been implicated in anxiety disorders, suggesting that salience network hyperactivity can be pathological [146]. Individuals scoring high on the trait neuroticism, the tendency to experience negative emotional states, demonstrate greater AI activation during decision-making even when the outcome of the decision is certain [147]. It is possible that an appropriate level of AI activity is necessary to provide an alerting signal that initiates brain responses to salient stimuli. If so, pathology could result from AI hyperactivity, as in anxiety, or hypoactivity, as might be the case in individuals is normal in the fusiform cortex, but not in the extended regions [152]. A decline in face perception with normal aging is also related to reduced structural integrity of the inferior fronto-occipital fasciculus [153].

Conclusions and future directions

We have reviewed emerging methods for the identification and characterization of large-scale structural and functional brain networks, and have suggested new concepts in cognitive brain theory from the perspective of large-scale networks. Although critical open questions remain (Box 3), the large-scale brain network framework described here offers a principled and systematic approach to the study of cognitive function and dysfunction [154,155].

Continued progress in understanding of cognitive function and dysfunction will depend on the development of new techniques for imaging structural and functional brain connectivity, as well as new methods for investigating dynamic interactions within and between networks. In the remainder of this section, we discuss important directions for future research and highlight areas in which progress is likely to occur.

Although we have reviewed studies that tend to map cognitive functions onto large-scale brain networks, we expect that attempts to equate individual brain networks with a set of cognitive functions could prove to be just as inadequate as attempts to equate single brain regions with specific cognitive functions. It is likely that the function of any cognitive brain network ultimately depends on its multidimensional context [156]. We predict that future studies will explicitly recognize the importance of context in the formation of large-scale functional networks, and will seek to determine the other factors contributing to context in addition to anatomical structure.

PNAS

High-cost, high-capacity backbone for global brain communication

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Edited by Terrence J. Sejnowski, Salk Institute for Biological Studies, La Jolla, CA, and approved May 16, 2012 (received for review March 3, 2012)

Network studies of human brain structural connectivity have identified a specific set of brain regions that are both highly connected and highly central. Recent analyses have shown that these putative hub regions are mutually and densely interconnected, forming a "rich club" within the human brain. Here we show that the set of pathways linking rich club regions forms a central high-cost, high-capacity backbone for global brain communication. Diffusion tensor imaging (DTI) data of two sets of 40 healthy subjects were used to map structural brain networks. The contributions to network cost and communication capacity of global cortico-cortical connections were assessed through measures of their topology and spatial embedding. Rich club connections were found to be more costly than predicted by their density alone and accounted for 40% of the total communication cost. Furthermore, 69% of all minimally short paths between node pairs were found to travel through the rich club and a large proportion of these communication paths consisted of ordered sequences of edges ("path motifs") that first fed into, then traversed, and finally exited the rich club, while passing through nodes of increasing and then decreasing degree. The prevalence of short paths that follow such ordered degree sequences suggests that neural communication might take advantage of strategies for dynamic routing of information between brain regions, with an important role for a highly central rich club. Taken together, our results show that rich club connections make an important contribution to interregional signal traffic, forming a central high-cost, high-capacity backbone for global brain communication.

connectome | graph | tractography

Integrative brain function depends on neuronal signaling within a complex network of connections linking brain regions (network nodes), the human connectome (1–3). A large proportion of cortico-cortical axonal connections link neurons locally through means of intracortical (gray matter) and short-range white matter axons (4, 5). In contrast, only a small fraction of axonal connections are involved in global communication between distant parts of the network. This long-distance cortico-cortical connectivity, accessible on the macroscopic scale to noninvasive diffusion imaging and tractography, is the primary focus of our study. Not all brain regions contribute equally to the global structure of the network. So-called "brain hubs" display an above-average level of connectivity and are more centrally embedded (6–11). In addition to being individually highly connected ("rich"), brain hubs exhibit a strong tendency to link to each other, forming a structural core (6) or "rich club" (7). A rich club is defined as a subset of nodes maintaining a large number of connections across the network (i.e., high degree) while at the same time forming mutual connections with a density significantly greater than expected on the basis of their degree alone (12, 13). The brain's cortical rich club was recently shown to consist of a selective set of frontoparietal hubs, including portions of bilateral precuneus and superior frontal cortex, together with regions overlapping the anterior and posterior cingulate cortex and the insula (7). Individually, these brain hubs engage in a wide range of behavioral and cognitive tasks and have been implicated in efficient integration of information between remote parts of the brain (14–16). Their aggregation into a connected rich club suggests the hypothesis that rich club regions do not act as separate entities but instead operate as a single coherent collective, a focal and centrally embedded network, with rich club connections forming a connectivity backbone linking diverse sets of regions across the brain.

In this report we investigate aspects of network cost and communication capacity for rich club connections based on in vivo diffusion magnetic resonance imaging (MRI) measurements, in relation to their topology and spatial embedding in the human brain network. Large-scale rich club connections are shown to be relatively high cost, with a tendency to link regions across long physical distances. At the same time, rich club connections participate in a large number of short communication paths, thus carrying a high proportion of the brain's signal traffic. Closer examination of the structure of these paths across the brain reveals a sequential organization suggestive of some efficient strategies for dynamic routing of interregional signals, with a central role for rich club connections.

Results

Rich Club Organization. Diffusion tensor imaging (DTI) data of 40 healthy subjects were used to map the large-scale connectivity structure of the brain network, parcellating the cortical sheet into 1,170 distinct evenly sized parcels and determining a group-averaged level of connectivity as the number of reconstructed streamlines between all parcels. A second set of 40 healthy subjects was used to replicate the findings of the principal dataset. Confirming an earlier report (7), the human connectome, mapped here in an independently acquired dataset, was again found to exhibit rich club organization, indicated by a significant tendency for highly connected hub nodes to show an above-random level of interconnectivity, with up to 40% more connectivity than expected by chance ($P < 0.05$, Bonferroni corrected, Fig. 1*A*). Confirming previous findings, the rich club comprised a set of spatially widely distributed brain regions (7, 17), including portions of the precuneus, anterior and posterior cingulate cortex, superior frontal cortex, superior parietal cortex and the insula, all in both hemispheres (Fig. 1*B*). All results reported here refer to the rich club with a degree $k > 10$ (Fig. 1*A*, other levels give

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Author contributions: M.P.v.d.H., R.S.K., J.G., and O.S. designed research; M.P.v.d.H. and O.S. performed research; M.P.v.d.H. and O.S. contributed new reagents/analytic tools; M.P.v.d.H. and O.S. analyzed data; and M.P.v.d.H., R.S.K., J.G., and O.S. wrote the paper.

The authors declare no conflict of interest.

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Data deposition: The group connectivity matrices of streamline densities and lengths reported in this paper are publicly available at the Web site of the Dutch Connectome Laboratory, Rudolf Magnus Institute of Neuroscience, The Netherlands, http://www.myconnectome.nl/data_depository.html.

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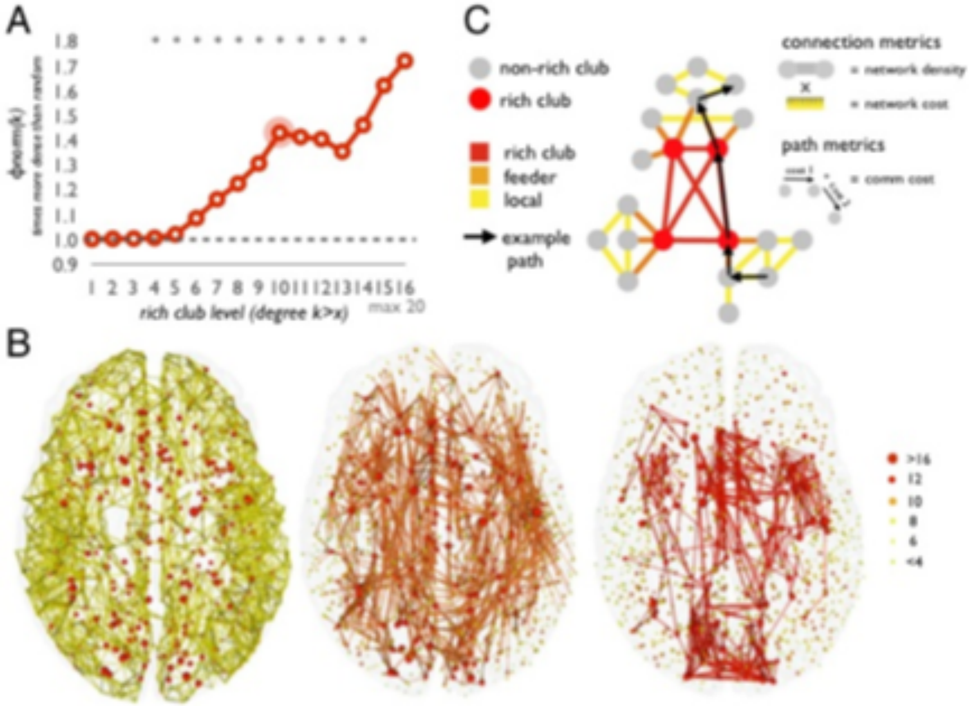

Fig. 1. (*A*) Rich club curve relative to random model, showing a rich club organization of the human connectome (*$P < 0.05$, Bonferroni corrected). The selected rich club level of $k > 10$ is indicated by a red circle. (*B*) Network representation of local (*Left*), feeder (*Center*), and rich club connections (*Right*). (*C*) Schematic illustration of local, feeder, and rich club connections.

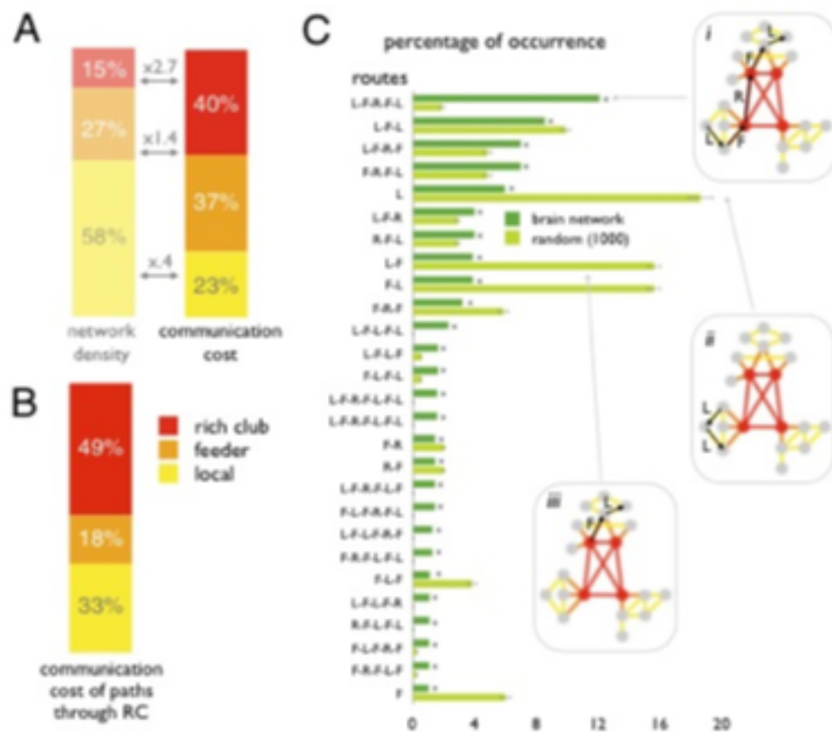

Fig. 3. (*A*) Contributions to communication cost of local feeder and rich club connections. (*B*) Communication cost of paths that pass through the rich club (69% of all paths). (*C*) Frequencies of a selection of path motifs in the brain network (main text), all occurring with a frequency greater than 1%, and their corresponding frequencies in a set of a 1,000 random networks, preserving degree sequence. L-F-R-F-L was the most common path motif in the brain network (*$P < 0.05$, Bonferroni corrected; *SI Materials and Methods*).

Discussion

Our findings suggest that rich club connections form a backbone for global brain communication, a coherent set of connections extending over long distances (high cost) and participating in a large proportion of short paths across the network (high capacity). Our analysis confirmed a rich club organization of the human connectome (7), with a cortical rich club that included portions of the precuneus, superior frontal cortex, superior parietal cortex, anterior and posterior cingulate cortex, and the insula (Fig. 1). These findings reinforce rich club observations in nonhuman species, reporting on the tendency of distributed brain regions to form a densely interconnected "hub complex" or "top hierarchical module," as reported for macaque and cat cortex (17, 18). Extending previous findings, we examined the topological and spatial organization of rich club connections, revealing aspects of their cost, as indexed by their volume, and their capacity, as indexed by their contribution to short communication paths between different parts of the network.

The rich club was found to constitute a high-cost, high-capacity feature of brain connectivity. Rich club tractography streamlines composed a relatively small proportion (15%) of the total network density, but consumed a disproportionately large share (24%) of the total network cost (Fig. 2*B*). Concordantly, rich club connections were found to span larger physical distances than feeder connections and local edges (Fig. 2 *A* and *C*), interconnecting the spatially distributed members of the rich club. Sixty-nine percent of all communication paths were found to pass through the rich club, and rich club connections together with connections feeding pathways into the rich club accounted for 77% of the total communication cost between all brain regions (Fig. 3*A*). The central role of rich club connections in global brain communication is further underscored by their high prevalence in communication paths (Fig. 3*B*), in particular those paths that span medium and long distances (Fig. 4). All metrics related to network density and network cost are greatly reduced in random networks that preserve node degrees but degrade global topology. Hence, the topology of the brain's network appears to be organized to create a focal network through which most of the brain's long-distance signal traffic must pass.

Importantly, signal traffic in brain networks goes beyond relaying and switching of messages. Instead neuronal information is integrated and elaborated as it is exchanged between regions. Intracortical and short-range axonal connections play a crucial role in this process and account for a large proportion of all cortical wiring (4, 5, 19, 20), but are not captured in diffusion MR imaging. The cortical rich club may therefore constitute a central network that not only attracts and propagates, but also transforms and integrates global signal traffic. The present structural study does not directly address functional aspects of rich club organization, but on the basis of their known physiological properties, most members of the rich club can be characterized as multimodal or "high-order" regions, receiving and integrating information from functionally diverse (nonrich club) brain regions (7, 17, 21). With rich club connections forming a backbone for global signal traffic, the rich club as a whole (i.e., its regions and connections) may thus be seen not only as a central attractor but also as an integrator of neuronal information. Future studies examining the intrinsic connectivity of rich club regions will therefore be of particular importance to fully characterize the role of the rich club in the integration of information across functional subdivisions of the human brain (7, 21).

Our findings support the idea that neural architecture is organized to achieve a high level of global information integration along short communication paths (14, 15), while at the same time conserving material resources such as metabolic energy and wiring volume (22–25). Previous analyses of connectivity in nonhuman primates suggested that long-distance projections, although violating strict minimization of wiring volume, act as long-distance shortcuts, ensuring high levels of global information integration while lowering the number of processing steps during communication (26). These shortcuts may confer important advantages, as a lower number of communication steps shortens transmission

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Drifting From Slow to "D'oh!": Working Memory Capacity and Mind Wandering Predict Extreme Reaction Times and Executive Control Errors

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A combined experimental, individual-differences, and thought-sampling study tested the predictions of executive attention (e.g., Engle & Kane, 2004) and coordinative binding (e.g., Oberauer, Süß, Wilhelm, & Sander, 2007) theories of working memory capacity (WMC). We assessed 288 subjects' WMC and their performance and mind-wandering rates during a sustained-attention task; subjects completed either a go/no-go version requiring executive control over habit or a vigilance version that did not. We further combined the data with those from McVay and Kane (2009) to (1) gauge the contributions of WMC and attentional lapses to the worst performance rule and the tail, or τ parameter, of reaction time (RT) distributions; (2) assess which parameters from a quantitative evidence-accumulation RT model were predicted by WMC and mind-wandering reports; and (3) consider intrasubject RT patterns—particularly, speeding—as potential objective markers of mind wandering. We found that WMC predicted action and thought control in only some conditions, that attentional lapses (indicated by task-unrelated-thought reports and drift-rate variability in evidence accumulation) contributed to τ, performance accuracy, and WMC's association with them and that mind-wandering experiences were not predicted by trial-to-trial RT changes, and so they cannot always be inferred from objective performance measures.

Keywords: working memory, executive control, mind wandering, individual differences, reaction time

People tend to make mistakes when they think too much (e.g., Beilock & Carr, 2001) or too little (e.g., Reason, 1990) about ongoing, routine activities. The present study explores whether executive control over thought content—and over mind wandering, in particular—contributes to individual differences in working memory capacity (WMC) and their cognitive and behavioral consequences. Attentional theories of WMC argue that domain-general, executive control capabilities contribute to performance on both WMC and higher order cognitive tasks, as well as to their shared variance (e.g., Braver, Gray, & Burgess, 2007; Hasher, Lustig, & Zacks, 2007; Hasher & Zacks, 1988; Kane, Conway, Hambrick, & Engle, 2007; Unsworth & Engle, 2007; Unsworth & Spillers, 2010). Some evidence for these views comes from studies showing that WMC measures predict not only complex cognitive skills, such as reasoning and reading (e.g., Daneman & Merikle, 1996; Kane, Hambrick, & Conway, 2005; Oberauer, Schulze, Wilhelm, & Süß, 2005), but also more simple attention functions, such as restraining habitual but contextually inappropriate responses (e.g., Hutchison, 2011; Kane & Engle, 2003; Long & Prat, 2002; Unsworth, Schrock, & Engle, 2004) or constraining conscious focus to target stimuli amid distractors (e.g., Colzato, Spapé, Pannebakker, & Hommel, 2007; Conway, Cowan, & Bunting, 2001; Fukuda & Vogel, 2009; Heitz & Engle, 2007; Poole & Kane, 2009; but see Colom, Abad, Quiroga, Shih, & Flores-Mendoza, 2008; Keye, Wilhelm, Oberauer & van Ravenzwaaij, 2009).

Our view of executive control, like others' (e.g., Braver et al., 2007; Cohen & Servan-Schreiber, 1992; De Jong, 2001; Jacoby, Kelley, & McElree, 1999; Roberts & Pennington, 1996), is that self-regulation of thought and behavior is sometimes accomplished proactively, in advance of stimuli or contexts that provoke distraction, conflict, or other challenges. We have proposed that proactive control is accomplished by the active maintenance of goal representations (Engle & Kane, 2004; Kane, Conway, et al., 2007): If goals are not kept accessible, then strong distractors or habits may inappropriately capture ongoing cognition and performance, resulting in *goal neglect* errors (Duncan, 1995) and action slips.[1] We also argue that goal maintenance, which varies with WMC, is fragile and can be disrupted by salient external stimuli or by task-unrelated thoughts (TUTs) that are mentally or environmen-

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[1] We have also proposed that control may be implemented reactively, by mechanisms specialized for resolving response conflict and distractor inhibition (Engle & Kane, 2004; Kane, Conway, et al., 2007; Kane & Engle, 2003; see also Braver et al., 2007; Hasher, Lustig, & Zacks, 2007; Jacoby et al., 1999).

Conclusions

The measurement of mind wandering, or TUTs, within a task contributes significantly to the understanding of individual differences in WMC and attention control. The negative correlation between WMC and TUT rate supports the executive attention theory of WMC, which claims that a primary factor underlying both tests of WMC and complex cognition (e.g., reading comprehension, scholastic achievement tests, and fluid intelligence tests) is executive control. Furthermore, our thought-report and evidence-accumulation modeling findings indicate that lapses of attention contribute to the worst performance rule, whereby subjects' longest RTs (and the ex-Gaussian τ parameter) correlate most strongly with cognitive ability. More broadly, the apparent impact of off-task thoughts on particular varieties of task performance demands a closer look at the ways in which thought control and action control interact to produce goal-directed behavior (see e.g., the hypothesized addition of a *Supervisory Attention Gateway* to classic models of the Supervisory Attention System; Burgess, Dumontheil, & Gilbert, 2007; Gilbert, Frith, & Burgess, 2005; Gilbert, Simons, Frith, & Burgess, 2006).

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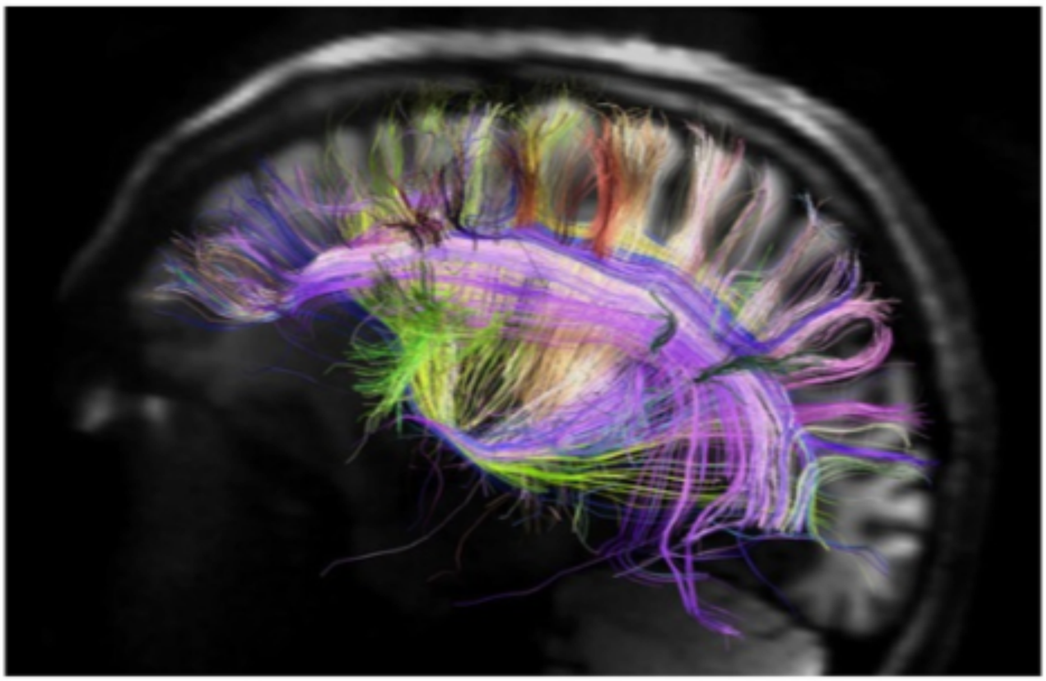
by JON HAMILTON

Audio for this story from All Things Considered will be available at approx. 7:00 p.m. ET

March 29, 2012



MGH-UCLA Human Connectome Project

This image shows the grid structure of the major pathways of the brain. It was created using a scanner that's part of the Human Connectome Project, a five-year effort which is studying and mapping the human brain.

(21)

(51)

It turns out your brain is organized even if you're not.

At least that's the conclusion of a study in *Science* that looked at the network of fibers that carry signals from one part of the brain to another.

Researchers used cutting-edge imaging technology to look at places where these fibers intersect. And they found a remarkably organized three-dimensional grid, says Van Wedeen of Harvard Medical School, the study's lead author.

The grid is a bit like Manhattan, Wedeen says, "with streets running in two dimensions and then the elevators in the buildings in the third dimension."

Of course the human brain has a lot of folds and curves. So, Wedeen says, you have to imagine Manhattan bent into some odd shapes. But the underlying grid doesn't change. The streets intersect at 90-degree angles and the buildings rise vertically.

The grid represents a big change from the traditional model of the brain's wiring, Wedeen says. In that model, he says, "the brain looked somewhat like a plate of spaghetti or perhaps like one of those old antique telephone switchboards with a million wires running more or less at random."

Wedeen says once he saw evidence of the brain's grid system, a lot of things began to make sense to him.

"I'd been looking at pictures of these monkey brains for years without being able to understand why the fibers were so often looking like sheets, why the curvatures were so well behaved and so organized," he says.

The grid model could help answer a question that has baffled geneticists and biologists for years, Wedeen says: How can a relatively small number of genes contain the blueprint for something as complex as the human brain?

The answer may be that in a highly organized grid system with consistent rules, a genetic blueprint doesn't have to describe every detail of the final product, he says.

"The grid structure shows how simple recipes can produce a very complicated outcome," Wedeen says.

The grid also may help explain how the rudimentary brain of a flat worm evolved into the complex brain found in people, Wedeen says.

The grid system, he says, would allow a species to gradually add new functions to its brain much the way an architect adds extra floors to a building or a city planner adds new streets.

"So you actually see the tools through which evolution builds a complicated human brain from more simply constructed ancestral brains," he says.

Not everyone thinks it's that simple, though.

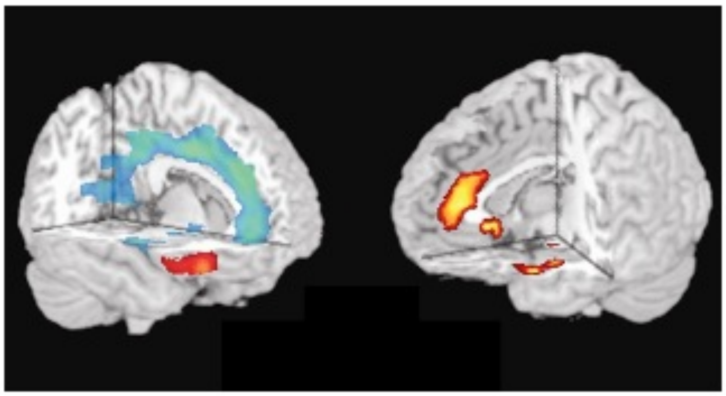
The results of the new study are surprising and intriguing, but not yet certain, says David Van Essen, a neuroscientist at Washington University School of Medicine in St. Louis.

"The evidence for their hypothesis is strong to some degree," Van Essen says. But he adds that "in a couple of important ways I think they may have oversimplified the story."

The brain's background noise

By Hannah Waters | March 25, 2012, 7:51 PM PDT

How many times have you read the headline "Brain scans show…?"



They've "shown" when patients are in pain, how psychopaths' brains are different, and why some people are shy. And they've even been used to reconstruct watched videos in what was widely described as "mind reading."

Most of the time, these brain scans are functional magnetic resonance imaging (fMRI) studies, which measure the amount of oxygen in different parts of the brain. And, presumably, where there is more oxygen, there is more activity.

But it's pretty hard to keep a brain quiet. Even when you're inactive, there is still plenty of oxygen flow. Now researchers are studying the brain under these "normal" conditions — when it's in resting state or performing simple tasks.

Two papers published last week showed that, when participants were just watching videos of peoples' faces or looking at patterns of numbers or letters, **the entire brain lit up.** You read that right: even when you're doing nothing in particular, the entire brain is active. And these studies were huge: in one, more than 1,300 peoples' brains were scanned, and in the other, three people each underwent the study 500 times each.

The findings suggest that most fMRI studies are presenting a "misleading picture of the brain," writes the blogger Neuroskeptic. If the whole brain is active most of the time, studies will only pick up the most extreme areas of activity, leaving smaller changes left unknown — "[a] bit like how we only hear the shouts and screams from through our neighbor's walls, not their normal conversations, which aren't loud enough to reach our ears," he wrote. "The idea that only small parts of the brain are 'involved' in any particular task may be a statistical artefact."

But studying the brain's background noise won't just improve fMRI studies: some researchers want to use the information to diagnose brain disease.

The premise is fairly straight-forward: if brain connections are damaged in people with Alzheimer's disease, epilepsy or ADHD, maybe their "normal" brain static will differ as well. Roxanne Khamsi writes in *Nature Medicine*:

> [I]ncreasingly, a group of neuroscientists believe that scientists focusing on task-based brain scans are missing the big picture. Over the last decade, momentum has swelled around the idea that examining resting-state fMRI, captured as people lie idle in the scanner, could reveal more intimate details about how brain regions communicate or fall out of sync as a result of disease. The approach, which might eventually be used as a diagnostic tool, has even caught the attention of some big-name drug developers.

Researchers are developing large databases, already with "resting brain" scans of more than 1,400 people, reports Khamsi.

The focus on "normal" brain states is compelling to me: before we start to pick apart behavior, shouldn't we first better understand the diversity among all human brains?

Brain Scanning - Just the Tip of the Iceberg? [Neuroskeptic]

Diagnosis by default [Nature Medicine]

nature medicine

Diagnosis by default

Roxanne Khamsi

Nature Medicine **18**, 338–340 (2012) | doi:10.1038/nm0312-338
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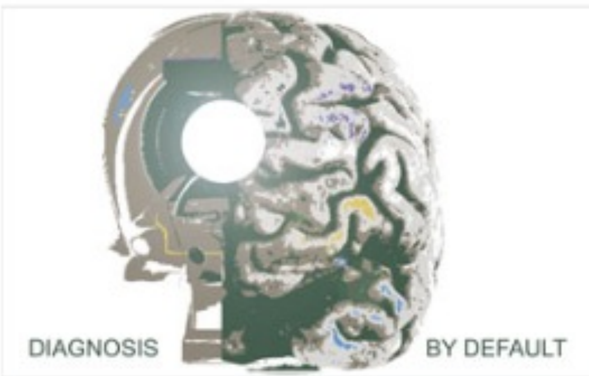
Brain scans that map differences in how brain regions communicate while people lie idle in the imaging machine could one day provide clues about afflictions ranging from Alzheimer's disease to attention disorders. Roxanne Khamsi **finds out why these so-called 'resting state' scans have made researchers and drug companies sit up and take notice.**

Even though the space inside a brain scanner is snug, volunteers in imaging studies usually have their hands full. Lying inside the machine, surrounded by hulking magnets, they might be asked to tap their fingers, listen to sounds or recognize faces flashing on a screen. While the subjects respond to these prompts, pulses of radio waves travel through their heads, knocking the protons in the brain out of order so that the machine can measure their resonance. Thankfully for researchers, oxygen-rich blood has a different magnetic resonance than oxygen-depleted blood, so they can detect variations in blood flow—and in brain activity by proxy.

Such functional magnetic resonance imaging (fMRI) studies have offered insights on everything from how people respond to advertising to how they process language. But, increasingly, a group of neuroscientists believe that scientists focusing on task-based brain scans are missing the big picture. Over the last decade, momentum has swelled around the idea that examining resting-state fMRI, captured as people lie idle in the scanner, could reveal more intimate details about how brain regions communicate or fall out of sync as a result of disease. The approach, which might eventually be used as a diagnostic tool, has even caught the attention of some big-name drug developers.



Lucas Gray and Kristin Slavin

"There's tremendous interest in the intrinsic activity in the brain," says Marcus Raichle, an early pioneer in the field at the Washington University School of Medicine in St. Louis. The growth in research into the brain's resting state has been "exponential," he adds.

Already, scientists have found inklings of differences in the resting-state brain activity of people with Alzheimer's disease and schizophrenia, among other neurological disorders. And only a year ago, a competition was launched to find the best analytical approach to detect attention deficit hyperactivity disorder (ADHD) from resting-state scans.

"We're on an amazing adventure. It really is," says James Hyde at the Medical College of Wisconsin in Milwaukee, who first published on the subject nearly two decades ago.

Signal to diagnoise

Scientists performed the first human MRI examination in the late 1970s, but it took about fifteen years for them to use the same technology to track brain signals with fMRI. In the early days of fMRI, the experts trying to analyze the data had a tough time discerning the 'signals' of altered brain activity from the 'noise' of regular, run-of-the-mill blood flow that sustains the organ. Neuroscientists hoping to tease this apart would compare fMRI scans of volunteers completing tasks with those of the same people when idle. The hope was to deduce the function of various brain regions by canceling out the background noise emitted by the brain during rest.

A twist came in 1995, when Hyde and his graduate student at the time, Bharat Biswal, became curious as to whether resting-state scans had distinct characteristics of their own.

The Wisconsin researchers had noticed that the noise in the fMRI data seemed to be unusually high, and they wondered whether the racket was coming from the brain itself. "I went around screaming about the noise in everyone's fMRI scans," says Hyde. "I gave [Biswal] the assignment and I said 'The noise is too high.'"

> **"Part of the mystique of the default network is no one knows what it does."**

For his PhD dissertation, Biswal looked at fMRI scans of eleven subjects who lay at rest for five minutes and later did a finger-tapping task for five minutes. After filtering out changes in blood flow caused by the participants' heart beats and breathing, the analysis revealed a sustained level of activity in the motor cortex of people at rest, indicating that the noise was indeed physiological and neurological in basis[1]. "I saw that there was still this low-frequency signal that was present in the brain at resting state," says Biswal, now at the University of Medicine and Dentistry of New Jersey in Newark. "Therefore, the question was, 'What was its role?'"

According to Biswal, who trained as an electrical engineer before joining Hyde's lab, neuroscientists had simply failed to appreciate that the circuitry of the resting brain functioned in a meaningful pattern, much like a computer in standby mode still has purposefully activated circuits.

Biswal's quest to understand whether the activity in the resting brain can have value came at a time when the imaging field in general still had not found its footing. "Back in 1995, people were still testing whether functional MRI was of any use," says Alexandre Coimbra, a senior clinical imaging scientist at Genentech, a South San Francisco–based subsidiary of the Swiss drug giant Roche. "It was very far-fetched at the time what he was proposing."

The idea started to pick up steam two years later when Raichle and his colleagues showed that certain brain regions are consistently more active during rest than during cognitive tasks[2]. In 2001, Raichle's group used brain scans obtained through positron emission tomography to show a 'default mode' of brain function related to a physiological baseline when the mind is at rest[3]. That notion gained further momentum two years later when a team led by Michael Greicius, a neurologist at the Stanford University School of Medicine in California, demonstrated that spontaneous activity detected by fMRI at rest was strongly correlated across regions within this default network[4].

The default mode network, one of the dozen or so networks in the brain, actually becomes more active during rest than during a novel task. Yet it remains unclear exactly why disparate regions of the default network—including the medial prefrontal cortex at the front of the brain and the lateral parietal cortex on the side—get going in concert when people are idle. "That's part of the mystique of the default network," Greicius says. "No one really knows what it does."

To better understand the healthy default network, researchers turned to studying faulty baseline states in people with various neurological and behavioral disorders, ranging from epilepsy and coma to depression and Parkinson's disease. One of the earliest studies of this kind, led by Mark Lowe, director of the High-Field MRI branch at the Cleveland Clinic Foundation in Ohio, analyzed finger-tapping and resting-state brain scans in 20 people with multiple sclerosis and 16 healthy controls and found that, compared with their control counterparts, individuals with the disease had less synchronicity in the 'sensorimotor regions' of the brain, which are involved in movement control and sensory perception[5].

Investigation into the default-mode network of people with Alzheimer's disease has also revealed intriguing results. Studies have found decreased coordinated activity between the hippocampus—a memory center—and other brain regions during the resting state[6]. And an experiment published a few years ago even found a link between a variant in the *APOE* gene that raises the risk of Alzheimer's and unusual activity in the default-mode network compared with controls[7].

Liz Williams

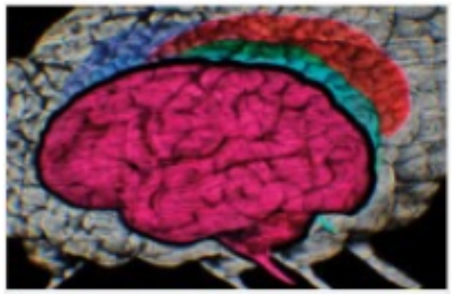
Together, these findings hint at a future when functional connectivity of brain regions could serve as a better early indicator of Alzheimer's than memory tests or measures of certain brain proteins.

Making the connection

As more teams attempt to obtain resting-state scans from patients and healthy volunteers, the research community has sought a way to bring the information all together. In December 2009, investigators from 35 centers around the world pooled resting-state fMRI records from more the 1,400 healthy subjects and released their data online through what became known as the 1,000 Functional Connectomes Project[8]. According to Michael Milham, founding director of the Center for the Developing Brain at the Child Mind Institute in New York and a co-creator of the project, the resource provided a repository of scans for people to evaluate using novel algorithms in hopes of finding improved diagnostic analyses.

But the project, as initially conceived, was limited in that each brain scan was tagged with only the age and sex of the individual, but not any clinical information. Also, the imaging speed of the fMRI machines used varied across sites, making it difficult to compare the data sets. So, Milham and his collaborators around the globe have morphed the effort to address these issues into what's known as the International Neuroimaging Data-Sharing Initiative, which has scans tagged with diagnostic background information and includes both prospective and retrospective data.

Meanwhile, in 2010 the US National Institutes of Health funded sites for its 'Human Connectome Project', much of it devoted to mapping the patterns of brain activity, including at resting state. Over the next five years, it will collect extensive behavioral details from the individuals who undergo brain scans—some of which will collect an hour's worth of resting state activity—and even compare the functional brain patterns between twins.



Liz Williams

In September 2010, Milham, along with Damien Fair of Oregon Health & Science University in Portland, conceived of the ADHD-200 Global Competition, a contest to characterize the disorder on the basis of resting-state scans. The initial goal was to collect scans of 200 subjects, 100 with ADHD and 100 control counterparts. But when word got out about the competition, close to 1,000 scans poured in from eight different labs around the world. “We really overachieved on this one,” Milham says.

In March of last year, Milham and his coorganizers released 285 scans from children with ADHD and 491 scans from healthy children—all stripped of any identifying information—for contenders to devise the optimal algorithm for detecting the attention disorder from fMRI imaging. Then, in July they released an additional 197 anonymized scans, without indicating which ones came from children with ADHD, as a final test of how well the teams had fared.

“Resting-state fMRI may be very important for drug companies.”

The competition, sponsored by the US National Institute on Drug Abuse (NIDA), culminated in October, when a team led by biostatistician Brian Caffo at the Johns Hopkins Bloomberg School of Public Health in Baltimore was declared the winner for the best diagnostic analysis. When the Hopkins algorithm said it found ADHD in resting-state patterns, it was correct 94% of the time. Competition winners received complementary trips to Washington, DC to receive recognition at a preview symposium at the Society for Neuroscience meeting.

Notably, although the Hopkins algorithm had a high degree of specificity, it only detected one out of every five confirmed cases of ADHD in the sample. In a clinical setting, that would mean many missed diagnoses. But on the upside, notes Milham, that's better than a test that has a many false positives, such as prostate-specific antigen testing for cancer. “Think about if your test picked up every kid with ADHD but also every kid without it,” he says, “You'd have a lot of scared parents.”

Attention scan

The ADHD-200 effort is also yielding results beyond the immediate aims of the competition. In December, for example, Nora Volkow, director of NIDA, and Dardo Tomasi of the US National Institute on Alcohol Abuse and Alcoholism used the resource to show that children with ADHD had lower connectivity in the default-mode network and superior parietal cortex, which is thought to be involved in regulating attention, of their brains. Conversely, they also had higher brain activity in reward networks[9].

Despite these insights into ADHD from the default network, not everyone is yet persuaded by this application. "I have a whole duffel bag of reservations" about using resting-state studies for ADHD, says Greicius, noting that the disorder is one of the tougher ones to define with traditional diagnostic criteria, let alone fMRI data. Even Milham, who definitely sees future promise in this approach for ADHD, is adamant that resting-state scans are not yet ready for the clinical prime time. "It's not appropriate," he says. "Trust me—I have a lot of people who ask me to use scanning to diagnose their child." Milham always declines.

As the algorithms get better and the scanning machines get more sensitive, that future might not be far off. In the meantime, scientists have begun exploring how medication for ADHD affects the default brain network in children with the disorder. Unpublished results from Yu-Feng Zang, a neuroscientist at the Hangzhou Normal University in Zhejiang, China, who contributed scans to the ADHD-200 sample, suggest that the psychostimulant drug methylphenidate, marketed as Ritalin, does seem to produce decreased activity in the motor cortex of individuals with ADHD during the resting state. The drug does not, however, affect signaling in the dorsal anterior cingulate cortex, an area thought to be involved in regulating attention that seems to be less active in ADHD.

Zang believes the pharmaceutical industry should take note. "I think resting-state fMRI may be very important for drug companies," he says. Indeed, drug developers such as Genentech and New York–based Pfizer have expressed interest in exploring the possibility of tracking brain changes in illnesses such as Alzheimer's disease through resting-state fMRI.

"An image is worth a thousand words. The same holds here," says Genentech's Coimbra. "The challenge is to find the few words or few sentences that can tell you how a patient is doing or how effective a drug is."

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NEUROSCIENCE NEWS Research news from the cutting edge of neuroscience.

Tuesday April 10th 2012

Researchers Use Brain Injury Data to Map Intelligence in the Brain

Scientists report that they have mapped the physical architecture of intelligence in the brain. Theirs is one of the largest and most comprehensive analyses so far of the brain structures vital to general intelligence and to specific aspects of intellectual functioning, such as verbal comprehension and working memory.

Their study, published in *Brain*: A Journal of Neurology, is unique in that it enlisted an extraordinary pool of volunteer participants: 182 Vietnam veterans with highly localized brain damage from penetrating head injuries.

"It's a significant challenge to find patients (for research) who have brain damage, and even further, it's very hard to find patients who have focal brain damage," said University of Illinois neuroscience professor Aron Barbey, who led the study. Brain damage – from stroke, for example – often impairs multiple brain areas, he said, complicating the task of identifying the cognitive contributions of specific brain structures.

But the very focal brain injuries analyzed in the study allowed the researchers "to draw inferences about how specific brain structures are necessary for performance," Barbey said. "By studying how damage to particular brain regions produces specific forms of cognitive impairment, we can map the architecture of the mind, identifying brain structures that are critically important for specific intellectual abilities."

The researchers took CT scans of the participants' brains and administered an extensive battery of cognitive tests. They pooled the CT data to produce a collective map of the cortex, which they divided into more than 3,000 three-dimensional units called voxels. By analyzing multiple patients with damage to a particular voxel or cluster of voxels and comparing their cognitive abilities with those of patients in whom the same structures were intact, the researchers were able to identify brain regions essential to specific cognitive functions, and those structures that contribute significantly to intelligence.

"We found that general intelligence depends on a remarkably circumscribed neural system," Barbey said. "Several brain regions, and the connections between them, were most important for general intelligence."

These structures are located primarily within the left prefrontal cortex (behind the forehead), left temporal cortex (behind the ear) and left parietal cortex (at the top rear of the head) and in "white matter association tracts" that connect them. (Watch a video about the findings.)

The researchers also found that brain regions for planning, self-control and other aspects of executive function overlap to a significant extent with regions vital to general intelligence.

The study provides new evidence that intelligence relies not on one brain region or even the brain as a whole, Barbey said, but involves specific brain areas working together in a coordinated fashion.

"In fact, the particular regions and connections we found support an emerging body of neuroscience evidence indicating that intelligence depends on the brain's ability to integrate information from verbal, visual, spatial and executive processes," he said.

The findings will "open the door to further investigations into the biological basis of intelligence, exploring how the brain, genes, nutrition and the environment together interact to shape the development and continued evolution of the remarkable intellectual abilities that make us human," Barbey said.

The research team also included scientists from Universidad Autónoma de Madrid; Medical Numerics, in Germantown, Md.; George Mason University; the University of Delaware; and the Kessler Foundation, in West Orange, N.J.

Barbey also is a professor of psychology and of speech and hearing science, an affiliate of the Beckman Institute, and the director of the Decision Neuroscience Laboratory at Illinois.

Notes about this intelligence research article

The U.S. National Institute of Neurological Disorders and Stroke at the National Institutes of Health provided funding for this research.

Take all those 90 degree intersections, for example.

Ptther studies show that the brain's structure also includes some diagonal pathways as well, Van Essen says. So he says it's possible the brain is neither pure spaghetti nor a perfect grid.

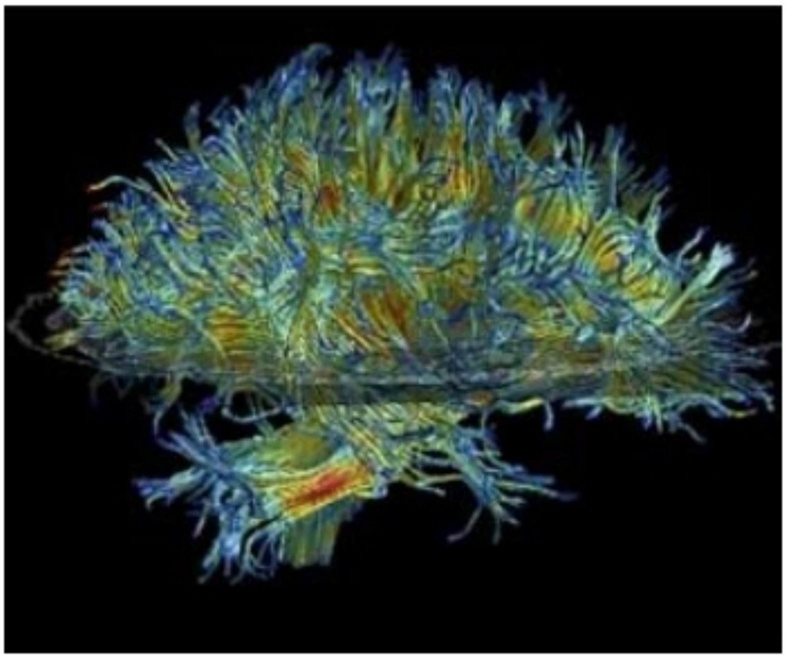
"I expect it will turn out to be somewhere in between," he says.

A definitive answer about the structure of the brain's wiring probably isn't far off, Van Essen says, thanks to something called the Human Connectome Project. It's a five-year brain-mapping effort supported by the National Institutes of Health.

Those findings should help explain how our brain wiring makes us who we are, Van Essen says, and what goes wrong in disorders like autism and Alzheimer's disease.

Multiple thought channels may help brain avoid traffic jams

Washington University School of Medicine | May 6, 2012 | Cognition / 0 / EDIT



Brain networks may avoid traffic jams at their busiest intersections by communicating on different frequencies, researchers at Washington University School of Medicine in St. Louis, the University Medical Center at Hamburg-Eppendorf and the University of Tübingen have learned.

"Many neurological and psychiatric conditions are likely to involve problems with signaling in brain networks," says co-author Maurizio Corbetta, MD, the Norman J. Stupp Professor of Neurology at Washington University. "Examining the temporal structure of brain activity from this perspective may be especially helpful in understanding psychiatric conditions like depression and schizophrenia, where structural markers are scarce."

The research will be published May 6 in *Nature Neuroscience*.

Scientists usually study brain networks — areas of the brain that regularly work together — using magnetic resonance imaging, which tracks blood flow. They assume that an increase in blood flow to part of the brain indicates increased activity in the brain cells of that region.

“Magnetic resonance imaging is a useful tool, but it does have limitations,” Corbetta says. “It only allows us to track brain cell activity indirectly, and it is unable to track activity that occurs at frequencies greater than 0.1 hertz, or once every 10 seconds. We know that some signals in the brain can cycle as high as 500 hertz, or 500 times per second.”

For the new study, conducted at the University Medical Center at Hamburg-Eppendorf, the researchers used a technique called magnetoencephalography (MEG) to analyze brain activity in 43 healthy volunteers. MEG detects very small changes in magnetic fields in the brain that are caused by many cells being active at once. It can detect these signals at rates up to 100 hertz.

“We found that different brain networks ticked at different frequencies, like clocks ticking at different speeds,” says lead author Joerg Hipp, PhD, of the University Medical Center at Hamburg-Eppendorf and the University of Tübingen, both in Germany.

For example, networks that included the hippocampus, a brain area critical for memory formation, tended to be active at frequencies around 5 hertz. Networks constituting areas involved in the senses and movement were active between 32 hertz and 45 hertz. Many other brain networks were active at frequencies between eight and 32 hertz. These “time-dependent” networks resemble different airline route maps, overlapping but each ticking at a different rate.

“There have been a number of fMRI studies of depression and schizophrenia showing ‘spatial’ changes in the organization of brain networks,” Corbettta says. “MEG studies provide a window into a much richer ‘temporal’ structure. In the future, this might offer new diagnostic tests or ways to monitor the efficacy of interventions in these debilitating mental conditions.”

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June 1, 2012 | 10:20 AM | By ***Annie Murphy Paul*** LEARNING SMARTER

Why Daydreaming Isn't a Waste of Time

FILED UNDER: **Learning Methods**, **Research**

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Allowing time for refleciton helps kids make meaning out of experiences and information they encounter.

Parents and teachers expend a lot of energy getting kids to pay attention, concentrate, and focus on the task in front of them. What adults don't do, according to University of Southern California education professor Mary Helen Immordino-Yang, is teach children the value of the more diffuse mental activity that characterizes our inner lives: daydreaming, remembering, reflecting.

Yet this kind of introspection is crucial to our mental health, to our relationships, and to our emotional and moral development. And it promotes the skill parents and teachers care so much about: the capacity to focus on the world outside our heads.

Our brains have two operating systems, Immordino-Yang and her coauthors **explain in an article to** be published in the journal *Perspectives on Psychological Science*. The first, which they call the "looking out system," orients our attention to the external environment, allowing us to get stuff done. The other, which they term the "looking in system," directs us inward, setting our thoughts

A lack of time to daydream may even hamper kids' capacity to pay attention when they need to.

free to wander. By scanning the brains of study subjects asked simply to rest and relax, scientists have discovered that our minds are anything but inactive in these moments. Relieved of the obligation to pay attention to what's going on around us, we engage instead with a rich internal environment: recalling the past, imagining the future, replaying recent interactions and sorting out our feelings. It's when we engage our brains' "looking in" mode, notes Immordino-Yang, that we make meaning out of the mass of experiences and information we encounter when we're "looking out."

Young people may have fewer opportunities to exercise the vital capacity of introspection. Immordino-Yang fingers two culprits: educational practices that demand constant attentiveness, even from young children, and a hyper-connected world that insistently draws attention away from the world inside. "If youths overuse social media, if they spend very little waking time free from the possibility that a text will interrupt them," the authors write, "we would expect that these conditions might predispose youths toward focusing on the concrete, physical and immediate aspects of situation and self, with less inclination toward considering the abstract, longer-term, moral and emotional implications of their and others' actions."

Ironically, a lack of time to daydream may even hamper kids' capacity to pay attention when they need to. The ability to become absorbed in our own thoughts is linked to our ability to focus intently on the world outside, research indicates. In **one recent neuro-imaging study**, for example, participants alternated periods of mental rest with periods of looking at images and listening to sounds. The more effectively the neural regions associated with "looking in" were activated during rest and deactivated while attending to the visual and auditory stimuli, the more engaged were the brain's sensory cortices in response to sights and sounds.

Focus and concentration are essential, of course. But so are introspection and reflection, and Immordino-Yang and her colleagues recommend that adults help children find a balance between the two modes: by regularly unplugging our kids' blinking, buzzing devices, and by providing time and space for a quieter, more inward kind of entertainment.-

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WEB VIEW

The Virtues of Daydreaming

by Jonah Lehrer • June 4, 2012

Humans are a daydreaming species. According to a recent study led by the Harvard psychologists Daniel Gilbert and Matthew A. Killingsworth, people let their minds wander forty-seven per cent of the time they are awake. (The scientists demonstrated this by developing an iPhone app that contacted twenty-two hundred and fifty volunteers at random intervals during the day.) In fact, the only activity during which we report that our minds are not constantly wandering is "love making." We're able to focus for that.

At first glance, such data seems like a confirmation of our inherent laziness. In a culture obsessed with efficiency, mind-wandering is often derided as useless—the kind of thinking we rely on when we don't really want to think. Freud, for instance, described daydreams as "infantile" and a means of escaping from the necessary chores of the world into fantasies of "wish-fulfillment."

In recent years, however, psychologists and neuroscientists have redeemed this mental state, revealing the ways in which mind-wandering is an essential cognitive tool. It turns out that whenever we are slightly bored—when reality isn't quite enough for us—we begin exploring our own associations, contemplating counterfactuals and fictive scenarios that only exist within the head.

Virginia Woolf, in her novel "To The Lighthouse," eloquently describes this form of thinking as it unfolds inside the mind of a character named Lily:

Certainly she was losing consciousness of the outer things. And as she lost consciousness of outer things, her mind kept throwing things up from its depths, scenes and names, sayings, memories and ideas, like a fountain spurting.

A daydream is that fountain spurting, spilling strange new thoughts into the stream of consciousness. And these spurts turn out to be surprisingly useful. A forthcoming paper in *Psychological Science* led by Benjamin Baird and Jonathan Schooler at the University of California at Santa Barbara helps explain why. The experiment itself was simple: a hundred and forty-five undergraduate students were given a standard test of creativity known as an "unusual use" task, in which they had two minutes to list as many uses as possible for mundane objects such as toothpicks, bricks, and clothes hangers.

Subjects were then given a twelve-minute break. During this time, they were randomly assigned to three different conditions: resting in a quiet room, performing a difficult short-term memory task, or doing something so boring that it would elicit mind-wandering. Following this interlude, the subjects were given another round of creative tests, including the unusual-use tasks they had worked on only a few minutes before.

Here's where things get interesting: those students assigned to the boring task performed far better when asked to come up with additional uses for everyday items to which they had already been exposed. Given new items, all the groups did the same. Given repeated items, the daydreamers came up with forty-one per cent more possibilities than students in the other conditions.

What does this mean? Schooler argues that it's clear evidence that those twelve minutes of daydreaming allowed the subjects to invent additional possibilities, as their unconscious minds pondered new ways to make use of toothpicks. This is why the effect was limited to those items that the subjects had previously been asked about—the question needed to marinate in the mind, "incubating" in those subterranean parts of the brain we can barely control.

On a more practical note, the scientists argue that their data show why "creative solutions may be facilitated specifically by simple external tasks that maximize mind-wandering." The benefit of these simple tasks is that they consume just enough attention to keep us occupied, while leaving plenty of mental resources left over for errant daydreams. (When people are left alone, such as those subjects forced to sit by themselves, they tend to perseverate on their problems. Unfortunately, all this focus backfires.) Consider the ping-pong tables that now seem to exist in the lobby of every Silicon Valley startup. While it's easy to dismiss such interior decorations as mere whimsy, the game turns out to be an ideal mind-wandering activity, at least when played casually. Another task that consistently leads to extended bouts of daydreaming is reading Tolstoy. In Schooler's earlier work on mind-wandering, he gave subjects a boring passage from "War and Peace." The undergraduates began zoning out within seconds.

Although Schooler has previously demonstrated a correlation between daydreaming and creativity—those who are more prone to mind-wandering tend to be better at generating new ideas, at least in the lab—this new paper shows that our daydreams seem to serve a similar function as night dreams, facilitating bursts of creative insight. Take a 2004 paper published in *Nature* by the neuroscientists Ullrich Wagner and Jan Born. The researchers gave a group of students a tedious task that involved transforming a long list of number strings into a new set of number strings. Wagner and Born designed the task so that there was an elegant shortcut, but it could only be uncovered if the subject had an insight about the problem. When people were left to their own devices, less than twenty per cent of them found the shortcut, even when given several hours to mull over the task. The act of dreaming, however, changed everything: after people were allowed to lapse into R.E.M. sleep, nearly sixty per cent of them discovered the secret pattern. Kierkegaard was right: sleeping is the height of genius.

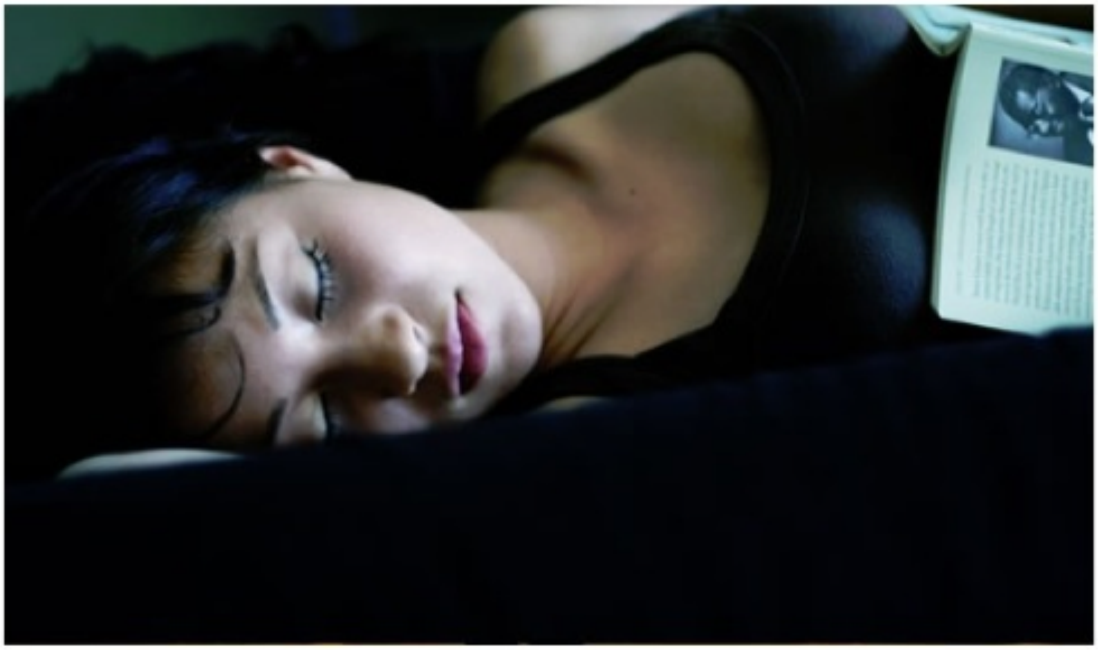
If this all sounds like scientific justification for afternoon naps, long showers, and Russian literature, you're right. "We always assume that you get more done when you're consciously paying attention to a problem," Schooler told me. "That's what it means, after all, to be 'working on something.' But this is often a mistake. If you're trying to solve a complex problem, then you need to give yourself a real break, to let the mind incubate the problem all by itself. We shouldn't be so afraid to actually take some time off."

Schooler has tried to apply this hypothesis to his own life. Although he used to take piles of work with him on vacation—he'd read papers and grant proposals on the beach—he now finds that he has better ideas when he lets himself really get away. "The good news is that there's no reason to feel guilty when taking a break or not checking your e-mail," he says. "Because it turns out that even when you're on vacation, the unconscious is probably still working on the problem."

A daydream, in this sense, is just a means of eavesdropping on those novel thoughts generated by the unconscious. We think we're wasting time, but, actually, an intellectual fountain really is spurting.

Photograph by Peter Marlow/Magnum.

How Much Do You 'Zone Out' While Reading?



Everyone zones out from time-to-time while reading, but how much is normal?

Everyone has had the experience of reading a few pages of a book and then suddenly noticing none of it has gone in. But how common is this experience?

A study by Schooler et al., (2004) suggests it's fairly common:

> "On average participants caught themselves zoning out approximately 5.4 times during the 45 min reading period. Several findings were consistent with the hypothesis that people are often (at least initially) unaware of the fact that they are zoning out."

This means you're not always aware of when you're zoning out. To combat this the experimenters used a system to catch people zoning out. This found that they were zoning out from reading about 13% of the time. And what were they thinking about while zoning out?

> "...they were only very rarely (less than 3%) thinking about what they were reading when they reported zoning out. Although they sometimes reported thinking about nothing at all (18%), more often participants reported thinking about specific things, such as school-related topics (27%), fantasies (19%), and themselves (11%)." (Schooler et al., 2004)

So we are often unaware that our minds are wandering from what we are reading, even when it's a gripping Amazon bestseller rather than a boring textbook.

In fact, mind wandering is very common:

> "Killingsworth and Gilbert (2010) sampled the experience of 2,250 US adults at random intervals. Each time participants reported, through their smartphone, how they were feeling and what they were doing. Almost half the time people were asked, at that moment their minds were wandering from whatever they were doing—43% to pleasant topics, 27% to unpleasant topics and the rest to neutral topics. The only time their minds weren't wandering was when they were having sex." (From: Does Keeping Busy Make us Happy?)

If our minds wander only 13% of the time when we're reading, that's actually pretty good compared to an average of 50% for everyday life.

Image credit: Mark Sebastian

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Review

The serendipitous discovery of the brain's default network

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A B S T R A C T

One of the most unexpected findings by functional neuroimaging has been the discovery of the brain's default network — a set of brain regions that is spontaneously active during passive moments. The default network's discovery was a fortunate accident that occurred due to the inclusion of rest control conditions in early PET and functional MRI studies. At first, the network was ignored. Later, its presence was shunned as evidence of an experimental confound. Finally, it emerged as a mainstream target of focused study. Here, I describe a personal perspective of the default network's serendipitous discovery.

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Full Length Articles

Circular representation of human cortical networks for subject and population-level connectomic visualization

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ABSTRACT

Cortical network architecture has predominantly been investigated visually using graph theory representations. In the context of human connectomics, such representations are not however always satisfactory because canonical methods for vertex–edge relationship representation do not always offer optimal insight regarding functional and structural neural connectivity. This article introduces an innovative framework for the depiction of human connectomics by employing a circular visualization method which is highly suitable to the exploration of central nervous system architecture. This type of representation, which we name a 'connectogram', has the capability of classifying neuroconnectivity relationships intuitively and elegantly. A multimodal protocol for MRI/DTI neuroimaging data acquisition is here combined with automatic image segmentation to (1) extract cortical and non-cortical anatomical structures, (2) calculate associated volumetrics and morphometrics, and (3) determine patient-specific connectivity profiles to generate subject-level and population-level connectograms. The scalability of our approach is demonstrated for a population of 50 adults. Two essential advantages of the connectogram are (1) the enormous potential for mapping and analyzing the human connectome, and (2) the unconstrained ability to expand and extend this analysis framework to the investigation of clinical populations and animal models.

Review

Cell PRESS

Top-down modulation: bridging selective attention and working memory

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Selective attention, the ability to focus our cognitive resources on information relevant to our goals, influences working memory (WM) performance. Indeed, attention and working memory are increasingly viewed as overlapping constructs. Here, we review recent evidence from human neurophysiological studies demonstrating that top-down modulation serves as a common neural mechanism underlying these two cognitive operations. The core features include activity modulation in stimulus-selective sensory cortices with concurrent engagement of prefrontal and parietal control regions that function as sources of top-down signals. Notably, top-down modulation is engaged during both stimulus-present and stimulus-absent stages of WM tasks; that is, expectation of an ensuing stimulus to be remembered, selection and encoding of stimuli, maintenance of relevant information in mind and memory retrieval.

Top-down modulation in perception and working memory

of sensory processing is not an intrinsic property of sensory cortices, but rather relies on long-range inputs from and interactions with a network of 'control' regions, including the prefrontal cortex (PFC) and parietal cortex [8,9]. We review evidence that a similar functional neural architecture of top-down modulation analogous to those that operate during perceptual analysis supports the prioritization of information in the service of WM.

In a typical visual WM task, participants are presented with an array of one or more items to be maintained in mind after the array is turned off over an interval of seconds (delay period) during which no stimulus information is present ('delayed-response' tasks). A single probe item or a probe array then appears, and the participant

Glossary

Selective attention: goal-directed focus on one aspect of the environment, while ignoring irrelevant aspects.
Working memory: maintenance and/or manipulation of task-relevant information in mind for brief periods of time to guide subsequent behavior.

Box 1. The concept of brain networks

Brain networks can be defined based on structural connectivity or functional interdependence. The structural network organization of the brain is based on the anatomical linkage of its neurons. Neurons are connected locally by synapses from short axons, dendrites and gap junctions. Although neuronal populations throughout the brain have a variety of different internal circuitry configurations, they can be represented as network nodes if they have a uniquely identifiable local structural organization, a large-scale structural connectivity pattern or a local functional activity pattern that allows them to be distinguished from their neighbors.

Some (projection) neurons in the brain have long axons that synapse at a distance from the cell body. Long axon pathways that project from one neuronal population to another can be represented as network edges. If the pathway between two populations (A and B) consists of axons only from A to B or only from B to A, then the edge can be considered to be directed. If the pathway consists of axons in both directions, then the edge can be considered to be bidirectional. If the method used to identify edges in the brain does not establish directionality, the edges can be treated as being undirected.

The functional interdependence of brain network nodes refers to joint activity in different brain structures that is co-dependent under variation of a functional or behavioral parameter. Most methods yield non-zero values of functional interdependence in all cases, so true functional interdependence must depend on values that are significantly different from zero or significantly different between cognitive conditions.

framework allows a more systematic examination of how cognitive functions emerge from, and are constrained by, core structural and functional networks of the brain. Finally, we suggest some directions in which we expect research in this field to proceed in the future.

Large-scale structural brain networks

The neuroanatomical structure of large-scale brain networks provides a skeleton of connected brain areas that facilitates signaling along preferred pathways in the service of specific cognitive functions. It is important to identify the brain areas that constitute structural network nodes and the connecting pathways that serve as structural network edges to know which configurations of interacting areas are possible. In the past, large-scale structural brain networks were often schematized by two-dimensional wiring diagrams, with brain areas connected by lines or arrows representing pathways. Currently, more sophisticated network visualization and analysis schemes are being developed and used [19]. We focus here first on the principal methods used to define structural nodes and edges in the brain. We then consider some possible functional consequences of the structural organization of large-scale brain networks.

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Cognitive-emotional interactions

Attention regulation and monitoring in meditation

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Meditation can be conceptualized as a family of complex emotional and attentional regulatory training regimes developed for various ends, including the cultivation of well-being and emotional balance. Among these various practices, there are two styles that are commonly studied. One style, focused attention meditation, entails the voluntary focusing of attention on a chosen object. The other style, open monitoring meditation, involves nonreactive monitoring of the content of experience from moment to moment. The potential regulatory functions of these practices on attention and emotion processes could have a long-term impact on the brain and behavior.

Meditation as an explanandum

Despite a large number of scientific reports and theoretical proposals [1–5], little is known about the neurophysiological processes involved in meditation and the long-term impact of meditation on the brain. The lack of statistical evidence, control populations and rigor of many of the early studies, the heterogeneity of the studied meditative states and the difficulty in controlling the degree of expertise of practitioners can, in part, account for the limited contributions made by neuroscience-oriented research on meditation. The absence of a clear operational definition of meditation limits this research. Here, we offer a theoretical framework, based on traditional meditation texts and modern neuroscientific conceptions, in which some standard meditations are grouped into two broad categories: focused attention (FA) and open monitoring (OM) meditation (Boxes 1,2; Table 1). These categories are used to delineate the specific psychological processes implicated in these two practices and to derive neurofunctional predictions. We also present key findings illustrating how meditation might affect mental processing and the brain. The overall purpose of this framework is to produce an operational definition for FA and OM meditative practices that can be adopted in the scientific study of effects of meditation training on the mind and the brain [6–8].

The term 'meditation' refers to a broad variety of practices, ranging from techniques designed to promote relaxation to exercises performed with a more far-reaching goal, such as a heightened sense of well-being. It is thus essential to be specific about the type of meditation practice under investigation. Failure to make such distinctions would be akin to the use of the word 'sport' to refer to all sports as if they were essentially the same. For example, the overly generic description of meditation as a mere relaxation technique [9] becomes extremely problematic when one attends to the details of many practices [4,10,11] (Boxes 1,2). By contrast, here, we conceptualize meditation as a family of complex emotional and attentional regulatory strategies developed for various ends, including the cultivation of well-being and emotional balance [7]. To narrow the explanandum to a more tractable scope, we use Buddhist contemplative techniques and their clinical secular derivatives as a paradigmatic framework [7,6,7]. Among the wide range of practices within the Buddhist tradition, we further narrow this review to two common styles of meditation, FA and OM (Boxes 1,2), which are often combined, whether within a single session or over the course of a practitioner's training. These styles are found with some variation in several meditation traditions, including Zen, Vipassana and Tibetan Buddhism [4,12,13]. Both styles are also implicated in secular interventions that draw on Buddhist practices, such as mindfulness-based stress reduction [14]. The first style, FA meditation, entails voluntary focusing attention on a chosen object in a sustained fashion. The second style, OM meditation, involves nonreactively monitoring the content of experience from moment to moment, primarily as a means to recognize the nature of emotional and cognitive patterns. A functional characterization of these states is proposed in Table 1.

Neuroscientific study of focused attention meditation

The selective nature of attention and its importance for guiding goal-directed behavior has been one of the most extensively studied areas of Western psychology and neuroscience. Notably, there are remarkable parallels between the processes involved in FA meditation, as described in many meditation texts (Table 1), and recent cognitive (neuro)science conceptualizations of attention. Both Western scientists and Buddhist scholars recognize that the ability to focus and sustain attention on an intended object requires skills involved in monitoring the focus of attention and detecting distraction, disengaging attention from the source of distraction, and (re)dir-

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Box 1. FA meditation

A widespread style of Buddhist practice involves sustaining selective attention moment by moment on a chosen object, such as a subset of localized sensations caused by respiration. To sustain this focus, the meditator must also constantly monitor the quality of attention. At first, the attention wanders away from the chosen object, and the typical instruction is to recognize the wandering and then restore attention to the chosen object. For example, while intending to focus on localized sensations around the nostrils caused by breathing, one might notice that the focus has shifted to the pain in one's knee. One then 'releases' this distraction, and returns to the intended object. Thus, while cultivating the acuity and stability of sustained attention on a chosen object, this practice also develops three skills regulative of attention: the first is the monitoring faculty that remains vigilant to distractions without destabilizing the intended focus. The next skill is the ability to disengage from a distracting object without further involvement. The last involves the ability to redirect focus promptly to the chosen object.

Progress in this form of meditation is measured, in part, by the degree of effort required to sustain the intended focus. The novice contends with more distractions, and the three regulative skills are frequently exercised. As one advances, the three regulative skills can be developed to the point that, for example, advanced practitioners have an especially acute ability to notice when the mind has wandered. Eventually, FA induces a trait change, whereby the attention rests more readily and stably on the chosen focus. At the most advanced levels, the regulative skills are invoked less and less frequently, and the ability to sustain focus thus becomes progressively 'effortless.'

In advanced practitioners, FA practices create a sense of physical lightness or vigor, and the need for sleep is said to be reduced. Advanced levels of concentration are also thought to correlate with a significant decrease in emotional reactivity. FA practices typically involve a relatively narrow field of focus, and as a result, the ability to identify stimuli outside that field of focus might be reduced.

ecting and engaging attention to the intended object. These

Impact of meditation training on the default mode network during a restful state

Impact of meditation training on the default mode network during a restful state.

Soc Cogn Affect Neurosci. 2012 Mar 24

Authors: Taylor VA, Daneault V, Grant J, Scavone G, Breton E, Roffe-Vidal S, Courtemanche J, Lavarenne AS, Marrelec G, Benali H, Beauregard M

Abstract. Mindfulness meditation has been shown to promote emotional stability. Moreover, during the processing of aversive and self-referential stimuli, mindful awareness is associated with reduced medial prefrontal cortex (MPFC) activity, a central default mode network (DMN) component. However, it remains unclear whether mindfulness practice influences functional connectivity between DMN regions and, if so, whether such impact persists beyond a state of meditation. Consequently, this study examined the effect of extensive mindfulness training on functional connectivity within the DMN during a restful state. Resting-state data were collected from 13 experienced meditators (with over 1000 h of training) and 11 beginner meditators (with no prior experience, trained for 1 week before the study) using functional magnetic resonance imaging (fMRI). Pairwise correlations and partial correlations were computed between DMN seed regions' time courses and were compared between groups utilizing a Bayesian sampling scheme. Relative to beginners, experienced meditators had weaker functional connectivity between DMN regions involved in self-referential processing and emotional appraisal. In addition, experienced meditators had increased connectivity between certain DMN regions (e.g. dorso-medial PFC and right inferior parietal lobule), compared to beginner meditators. These findings suggest that meditation training leads to functional connectivity changes between core DMN regions possibly reflecting strengthened present-moment awareness.

Meditation experience is associated with differences in default mode network activity and connectivity

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Many philosophical and contemplative traditions teach that "living in the moment" increases happiness. However, the default mode of humans appears to be that of mind-wandering, which correlates with unhappiness, and with activation in a network of brain areas associated with self-referential processing. We investigated brain activity in experienced meditators and matched meditation-naive controls as they performed several different meditations (Concentration, Loving-Kindness, Choiceless Awareness). We found that the main nodes of the default-mode network (medial prefrontal and posterior cingulate cortices) were relatively deactivated in experienced meditators across all meditation types. Furthermore, functional connectivity analysis revealed stronger coupling in experienced meditators between the posterior cingulate, dorsal anterior cingulate, and dorsolateral prefrontal cortices (regions previously implicated in self-monitoring and cognitive control), both at baseline and during meditation. Our findings demonstrate differences in the default-mode network that are consistent with decreased mind-wandering. As such, these provide a unique understanding of possible neural mechanisms of meditation.

mindfulness | task-positive network | attention

broaden the scope of mindfulness to all aspects of experience, whether during formal meditation practice or everyday life, via directly attending to whatever arises in one's conscious field of awareness at any moment (11, 16). During such training, meditators learn to clearly identify when self-related thoughts, emotions, and body sensations are occurring, and to differentiate identification of these from identifying with them (e.g., awareness that anger is present vs. "I am angry"). That is, meditators practice noticing when they are identifying with an object, and when this occurs, to "let go" and bring their attention back to the present moment. Across these practices, one common aim is to reverse the habit of mind-wandering, which has been defined as "thinking about something other than what [one is] currently doing" (1). In other words, the meditator's task is to remain aware from moment to moment, and self-identification is included in the off-task category of mind-wandering. Importantly, this information-processing task, common to all three of these meditation techniques, is a training of attention away from self-reference and mind-wandering, and potentially away from default-mode processing.

Clinically, mindfulness training has shown benefit for the treatment of pain (13), substance-use disorders (15, 17), anxiety disorders (18), and depression (14), and also helps to increase

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The Psychological Effects of Meditation: A Meta-Analysis

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In this meta-analysis, we give a comprehensive overview of the effects of meditation on psychological variables that can be extracted from empirical studies, concentrating on the effects of meditation on nonclinical groups of adult meditators. Mostly because of methodological problems, almost ¾ of an initially identified 595 studies had to be excluded. Most studies appear to have been conducted without sufficient theoretical background. To put the results into perspective, we briefly summarize the major theoretical approaches from both East and West. The 163 studies that allowed the calculation of effect sizes exhibited medium average effects ($\bar{r} = .28$ for all studies and $\bar{r} = .27$ for the $n = 125$ studies from reviewed journals), which cannot be explained by mere relaxation or cognitive restructuring effects. In general, results were strongest (medium to large) for changes in emotionality and relationship issues, less strong (about medium) for measures of attention, and weakest (small to medium) for more cognitive measures. However, specific findings varied across different approaches to meditation (transcendental meditation, mindfulness meditation, and other meditation techniques). Surprisingly, meditation experience only partially covaried with long-term impact on the variables examined. In general, the dependent variables used cover only some of the content areas about which predictions can be made from already existing theories about meditation; still, such predictions lack precision at present. We conclude that to arrive at a comprehensive understanding of why and how meditation works, emphasis should be placed on the development of more precise theories and measurement devices.

Keywords: meditation, meta-analysis, psychological variables, nonclinical population

Supplemental materials: http://dx.doi.org/10.1037/a0028168.supp

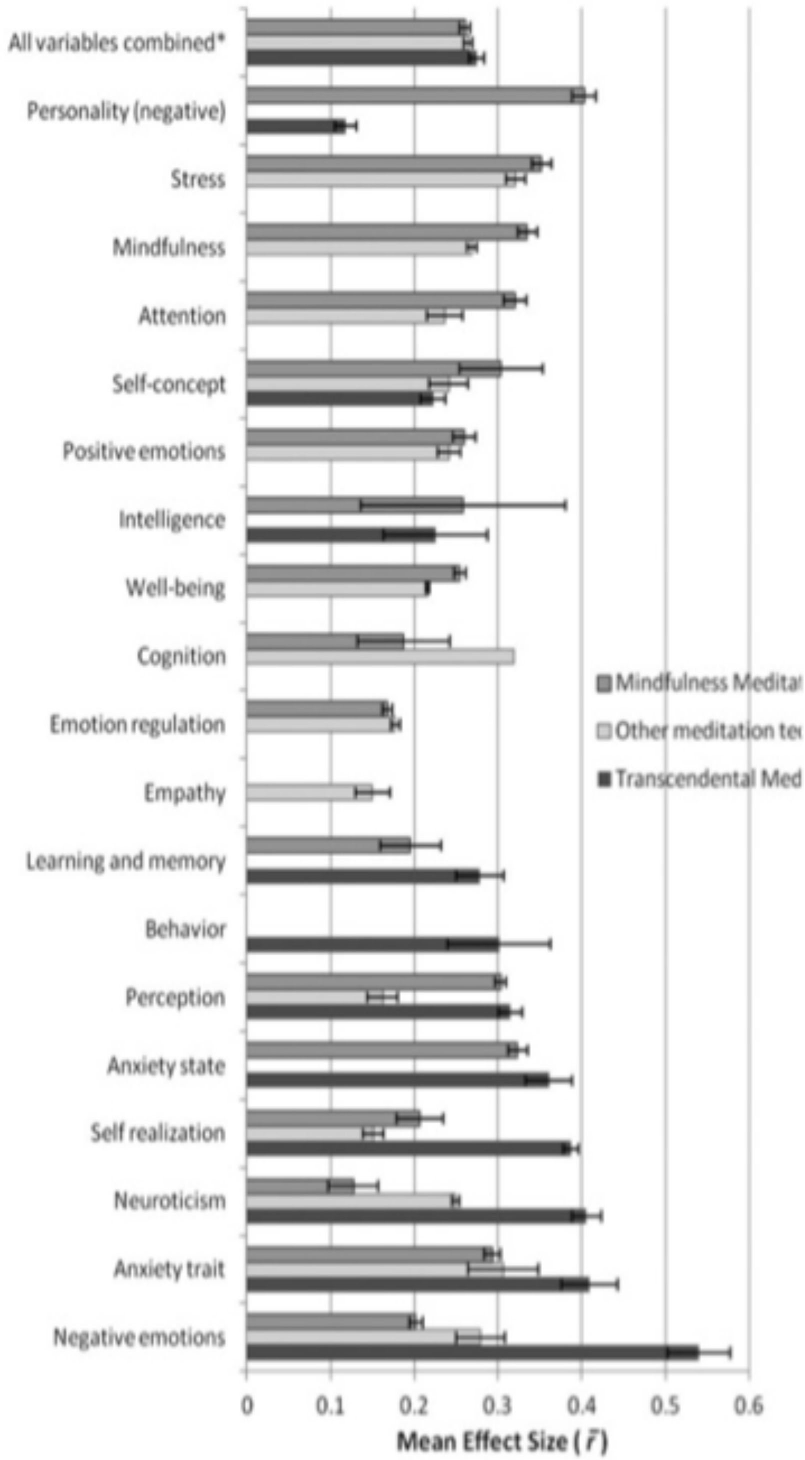

Figure 9. Differential effects of the kind of meditation for specific categories of dependent measures. Shown are effect sizes ($\bar{r}$) and 95% confidence intervals for all dependent measures that were used in three or more studies. The category "All variables combined" also includes data for variables that were examined in $k < 3$ studies.

Figure 7. Effect sizes, number of studies (articles only) used to calculate them, and 95% confidence intervals for all categories listed in Table 1, as well as for the overall effect size ("All variables combined*"). The specific categories include results for $k \geq 4$ studies. The category "All variables combined*" also includes data for variables that were examined in $k < 4$ studies.

What Is Meditation?

There are many varieties of meditation. According to Shear (2006b), approaches to meditation differ in the mental faculties they use (e.g., attention, feeling, reasoning, visualization, memory, bodily awareness), in how these faculties are used (e.g., actively, passively, effortlessly, forcefully), and the objects to which these faculties are directed (e.g., thoughts, images, concepts, internal energy, aspect of the body, love, God). In practice, however, it is difficult if not impossible to find an approach to meditation that can be reduced to a single mechanism.

Some distinctions are frequently mentioned in the literature, such as the type of attention cultivated (concentration vs. awareness) and the relationship to cognitive processes (e.g., simply observing cognitions vs. deliberately modifying them; see Feuerstein, 2001; Shear, 2006a; Walsh & Shapiro, 2006). A primary distinction is that between concentrative and mindfulness techniques (Goleman, 1988; Kristeller & Rikhye, 2008; Naranjo & Ornstein, 1971), although the two techniques are often used together in actual approaches to meditation such as Zen meditation (e.g., Kapleau, 2000; Samy, 2002). Concentrative techniques use an object of focus or attention, which can be a mantra (mostly a spiritually meaningful word or phrase),[2] one's breathing, or a picture or physical experience. Meditators train their ability to rest their attention on a single object and thereby to disengage their usual mental processes. Take, for instance, breathing as the object of attention. First, trying to stay focused on each breath, meditators experience a heightened awareness of how the mind jumps around (like a monkey, it is often said). They then learn to disengage their responses to thoughts, emotions, actions, or other cognitions, and with much practice, they may be able to effortlessly maintain the awareness of their breathing in the back of the mind, thus producing a calming effect that might even extend to everyday activities.

Whereas concentrative meditation is usually seen to stem from Hinduism (but is also found in many Buddhist approaches), mindfulness meditation is closely connected to Buddhism (Feuerstein, 2001). Mindfulness meditation emphasizes staying present in the moment and maintaining an alert, aware state in a nonjudgmental way (e.g., Kabat-Zinn, 1994). Meditators learn not to let the mind

Specific effects of mindfulness practice. According to some Western approaches, mindfulness practice can be expected to improve attention control and to lead to a shift in perspective.

Effects via attention control. Lutz, Slagter, Dunne, and Davidson (2008) argued that (as in most Hindu approaches to meditation) Buddhist approaches have meditators focus and sustain their attention on an object. This practice is thought to train skills in sustaining the focus of attention, detecting distractions, disengaging from such distractions, and redirecting the attention to the object one should focus on. These skills have been identified as basic attentional processes, and they are well connected to specific brain regions (for a wealth of references, see Chapter 3 in E. D. Smith & Kosslyn, 2007). According to Lutz et al., continued focused attention practice goes along with improvements in concentration tasks, such as continuous performance tasks, binocular rivalry tasks, and selective attention tasks. Therefore, according to these authors, meditators' concentration should eventually become more and more effortless, thus creating a sense of physical lightness and vigor that reduces the need for sleep and in addition leads to a significant decrease in emotional reactivity.

ADHD as a brain network dysfunction—IM as a tool to “fine tune” and control this network.

Dr. Kevin McGrew · Mar 28 · Science · 0 Comments

ADHD as a brain network dysfunction—IM as a tool to “fine tune” and control this network.

The explosion of research on *large scale brain networks*, and the “resting state” or “default mode or default network” in particular, has been dizzying. I previously reviewedkey brain network research describing the interaction between the *default*, *salience* (attention) and *executive controlled* networks. The most important conclusion, which was reinforced by my personal experiencewith Interactive Metronome (IM), is that problems with controlled attention (focus) may be responsible for a number of the behavioral symptoms of ADHD—and this is due to the poor ability to suppress the random self-talk “background noise” of the default brain network. [Click herefor related IM-HOME ADHD posts; click herefor ADHD- related Brain Clock.]

In prior posts I advanced the position that the efficacy of IM technology in improving focus or controlled attention is that it helps to "quiet the busy mind" due to the REST (random, episodic, spontaneous thought or thinking) of the default brain network. In simple terms, poor ability to suppress or quiet the default network results in poor controlled attention when trying to engage in controlled, deliberate cognitive tasks. The pirates of the default network are constantly engaged in “attentional capture” escapades—efforts to capture the brains gold—focus and controlled attention.

A new research review in Trends in Cognitive Sciences (January 2012, Vol. 16, No. 1) supports the hypothesis that ADHD may be a default brain network disorder. The authors state "*In 2007, Sonuga-Barke and Castellanos suggested that ADHD could be considered a default network disorder*"...and the authors of the current article agree.

Individuals with ADHD may have trouble stopping (inhibiting) the spontaneous intrusion of default network generated random thoughts when engaged in tasks that require laser-beam focus on a cognitively demanding task (e.g., solving math problems; reading). Either the default network does not function properly or is not synchronized well with other brain networks responsible for engaging controlled attention to shut down or inhibit the intrusion of thoughts generated by a busy mind. A comprehensive review of the ADHD research in Neuropsychopharmacologyalso concluded that studies of the brain when it is at "rest" (default mode) reveal that one of the primary problems in ADHD "may lie in dysfunction of brain regions that, as discussed above, support a proposed 'default network'. Specifically, it may be the case that an abnormally high default mode network activity may interfere with CFP attention network activity." CFP refers to cingulo-fronto-parietal activation.

I am not alone in my belief that a faulty default network, or a default network that is not well controlled by other cognitive control networks (sometimes referred to as poor network *coherence*), is important for understanding ADHD and other cognitive disorders. Check out "The Brains Background Noise" and "Diagnosis by Default" for other reports along these lines. Also, a very interesting studylinking the busyness of one's wandering mind and working memory and attention fits nicely into this growing body of literature.

The ability to invoke "on-demand-focus", to quiet the spontaneous internal self-talk and thinking we all enjoy when appropriate, is an important cognitive tool that can be trained. Forms of meditationappear to operate along these lines. As summarized in my prior posts, IM is a cognitive tool that can help individuals hone their ability to invoke on-demand-focus. The attention-capturing pirates need to be kept at bay when the brain's precious limited golden resource of attentional control (focus) is needed.

Tags: ADD/ADHD, brain timing, timing in the brain

Altered Small-World Brain Functional Networks in Children With Attention-Deficit/Hyperactivity Disorder

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Abstract: In this study, we investigated the changes in topological architectures of brain functional networks in attention-deficit/hyperactivity disorder (ADHD). Functional magnetic resonance images (fMRI) were obtained from 19 children with ADHD and 20 healthy controls during resting state. Brain functional networks were constructed by thresholding the correlation matrix between 90 cortical and subcortical regions and further analyzed by applying graph theoretical approaches. Experimental results showed that, although brain networks of both groups exhibited economical small-world topology, altered functional networks were demonstrated in the brain of ADHD when compared with the normal controls. In particular, increased local efficiencies combined with a decreasing tendency in global efficiencies found in ADHD suggested a disorder-related shift of the topology toward regular networks. Additionally, significant alterations in nodal efficiency were also found in ADHD, involving prefrontal, temporal, and occipital cortex regions, which were compatible with previous ADHD studies. The present study provided the first evidence for brain dysfunction in ADHD from the viewpoint of global organization of brain functional networks by using resting-state fMRI. *Hum Brain Mapp 30:638–649, 2009.*

Key words: ADHD; connectivity; efficiency; functional magnetic resonance imaging; networks; resting-state; small-world

Review

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Special Issue: Cognition in Neuropsychiatric Disorders

Large-scale brain systems in ADHD: beyond the prefrontal–striatal model

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Attention-deficit/hyperactivity disorder (ADHD) has long been thought to reflect dysfunction of prefrontal–striatal circuitry, with involvement of other circuits largely ignored. Recent advances in systems neuroscience-based approaches to brain dysfunction have facilitated the development of models of ADHD pathophysiology that encompass a number of different large-scale resting-state networks. Here we review progress in delineating large-scale neural systems and illustrate their relevance to ADHD. We relate frontoparietal, dorsal attentional, motor, visual and default networks to the ADHD functional and structural literature. Insights emerging from mapping intrinsic brain connectivity networks provide a potentially mechanistic framework for an understanding of aspects of ADHD such as neuropsychological and behavioral inconsistency, and the possible role of primary visual cortex in attentional dysfunction in the disorder.

reasonable assumption that unexpected results probably represent false positives. However, accumulating evidence suggests that the prefrontal–striatal model of ADHD should be extended to include other circuits and their interrelationships from the perspective of systems neuroscience [10,11]. We suggest that formulation of a more inclusive brain model of ADHD is facilitated by the new paradigm of resting-state functional magnetic resonance imaging (R-fMRI), which is increasingly revealing the intrinsic functional architecture of the brain [12]. Finally, we speculate that modulation of neural networks through imaging-guided transcranial direct current electrical stimulation (tDCS) may provide novel therapeutic opportunities for disorders such as ADHD.

Resting-state functional magnetic resonance imaging

Resting-state functional imaging, that is, imaging without a specific task (Box 1), is not new. It dates from the earliest

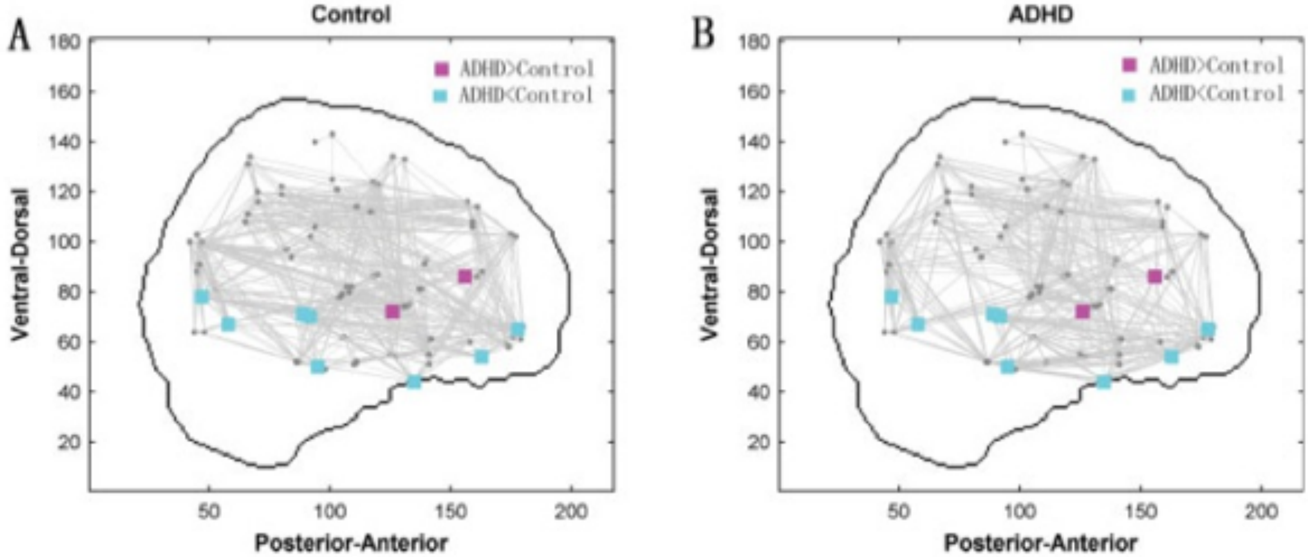

Figure 5.

ADHD-related changes in nodal efficiency in topological maps. The networks were constructed by converting the individual correlation matrices to generate sparse networks with the cost of 0.15 (the vertical lines in Fig. 2) and shown in a sagittal view of the brain. These black dots represent the brain regions that were visualized by locating their *y* and *z* centroid coordinates in the anatomical space. Cyan and magenta squares show significantly lower and higher nodal efficiency of brain regions in the ADHD patients compared with the controls, respectively. See Table II for the details of the regions.

DISCUSSION

This is the first study, to our knowledge, to investigate small-world properties of brain functional networks in children with and without ADHD. We found that brain functional networks exhibited economical small-world topology in both groups. An altered functional network, however, was found in the brain of ADHD. In particular, a tendency of shift toward regular networks was demonstrated in ADHD when compared with normal controls. Moreover, our study revealed that nodal efficiency was profoundly affected at several regions of prefrontal, temporal, and occipital cortices, which were compatible with previous studies in ADHD. Our results suggested that the widely distributed functional brain networks are altered in ADHD, thus providing further evidence for brain dysfunction associated with this disease [Bush et al., 2005; Seidman et al., 2004].

Since small-world networks were quantitatively described by Watts and Strogatz [1998], human brain functional networks with a small-world configuration have been validated by using various imaging techniques, such as MEG, EEG, and fMRI [for reviews, see Bassett and Bullmore, 2006; Stam and Reijneveld, 2007]. In agreement with these previous findings, in the present study, we also observed the features of small-world architecture in the functional brain networks in children both with and without ADHD using the resting-state fMRI (see Fig. 1), thus providing further support for the opinion that small-world brain networks have the ability to display tolerance in the face of developmental aberration or disease [Achard et al., 2006]. Moreover, the functional networks with small-world features were also found to show economical properties (see Fig. 2), consistent with previous studies [Achard and Bullmore, 2007]. Together, these findings supported the standpoint that brain networks might have been evolved to maximize cost efficiency of parallel information processing, i.e., high efficiency of parallel information transfer at low cost [Kaiser and Hilgetag, 2006; Sporns et al., 2004].

Although both of ADHD and control groups had economical small-world properties as elucidated earlier, the topology of the ADHD group was altered compared to the control group. A tendency of decreased global efficiency of the brain networks was found in ADHD over the whole cost range. It has been suggested that the global efficiency is affected by the loss of long-range connections [Latora and Marchiori, 2001]. Structural and diffusion imaging studies found that the regions showing the ADHD-related abnormality are associated with long fibers in ADHD children, such as the corpus callosum (connecting the left and right cerebral hemispheres) [Hill et al., 2003; Hynd et al., 1991; Semrud-Clikeman et al., 1994] and the anterior limb of internal capsule (containing thalamocortical fibers and corticopontine fibers) [Ashtari et al., 2005]. The abnormalities may incur the disruption to the long-range communication among parts of the brain. A recent research has also indicated abnormal long-range connections (dorsal anterior cingulate and medial parietal lobe) in ADHD [Castellanos et al., in press]. All these abnormalities may contribute to the decreasing tendency of global efficiency of brain network in ADHD. In the current study, significantly increased local efficiency of the brain networks was also found in ADHD children compared to the controls. The underlying mechanisms of increased local efficiency of a network have been widely discussed in various studies. For example, De Vico Fallani et al. [2007] reported that increased local efficiency in spinal cord injured patients could be attributable to a functional reorganization (i.e. brain plasticity). Latora and Marchiori [2001] indicated that the higher the local efficiency of a network, the larger fault tolerance was the network at the face of external attack. We thus suspected that the higher value of local efficiency in ADHD observed here might suggest a kind of defense mechanism responsible for suppressing the disorder affection.

Although both the ADHD children and controls showed small-world attributes in their brain functional networks, the increased local efficiency combined with slightly decreased global efficiency made their networks topology exhibit the tendency of a shift toward regular networks (see Fig. 1). It has been suggested that the small-world structure reflects an optimal balance between local processing and global integration [Sporns and Tononi, 2002]. Therefore, any abnormal shift caused by brain diseases toward either random [Bartolomei et al., 2006; Micheloyannis et al., 2006b; Ponten et al., 2007] or regular [De Vico Fallani et al., 2007] networks may reflect a less optimal network organization. Though the biological causes of underlying the shift remain still unclear, the regular configurations in complex networks have been found to demonstrate low global coordination and slow information flow compared to small-world arrangements [Barahona and Pecora, 2002; Lago-Fernandez et al., 2000; Nishikawa et al., 2003; Strogatz, 2001]. Hence, our results suggested that the ADHD-related network shift may reflect the abnormalities of network architecture.

As described by Achard and Bullmore [2007], the nodal efficiency measures the extent to which the node connects all other nodes of a network, which may indicate the importance of the nodal area in the whole brain network. Using this measure, we here found abnormal nodal efficiency in several regions, involving the prefrontal, temporal, occipital, and subcortical regions (Table II) that were, in general, concerned in ADHD studies. The orbital frontal cortex (OFC) is associated with executive function network [Makris et al., 2007]. The decreased nodal efficiency in the OFC was in accordance with several structural and functional imaging studies that have found cortical atrophy and reduced activity in this region in the ADHD patients [Lee et al., 2005; Makris et al., 2007], which might suggest the abnormalities of executive function in the patients. In addition, several regions belonging to temporal and occipital cortices were also found to have significant decreases in nodal efficiency (Table II), which were compatible with previous studies showing ADHD-related structural and functional abnormalities in these regions [Castellanos