

The Default Network: Your Mind, on Its Own Time

By Trey Hedden, Ph.D.

Editor's note: Studies about the brain usually focus on neural activity during the completion of a specific task—remembering a series of words, for example. But over the last 20 years, researchers have been interested in what the brain does during periods of supposed inactivity. They discovered that when someone appears to be doing nothing at all, a network of brain regions—named the default network—is hard at work, allowing for the rich inner lives inside our heads. Applying what is known about the default network to diseases like Alzheimer's allows for new possibilities for diagnosis and evaluation of treatments.

Article available online at <http://dana.org/news/cerebrum/detail.aspx?id=29194>

You're lying in a brain scanner in the dark, looking up at a small white crosshair, left alone with your thoughts for the next six minutes. What goes through your mind? Perhaps you think about why you volunteered for this, or what you'll do with the money you earn from this experiment. Perhaps you plan out the rest of your day, or start replaying a conversation from yesterday. New techniques in neuroimaging are helping scientists understand how your brain represents such internally directed and spontaneous thoughts.

Beginning in the 1980s, technological developments in brain imaging (primarily with positron-emission tomography and magnetic resonance imaging of blood flow) brought the fields of psychology and neuroscience closer together. Cognitive neuroscientists, as researchers at this intersection of disciplines came to be called, focused almost exclusively on how people's brains represent and respond to goal-directed tasks—that is, thoughts about the external world directed by external stimulation. Imagine, for example, that you're asked to remember a series of pictures. The pattern of blood flow in your brain while you study the pictures compared to periods when you're not looking at the pictures tells researchers which portions of the cortex are involved in memory encoding, as well as visual perception and other mental processes. This type of study became a common way to compare what happens in the brain during a task with what happens during a so-called control state, very often a resting period when a person is simply left to his or her thoughts.

Because of the ubiquitous use of such control states in study design, nearly every lab conducting neuroimaging had disks full of data recorded when a person was left to his or her own devices. For years, these data were mostly ignored because the control state was thought to be too unconstrained to understand. This opinion was based on the knowledge that one-third or more of our thoughts consist of spontaneous daydreams or mind wandering.¹ Scientists established this estimate through questionnaires and with a technique known as experience sampling, in which individuals carry around a beeper that goes off at random times during the day. When it beeps, study participants report their current activities and thoughts. The uncertainty about what people are actually thinking and doing during such unconstrained times has led some researchers to reject the idea of using resting periods as a control state, favoring very simple directed tasks instead.²

But just because something is random or uncertain does not mean that it cannot be understood. In the mid- to late 1990s, a few scientists, notably Marcus Raichle and his colleagues at Washington University, realized that it might be worthwhile to examine what our brains do

during these seemingly quiescent periods. They made two important observations. First, when a resting period was compared to activity during a goal-directed task (it almost didn't matter what task), a particular network of brain regions was consistently involved (see figure, page 10).³ This set of brain regions had not previously been thought of as a unified network of structures that can work together, so this was a major discovery. The second observation was that these regions, along with the rest of the brain, were exceedingly busy during resting periods.

Raichle and his colleagues labeled this network of brain regions the default network, partly because it seemed to be involved when people returned to whatever they were doing when not performing the researchers' tasks and partly because the energy consumption of the brain seemed to be at equilibrium during resting periods.⁴ At equilibrium, the brain consumes approximately one-fifth of the body's oxygen and produces a large amount of activity. This high-energy equilibrium seems to prominently involve the default network and occurs even though the person may appear to be doing nothing at all. Of course, it is only when looked at from the outside that the person appears to be doing nothing; scientists had been so focused on the tasks they asked people to perform that they had largely ignored the rich inner lives inside all of our heads. Researchers are now actively investigating what thought processes engage this so-called default network. The primary candidates share the property of being internally directed and tend to involve memory or imagination.

Intrinsic Activity in the Default Network

The idea that this network might be involved in unconstrained thought such as spontaneous recollection of memories or imaginative daydreams made it a natural target for new techniques that measure the intrinsic organization of the brain. In the early 1990s, a technique known as intrinsic activity correlations was introduced.⁵ This technique measures fluctuations in the brain's activity over time and relates the fluctuations in one region to those elsewhere in the brain. This is a powerful technique for identifying sets of brain regions that are united in their activity patterns—in other words, regions that form coherent brain networks. After the default network had become a topic of more vigorous investigation in the early 2000s, researchers applied the technique of intrinsic activity correlations and found that the exact same regions that were so active during control periods compared to task periods could also be identified solely on the basis of their correlated activity patterns during resting periods (see middle panel of figure, page 10).⁶ Suddenly, the use of a task was not necessary for investigating the default network,

opening up the possibility of using resting period scans to identify the network and relate its properties to behavior even in patients too severely impaired to perform a complicated task. While you simply lie in the dark for a few minutes looking at a crosshair and thinking your own thoughts, a researcher can map the correlated networks in your brain.

It is important to recognize that these correlated activity patterns during a resting period do not necessarily represent unconstrained mental activity that is nonetheless consciously directed (such as planning a shopping list). These patterns may instead represent the spontaneous and synchronous firing of neurons that form a brain network—that is, this technique may be well suited to identifying structural properties of the brain’s organization into networks but may not always be informative about how those networks function. One reason the regions within the default network are so readily identifiable by their correlated activity may be because they happen to be among the most highly interconnected areas of the brain during both rest and task-directed activities.⁷ That is, certain regions of the default network may act as information hubs or switching stations that allow for communication between more remote regions or between regions that reside in different networks.

It should also be noted that many other brain networks can be identified by their correlated activity patterns during resting periods, so the term “default network” may inadvertently create confusion. Many scientists have taken to calling this the “core” network because of its high degree of interconnectivity to other regions, suggesting that it may act as a connector for information processing that involves multiple networks. In keeping with the labeling of networks according to their function (attention network, motor network, auditory network, etc.), it might be useful to refer to this as the internally oriented network (ION), suggesting the wide range of internally directed functions that have been attributed to these regions. But for now, “default network” remains the most commonly used label.

Functions of the Default Network

The problem with a network that seems to be most active during unconstrained resting periods is that it can be difficult to measure exactly what the network is doing. Scientists have started to tackle this problem by using tasks that mirror some of what might be going on during such resting periods. By changing which parts of the resting period (memory, planning and imagination, visualization, etc.) the tasks replicate, they are beginning to home in on what types of spontaneous thoughts primarily contribute to activity in the default network.

Confirming the role of the default network in spontaneous (as opposed to task-directed) thought is one top-level goal of such research. In one study by Malia Mason and colleagues, then at Dartmouth University, individuals received several days of practice on a task until they were extremely fluent in performing it.⁸ After extensive practice, participants reported more mind wandering during performance of the well-rehearsed task (presumably because they were able to easily keep up with the task) than during performance of a novel version of the task. When they performed the same highly practiced and novel tasks in an MRI scanner, activity in the default network was more evident during the well-rehearsed task than during the novel task. This activity was related to an individual's self-reported propensity to mind-wander. Although it did little to separate the types of thought that might contribute to default-network activity during mind wandering, this and other related studies represent an important confirmation that the default network can be manipulated by encouraging individuals to mind-wander.

What types of thoughts are we likely to engage in when our minds wander? Intuition tells us that thoughts about ourselves in various scenarios, real or imagined, may occupy our self-absorbed minds. Several studies have shown that regions of the default network are engaged by self-referential thinking, including when we make decisions about personal preferences.⁹ Still others have shown that when we consider the thoughts of others (using a so-called theory of mind), certain regions of the default network become more engaged.¹⁰ It appears that simulating how we might react in the shoes of another involves the same network as when we think about our own thoughts, feelings, and desires. Disorders that potentially affect self-referential thinking, such as autism, schizophrenia, and depression, appear to alter the function of the default network. For example, default network activity is disrupted in depressed patients when they try to regulate their emotional response to a negative image, suggesting that the default network may be involved in distortions of self-relevant thoughts that occur with depression.¹¹

Another important function of the default network is thought to be bringing to mind memories of the past. Given the default network's role in self-referential thinking, self-relevant or autobiographical memories are believed to be especially engaging for this network. But how can one distinguish an autobiographical memory from the act of visualization of an imagined (i.e., not remembered) scene? Donna Addis and her colleagues at Harvard University attempted to answer this question by collecting extensive reports of autobiographical memories from their study participants.¹² They then took key details about these memories and asked people to re-imagine them while undergoing an MRI scan. In some cases, the researchers provided the same

details from a single memory to cue the person to think of that memory again. In other cases, they combined details from multiple memories and asked individuals to imagine a past event involving details that never actually occurred together, or they asked them to imagine a future event involving those details. Although the entire default network was involved in thinking of both actual and imagined events, they found that when actual memories were being remembered, regions in the hippocampus and medial temporal lobes were most involved. These regions were already known to be critically involved in memory. In contrast, when imagined past or future events were being constructed, the midline regions in the posterior cingulate and frontal cortex were most involved. Such results suggest that different parts of the default network are involved in memory and imagination, and that the content of inwardly directed thoughts might influence how the default network interacts with other regions.

The idea that the default network may be made up of multiple subnetworks has been verified using the technique of intrinsic activity correlations. By ranking the strength of association among the fluctuating patterns of activity during rest across different brain regions, Jessica Andrews-Hanna and colleagues at Harvard found three distinct systems within the default network: a core system involved across many functions ascribed to the default network and comprising the midline areas of the posterior cingulate and frontal cortex; a medial temporal lobe subsystem involving the hippocampus and other memory-related regions; and another subsystem involving those areas most commonly associated with self-referential thought.¹³ They further showed that these systems were differently engaged by thinking about oneself in the present and in the future, with the medial temporal lobe memory subsystem being more engaged in the hypothetical imagining of the future and the self-referential subsystem being more engaged in thinking about oneself in the present.

Relevance to Disease: The Case of Alzheimer's

Much research has been devoted to understanding the thought processes performed by the default network, but a more practical consequence of this research is that it may have relevance for understanding common diseases of the nervous system. Several disorders, including autism, depression, schizophrenia, and Alzheimer's disease, have been linked to dysfunctional activity within the default network.¹⁴ As a case study, we will examine Alzheimer's disease and how understanding the default network's role in the disease may eventually help in the quest for development of treatment and prevention.

There is no doubt that Alzheimer's is a frightening and devastating disorder. It is especially frightening because it is so prevalent in our rapidly aging society—approximately 5.1 million (or one in eight) people over 65 in the United States have the disease¹⁵—and because there is no known cure. The disease is devastating not because it weakens our bodies, but because it takes from us what we most associate with ourselves: our memories and our innermost mental lives. Alzheimer's is characterized by a loss of memory that disrupts daily life, usually beginning with an inability to form new and lasting memories and progressing to loss of long-held memories. Because they can't remember who close relatives are or what they did earlier, patients in more advanced stages of the disease often experience confusion, poor judgment, emotional outbursts, and difficulty completing familiar tasks. Although their lives may still be punctuated by periods of lucidity, patients often seem to have largely lost hold of their inner lives and experience severe reductions in the types of internal mental activity associated with the function of the default network.

Since the characterization of this disease by Alois Alzheimer in 1906, the only certain way to confirm a diagnosis of Alzheimer's disease has been examination of the brain after the patient's death. The hallmark cell abnormalities known as neuritic plaques and neurofibrillary tangles create a dense thicket of distorted cells in the brains of those suffering from Alzheimer's. Neuritic plaques consist mainly of a substance called amyloid beta that is normally produced by the body but appears to become toxic when longer chains of it accumulate and eventually are deposited in the brain as plaques. Neurofibrillary tangles form inside nerve cells when a protein called tau, which normally helps to stabilize the cellular infrastructure, becomes defective. New imaging techniques have made it possible to recognize plaques in the brain while a person is still alive.¹⁶ Although techniques that make it possible to specifically image tau are not yet in routine use in humans, scientists are actively working on their development. The advent of plaque-visualization techniques constitutes a breakthrough in our ability to understand amyloid pathology and its potential role in the progression of Alzheimer's disease.

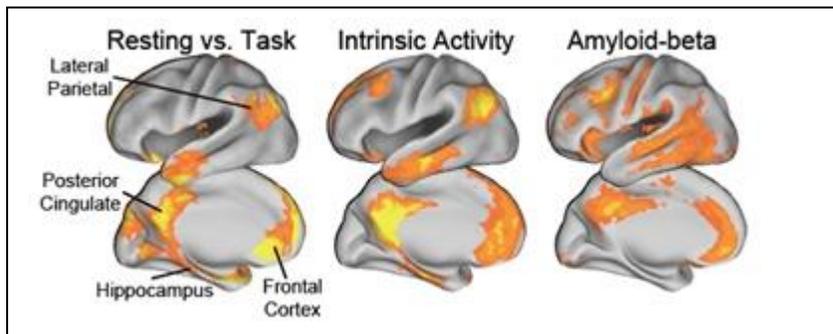
One important finding that emerged from these new techniques was that the amyloid plaques were extremely widespread throughout the cortex, expressing an unexpected yet recognizable pattern. It was immediately apparent that the pattern of amyloid deposits in living Alzheimer's patients was similar to the regions that make up the default network (see right panel of figure, page 10).¹⁷ Cindy Lustig, now at the University of Michigan, Michael Greicius at Stanford, and others had previously shown that Alzheimer's patients had abnormal activity in the

default network.¹⁸ We now know that amyloid plaques appear to preferentially accumulate in certain regions of the default network. Upon seeing the substantial, although not complete, overlap between amyloid and core regions of the default network, researchers hypothesized that perhaps the amyloid plaques lead to a failure of function within the default network and disrupt its ability to communicate with other regions, especially memory-related regions in the medial temporal lobes. Research that combines imaging during task performance, intrinsic activity correlations, and amyloid imaging techniques has confirmed that abnormal default network activity is associated with high levels of amyloid in the brain.¹⁹ Some studies suggest that a severe reduction of intrinsic activity correlations within the default network may be sufficient to distinguish Alzheimer's patients from healthy individuals of the same age.²⁰ Even older adults who do not show clinical impairments or dementia but who have high amyloid levels show disruptions in the relationship between the default network and the medial temporal lobes. These results suggest that amyloid deposition leads to dysfunction of the default network, which may also contribute to the devastating loss of memory.

This leads to a speculative, but hopeful, possibility. By combining several imaging techniques, we may be closer to understanding why the large-scale and devastating effects of Alzheimer's disease occur. When an Alzheimer's patient loses the inner life that most of us consider to be central to our very being, it points to the possibility that functions ascribed to the default network, such as self-referential thought, autobiographical memory, imagining the future, and planning and decision making, may be precisely those most affected by the hallmark amyloid pathology of Alzheimer's disease. The ability to measure amyloid plaques (and eventually neurofibrillary tangles) in living individuals may allow us to begin to predict with more precision who is most at risk of developing Alzheimer's disease. If sufficiently validated, it may eventually be possible to use these imaging techniques as an end point in clinical trials of therapies with the aim of reducing plaque burden and restoring brain function. This is potentially important because recently publicized trials not involving neuroimaging techniques have had disheartening results.²¹ Several clinical trials of anti-amyloid therapies in Alzheimer's patients did not demonstrate a benefit of treatment, and some potentially serious side effects were encountered. As is often the case in drug development, new and more extensive trials are needed to determine whether treatments aimed at reducing plaques can successfully and safely halt the progression of the disease. Such trials are currently under way and will eventually provide an answer.

However, it may be critically important that the treatments be applied very early in the course of the disease before irreversible damage has occurred. Using neuroimaging to examine the function of the default network and the presence of amyloid plaques in these same regions, we may be able to observe the effects of new and safe therapies in people who are in early stages of the disease before cognitive deficits occur or who possess certain characteristics that make them good candidates for preventive treatments. Plaques and tangles could be identified early and treatments tested for efficacy during this early phase, when they may be most likely to be effective.²² These developments are likely still many years away, but they offer hope that we can observe, understand, and prevent the once-hidden signs of Alzheimer's in ways that have never before been possible.

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Figure: Three Views of the Default Network

Adapted from data reported in T. Hedden, K. R. Van Dijk, J. A. Becker, A. Mehta, R. A. Sperling, K. A. Johnson, and R. L. Buckner, "Disruption of Functional Connectivity in Clinically Normal Older Adults Harboring Amyloid Burden," *Journal of Neuroscience* 29 (2009): 12686–12694.

All images are from the same group of elderly individuals (aged 60–88), none with diagnosed Alzheimer's disease. Upper images in each panel provide a lateral (side) view of the brain, lower images provide a medial (midline) view.

Left: The default network identified by comparing activity during a resting period with activity during a directed-attention task. Coloration indicates increased activity during rest. Key regions of the default network are labeled, including midline areas in the posterior cingulate and frontal cortex, lateral areas of the parietal lobe, and the hippocampus and adjacent regions in the medial temporal lobe.

Middle: The default network identified by intrinsic activity correlations during a resting period. Coloration represents the degree of correlated activity of each region of the brain with the posterior cingulate cortex.

Right: The pattern of amyloid deposition measured with positron-emission tomography. Although not identical to the default network, substantial overlap between regions of high amyloid deposition and regions of the default network is apparent. Coloration indicates increased retention of the amyloid marker.

References

1. M. J. Kane, L. H. Brown, J. C. McVay, P. J. Silvia, I. Myin-Germeys, and T. R. Kwapil, "For Whom the Mind Wanders, and When: An Experience-Sampling Study of Working Memory and Executive Control in Daily Life," *Psychological Science* 18 (2007): 614–621.
2. For a recent version of this critique and other potential issues with the interpretation of the default network, see A. M. Morcom and P. C. Fletcher, "Does the Brain Have a Baseline? Why We Should Be Resisting a Rest," *Neuroimage* 37 (2007): 1073–1082. There are several replies to this article discussing many of the arguments.

3. G. L. Shulman, J. A. Fiez, M. Corbetta, R. L. Buckner, F. M. Miezen, M. E. Raichle, and S. E. Petersen, "Common Blood Flow Changes Across Visual Tasks: II. Decreases in Cerebral Cortex," *Journal of Cognitive Neuroscience* 9 (1997): 648–663.
4. The pivotal report that introduced the concept of the default network is M. E. Raichle, A. M. MacLeod, A. Z. Snyder, W. J. Powers, D. A. Gusnard, and G. L. Shulman, "A Default Mode of Brain Function," *Proceedings of the National Academy of Sciences, USA* 98 (2001): 676–682.
5. This technique was based on work in positron-emission tomography, as described in K. J. Friston, C. D. Frith, P. F. Liddle, and R. S. J. Frackowiak, "Functional Connectivity: The Principal-Component Analysis of Large (PET) Data Sets," *Journal of Cerebral Blood Flow and Metabolism* 13 (1993): 5–14. The application of intrinsic activity correlations to MRI data during a resting period is described by B. Biswal, F. Z. Yetkin, V. M. Haughton, and J. S. Hyde, "Functional Connectivity in the Motor Cortex of Resting Human Brain Using Echo-planar MRI," *Magnetic Resonance in Medicine* 34 (1995): 537–541.
6. M. D. Greicius, B. Krasnow, A. L. Reiss, and V. Menon, "Functional Connectivity in the Resting Brain: A Network Analysis of the Default Mode Hypothesis," *Proceedings of the National Academy of Sciences, USA* 100 (2003): 253–258.
7. The initial demonstration of default network regions as highly interconnected hub regions was provided in P. Hagmann, L. Cammoun, X. Gigandet, R. Meuli, C. J. Honey, V. J. Weeden, and O. Sporns, "Mapping the Structural Core of Human Cerebral Cortex," *PLoS Biology* 6 (2008): e159. An application of this idea and its potential relevance to Alzheimer's disease is described by R. L. Buckner, J. Sepulcre, T. Talukdar, F. M. Krienen, H. Liu, T. Hedden, et al., "Cortical Hubs Revealed by Intrinsic Functional Connectivity: Mapping, Assessment of Stability, and Relation to Alzheimer's Disease," *Journal of Neuroscience* 29 (2009): 1860–1873.
8. M. F. Mason, M. I. Norton, J. D. Van Horn, D. M. Wegner, S. T. Grafton, and C. N. Macrae, "Wandering Minds: The Default Network and Stimulus-Independent Thought," *Science* 315 (2007): 393–395.
9. J. M. Moran, T. F. Heatherton, and W. M. Kelley, "Modulation of Cortical Midline Structures by Implicit and Explicit Self-Relevance Evaluation," *Social Neuroscience* 4 (2009): 197–211.
10. R. N. Spreng and C. L. Grady, "Patterns of Brain Activity Supporting Autobiographical Memory, Propection, and Theory of Mind, and Their Relationship to the Default Mode Network," *Journal of Cognitive Neuroscience* 22 (2010): 1112–1123.
11. Y. I. Sheline, D. M. Barch, J. L. Price, M. M. Rundle, S. N. Vaishnavi, A. Z. Snyder, et al., "The Default Mode Network and Self-referential Processes in Depression," *Proceedings of the National Academy of Sciences, USA* 106 (2009): 1942–1947.

12. D. R. Addis, L. Pan, M. A. Vu, N. Laiser, and D. L. Schacter, "Constructive Episodic Simulation of the Future and the Past: Distinct Sub-systems of a Core Brain Network Mediate Imagining and Remembering," *Neuropsychologia* 47 (2009): 2222–2238.
13. J. R. Andrews-Hanna, J. S. Reidler, J. Sepulcre, R. Poulin, and R. L. Buckner, "Functional-Anatomic Fractionation of the Brain's Default Network," *Neuron* 65 (2010): 550–562.
14. For a review of the default network's involvement in multiple disorders, see S. J. Broyd, C. Bemanuele, S. Debener, S. K. Helps, C. J. James, and E. J. Sonuga-Barke, "Default-Mode Brain Dysfunction in Mental Disorders: A Systematic Review," *Neuroscience and Biobehavioral Reviews* 33 (2009): 279–296.
15. Alzheimer's Association, "2010 Alzheimer's Facts and Figures," *Alzheimer's and Dementia* 6 (2010): 158–194.
16. There are now several amyloid agents available for use in neuroimaging. The first of these new-generation agents is described by W. E. Klunk, H. Engler, A. Nordberg, Y. Wang, G. Blomqvist, D. P. Holt, et al., "Imaging Brain Amyloid in Alzheimer's Disease with Pittsburgh Compound-B," *Annals of Neurology* 55 (2004): 306–319. For reporting on recent advances using amyloid imaging, see <http://www.alzforum.org/new/detail.asp?id=2389> and <http://www.nytimes.com/2010/06/24/health/research/24scans.html>.
17. The article that pointed out this remarkable similarity and posited several hypotheses that still drive investigation is R. L. Buckner, A. Z. Snyder, B. J. Shannon, G. LaRossa, R. Sachs, A. F. Fotenos, et al., "Molecular, Structural, and Functional Characterization of Alzheimer's Disease: Evidence for a Relationship Between Default Activity, Amyloid, and Memory," *Journal of Neuroscience* 25 (2005): 7709–7717.
18. C. Lustig, A. Z. Snyder, M. Bhakta, K. C. O'Brien, M. McAvoy, M. E. Raichle, et al., "Functional Deactivations: Change with Age and Dementia of the Alzheimer Type," *Proceedings of the National Academy of Sciences, USA* 100 (2003): 14504–14509. M. D. Greicius, G. Srivastava, A. L. Reiss, and V. Menon, "Default-Mode Network Activity Distinguishes Alzheimer's Disease from Healthy Aging," *Proceedings of the National Academy of Sciences, USA* 101 (2004): 4637–4642.
19. R. A. Sperling, P. S. Laviolette, K. O'Keefe, J. O'Brien, D. M. Rentz, M. Pihlajamaki, et al., "Amyloid Deposition Is Associated with Impaired Default Network Function in Older Persons Without Dementia," *Neuron* 63 (2009): 178–188. T. Hedden, K. R. Van Dijk, J. A. Becker, A. Mehta, R. A. Sperling, K. A. Johnson, and R. L. Buckner, "Disruption of Functional Connectivity in Clinically Normal Older Adults Harboring Amyloid Burden," *Journal of Neuroscience* 29 (2009): 12686–12694.
20. Although diagnostic specificity and robustness to differences in analytic methods remain to be confirmed, the possibility of using such images to detect Alzheimer's is described by W. Koch, S. Teipel, S. Mueller, J. Benninghoff, M. Wagner, A. L. Bokde, et al., "Diagnostic

Power of Default Mode Network Resting State fMRI in the Detection of Alzheimer's Disease," *Neurobiology of Aging* (2010), e-publication ahead of print.

21. Recent reporting on setbacks in clinical trials includes:
<http://www.alzforum.org/new/detail.asp?id=2536>
<http://www.nytimes.com/2008/07/01/business/01gene.html>
<http://www.alzforum.org/new/detail.asp?id=1647>
<http://www.economist.com/node/16374470>
22. A working group convened by the National Institute on Aging at the National Institutes of Health and the Alzheimer's Association has proposed a new set of criteria for the earliest stages of Alzheimer's disease that include certain neuroimaging techniques. See <http://www.alzforum.org/new/detail.asp?id=2521> and <http://www.telegraph.co.uk/health/healthnews/7965818/Alzheimers-disease-being-tackled-too-late-Lancet.html> for reporting on why these criteria may represent an important step for diagnosis and evaluation of treatments. These criteria are still in the discussion and review stage; detailed information on the proposal can be found at http://www.alz.org/research/diagnostic_criteria.

Recommended Reading:

The following lay-friendly articles provide an in-depth review of the concepts discussed here:

R. L. Buckner, J. R. Andrews-Hanna, and D. L. Schacter, "The Brain's Default Network: Anatomy, Function, and Relevance to Disease," *Annals of the New York Academy of Sciences* 1124 (2008): 1–38.

M. E. Raichle, "The Brain's Dark Energy," *Scientific American* 302 (2010): 44–49.

D. Zhang and M. E. Raichle, "Disease and the Brain's Dark Energy," *Nature Reviews Neurology* 6 (2010): 15–28.