Assessing Cognition and Brain Function

Neal J. Cohen, PhD

Overview

Cognition and brain function can be assessed through a variety of powerful behavioral and cognitive neuroscience tools. In addition to assessment strategies that provide global measures of cognitive and brain health, it is possible to use more specialized tests to sample specific domains of cognition and brain function. In the work reviewed here, we target the assessment of memory specifically. But even the domain of memory is large, encompassing a range of capacities supported by multiple systems of the brain. The emphasis here is on one particular memory system, supporting relational (or declarative) memory, which depends critically on the hippocampus and related medial temporal-lobe (MTL) structures. The hippocampus and relational memory provide a favorable target for investigations of the effects of nutrition, because this memory system is highly modifiable, susceptible to damage or disruption, and also susceptible to enhancement by experience and by certain interventions, such as exercise or fitness. This paper highlights a few powerful and sensitive tests of relational memory and hippocampal function, and illustrates some findings that emphasize the modifiability of this system.

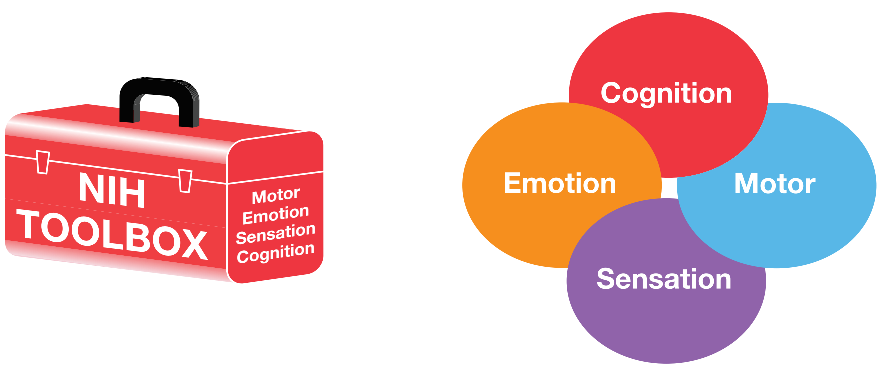
Cognition and Brain Function

Assessment of the potentially beneficial effects of nutrition can be addressed using powerful assays of the status of cognition and brain function. Cognition refers to the abilities that derive from the acquisition, processing, and use of information or knowledge, and the mental processes that support them. Assessing cognitive function usually entails examining various behavioral performances and abilities. Cognitive functions are implemented in the biological processes of the brain: however, a fuller assessment of cognitive function also would include examination of the brain systems and brain mechanisms that underlie those mental processes, which is an approach favored in modern-day cognitive neuroscience.

Assessment Strategies

The effects of various types of intervention, whether pharmaceutical, lifestyle choice (such as physical activity), or nutritional, may be assessed using very different approaches. Some intervention studies involve assessments conducted via purely behavioral tests, while other assessments are directed at brain function more directly, through human electrophysiology and/or brain imaging. Another critical way in which assessment strategies differ is with regard to whether global measures of overall cognitive and brain health are used; or assessment of cognitive and brain function is broad and comprehensive, sampling across a range of different cognitive domains supported by disparate brain systems; or assessment is of a particular domain of cognition and brain function that is seen as an especially favorable target of the intervention.

Assessing multiple domains of cognition is often accomplished, when possible, with one or another ambitious battery of tests, each focused on one or another cognitive process or mental ability. One increasingly used example is the National Institutes of Health (NIH) Toolbox, which provides a computer-based examination of cognition that includes various measures of attention, episodic memory, working memory, language, executive function, and processing speed (Fig 1).[1,2]



Assessment via behavioral tests
For example, with the NIH Toolbox

Fig 1. The National Institutes of Health (NIH) Toolbox is used to assess cognition and brain function.[1,2]

Here, we focus specifically on memory, reflecting the emphasis of the Center for Nutrition, Learning, and Memory, University of Illinois at Urbana-Champaign (http://cnlm.illinois.edu/). In the remainder of this review we briefly consider the nature and organization of memory; introduce a particular form or type of memory and illustrate how to assess it with sensitive, targeted measures; and explain why it might be a favorable target for the beneficial effects of nutrition on brain and cognition.

Multiple Memory Systems

Memory is itself a large domain, encompassing a collection of abilities that are supported by various brain mechanisms. Cognitive neuroscience research has shown that there are multiple memory systems in the brain.[3,4] Various taxonomies of memory have been proposed, but most investigators agree that important distinctions can be drawn between *declarative*, or *relational*, memory, and *procedural* memory. Declarative or relational memory refers to memory for facts and events, and the relations among them (eg, remembering the who, what, where, and when of experienced events, and the calendar of upcoming events; spatial layouts and maps; face-name pairings; and richly interconnected knowledge about various domains of interest, such as detective novels, or professional football, or Academy Award-winning movies, or nutritional supplements). Non-declarative or *procedural* memory refers to memory supporting the acquisition and expression of skills (eg, supporting ability in tennis, typing, dancing, wine tasting, dog judging, or detecting tumors in magnetic resonance imaging [MRI] scans).[3,4]

Relational Memory

Relational memory depends critically on the hippocampus and related MTL structures. Why is this aspect or form of memory so important for our purposes? First, in supporting the ability to acquire, retain, retrieve, and flexibly use knowledge about facts and events, relational memory provides a critical foundation for many cognitive abilities, including aspects of language,[5,6] decision making[7] and other strategic behaviors,[8] inferential reasoning,[9] and creative thinking.[10] Accordingly, interventions that can alter relational memory will have broad consequences for cognitive function. Second, this memory system is highly modifiable, susceptible to damage or disruption in various neurological and psychiatric conditions, and also susceptible to enhancement by experience and by certain interventions, such as exercise or fitness. Accordingly, it may be a promising target for enhancement by nutrition.

Assessing Relational Memory

We have developed several especially powerful and sensitive tests for assessing the status of relational memory and hippocampal function. In one, participants are shown a series of arbitrary face-scene pairings, and are subsequently tested with scenes on each of which are superimposed a test display with three equally familiar faces. The task is to identify the particular face that had been studied with that scene. Performance is assessed via both behavioral accuracy and eye movements. Tracking of eye movements has proven to provide a uniquely robust measure of memory.[11] The degree of preferential viewing of the "matching" face (the one that had been previously studied with that scene) relative to the other, equally familiar, faces in the test display constitutes the measure of relational memory.[12] Preferential viewing of the matching face occurs automatically and obligatorily early in viewing (within 500-750 msec)[12]; fails to occur in patients with amnesia following damage to the hippocampus[12]; is associated with hippocampal activity in functional MRI studies of normal participants, activity which predicts eye movements even when the behavioral response is inaccurate[13]; and is reduced in magnitude and delayed in onset in patients with schizophrenia,[14] a disorder associated with pathological changes of the hippocampus.[15]

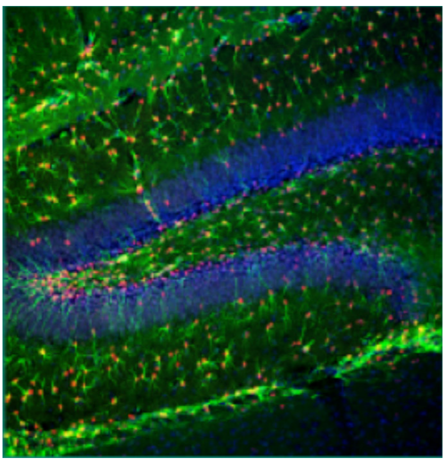
A second test that has proven very sensitive to relational memory and hippocampal function involves spatial reconstruction of (even small) arrays of objects.[16] In this task, a particular type of memory error, involving the swapping of positions of pairs of objects ("swap errors")—ie, failure to keep track of the arbitrary bindings of objects to their positions in the array—turns out to be diagnostic of hippocampal damage. Patients with amnesia following damage to the hippocampus made 40 times more errors of this type than did matched comparison participants, and the patients made swap errors even when only two objects had to be remembered across only a few seconds.[16]

Modifiability of the Hippocampus and Relational Memory

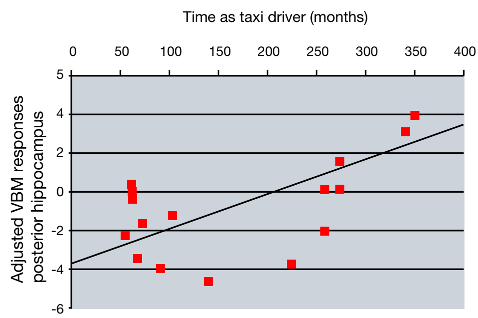
Hippocampal function and relational memory are highly susceptible to damage or disruption. In the examples above and in others,[17,18] damage to the hippocampus produced a deficit in memory that was highly selective, affecting memory for the relations among items while leaving intact memory for the items themselves tested individually.

The modifiability of the hippocampus and relational memory also is seen in the opposite direction, with clear capability to show enhancement or growth. The hippocampus is one of only two structures in the brain that exhibit *neurogenesis*, the addition of new neurons, in adulthood. This process is shown to occur even in humans.[19,20] In animals, neurogenesis is increased by exercise and by living in enriched environments, and has been shown to be associated with enhancement of synaptic plasticity and memory function.[21] In humans, the volume of the hippocampus likewise has been shown to increase in response to experiential factors and exercise or fitness. One well-known study found that the size of (posterior) hippocampus in London taxi drivers was proportional to the amount of experience they had in (months of) professional driving (Fig 2).[22]

Changes in the Hippocampus



Visualizing creation of new neurons *(neurogenesis)* in the hippocampus



The volume of the hippocampus of London taxi drivers increased as a function of the number of years of experience driving

Fig 2. Neurogenesis in the hippocampus of London taxi drivers.[22]

VBM=voxel-based morphometry

Source: Maguire EA et al. Navigation-related structural change in the hippocampi of taxi drivers. *Proc Natl Acad Sci U S A.* 2000;97(8):4398-4403. © 2000 National Academy of Sciences, U.S.A.

Other studies show increased hippocampal volume in healthy elderly individuals who underwent an exercise intervention[23] and in higher-fit (relative to lower-fit) preadolescent children.[24] In the latter study, higher fitness and increased hippocampal volume were associated with better relational memory.

Finally, in rodents, there is promising evidence concerning the synergistic effects of nutrition plus exercise. Exercise reduced or overcame the negative effects of a diet high in saturated fats and refined sugar in the levels of brain-derived neurotrophic factors (BDNF) that are associated with synaptic plasticity, and the combination of exercise with dietary supplementation with docosahexaenoic acid (DHA) had stronger effects on spatial learning and on BDNF-mediated synaptic plasticity than did either factor alone.[25-27]

Summary

Taken altogether, these studies suggest that the hippocampus and relational memory may provide a favorable target for investigations of the effects of nutrition such as dietary intake of omega-3 fatty acids, antioxidants, and flavonoids.[26] This memory system is highly modifiable, including in response to exercise or fitness interventions, and we have assessment tools powerful and sensitive enough to detect enhancement by nutrition.

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