

LE Magazine March 2004

## REPORT

### Life Extension for the Brain

By Bruce Scali



What is your name? How old are you? What day is it?

Simple questions such as these are the basis for the mental state assessment (MMSE) commonly accepted and administered in a couple of minutes in primary care settings.<sup>1</sup> But how valuable to you or your physician would a perfect score be? Or, on the other hand, would a failing score be?

In the first case, not very valuable, as most people would rattle off the correct answers, even if they had lost 30% or more of their peak cognitive ability. In the latter case, a failing score would not be very valuable either. Why? Because if one could not answer most of these questions correctly, one would be so diminished mentally that corrective measures would be of little, if any, use.

More than 2 million Americans have been diagnosed with Alzheimer's disease. If we do not do a better job now of preventing or slowing cognitive decline, this number will jump dramatically when the baby-boom generation reaches age 65.<sup>2,3</sup> Fortunately, we have at our disposal tests that provide more-meaningful memory assessments that can be administered earlier when effective interventions can be prescribed.

#### Forewarned Is Forearmed

Just as cardiovascular disease is preceded by 20 years of cholesterol buildup and hypertension—conditions that now are being controlled or reversed—diseases such as Alzheimer's and dementia are preceded by a long, steady decline in mental faculties, including memory function.

According to Eric Braverman, MD, an expert on brain function, "It is so sad when children bring 65-year-old parents to me who are so far gone mentally. If only I had seen these patients [while they were] in their early 50s, much heartbreak could have been avoided. Whole communities used to be wiped out by storms before the advent of radar, satellites, and sophisticated forecasting models. There's no reason for future seniors to be deprived of vitality prematurely when we know what can be done 15 or 20 years prior to age 70. I have seen many patients experience a complete reversal of memory loss when it is diagnosed and treated in its early stages. I have also treated patients with advanced dementia who have, on rare occasions, experienced a return of speech and memory function."

While age is the primary risk factor for dementia, recent studies have suggested that regular administration of memory tests can identify non-demented persons at greater or lesser risk for conversions to frank dementia.<sup>4</sup> Tests such as the Wechsler Memory Scale (WMSIII) can be given in a primary care setting to quantify the decline toward Alzheimer's. Although these tests take upwards of an hour to administer, their results provide a comprehensive assessment for baseline values and treatment protocols, and the tests are far more effective than the MMSE for early identification of cognitive impairment.<sup>5</sup>

#### The "Cholesterol Test" for Brain Function

Another test can now be used for an easier early assessment of memory function. Dr. Braverman and other doctors (see sidebar on p. 52, "Sources of P300 Testing") use brainwave testing in a primary care setting as an early-warning signal of memory decline. Such tests are noninvasive and can be administered in 10 minutes using electrodes similar to those used in an EKG. As part of a quantitative electroencephalography (QEEG) test, the P300 wave shows a patient's reaction time to an audio tone. Normal response is 300 milliseconds (ms) plus the patient's age. So a 40-year-old patient should react to a sound 340 ms after he hears it.

An extensive study conducted by Dr. Braverman with more than 1,500 of his patients correlated age with P300 readings and has shown that readings in excess of 400 ms would correlate to a chronological age in excess of 100, which are typical of patients suffering dementia. The same study reviewed age-related P300 values with MMSE and WMSIII scores to correlate the P300 readings with actual memory impairment.<sup>5</sup> Other studies have confirmed the correlation between P300 readings and age.<sup>6-8</sup>

How can this knowledge be used in a clinical setting? In cardiology, an established protocol exists for heart and vascular health assessment: electrocardiogram (EKG), echocardiogram, stress test, and blood analysis, with cholesterol levels as an early

marker for future disease. A parallel can be drawn for the assessment of brain function: QEEG, attention, intelligence quotient (IQ), memory, and psychological testing, with the P300 reading as an early marker for future cognitive impairment. "I consider the P300 to be the cholesterol test for the brain," says Braverman.

Other doctors recognize the value of P300 as an early diagnostic tool. "At a time when the US population is aging, the electrophysiological findings [of the study] bode well as a valuable prognostic tool for brain impairment," says Ernest Noble, MD, PhD, professor of psychiatry at UCLA and former director of the National Institute on Alcohol Abuse and Alcoholism (NIAAA), a division of the National Institutes of Health.

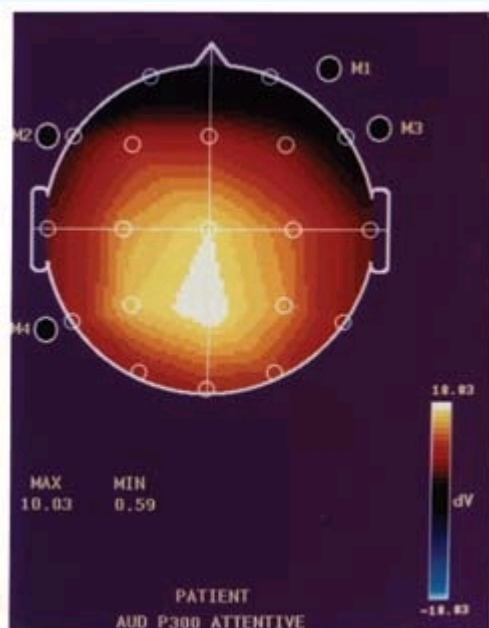
"The use of quantitative EEG measures is a promising technique to assess memory and other cognitive functions," adds Orrin Devinsky, MD, professor of neurology, neurosurgery, and psychiatry at the New York University School of Medicine.

If a 50-year-old patient has a P300 reading of 370 ms, that would indicate his brain is functioning as though he were 70 years old, and he would likely exhibit cognitive declines consistent with that advanced age. In such cases, the WMSIII should be administered and additional tests of attention and IQ should be ordered to quantify such declines. Test results would be used as a baseline for future assessments after treatments are implemented. Just as a cholesterol test is instructive when evaluating future cardiovascular health, the P300 is an early-warning signal for cognitive impairment.

The value of the P300 is perhaps best summarized by John Polich, PhD, associate professor of neuropharmacology at the Scripps Research Institute in La Jolla, CA: "It's a better cornerstone than anything available today for Alzheimer's early detection."

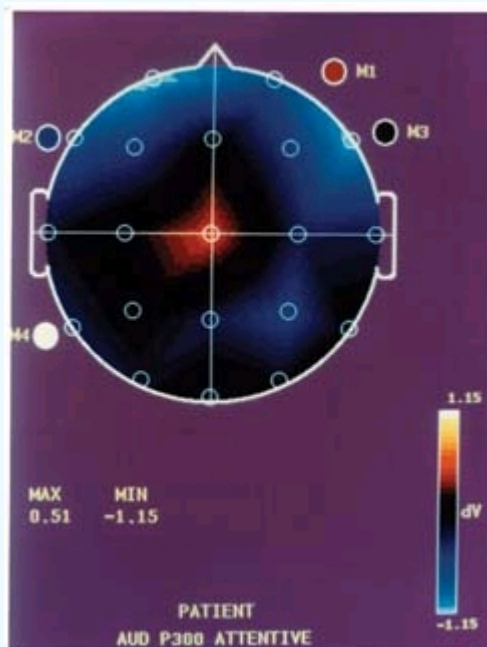
### P300 Component of Event-Related Potential as a Function of Age\*

Normal Brain



P300 Latency is 320 ms and voltage is 10.03dV

Aged Brain



Prolonged latency, decreased amplitude.  
P300 Latency is 380 ms and voltage is 0.51dV

\*Note: P300 max occurs at bright yellow peak at PZ on left, and red peak at CZ on right.  
Circles represent 10/24 electrode placement.

### Function Follows Form

The study of the brain over two millennia has resulted in an entire body of knowledge related to anatomy, physiology, and psychology. Much is now understood about the four lobe pairs, each of which has a primary neurotransmitter (biochemical) that initiates brain activity, a primary function associated with it, a dominant brainwave, and dominant psychological traits.

The frontal lobes, where dopamine provides energy, generates beta waves and controls thought. The temporal lobes, where gamma aminobutyric acid (GABA) provides calm, generates theta waves and controls hearing. The parietal lobes, where acetylcholine provides brain speed, generates alpha waves and controls memory. The occipital lobes, where serotonin provides restorative ability, generates delta waves and controls sight. As for psychological temperaments, strategic thinkers would be dominated by their frontal lobes, traditionalists would be dominated by their temporal lobes, idealists would be dominated by their

parietal lobes, and artisans would be dominated by their occipital lobes.

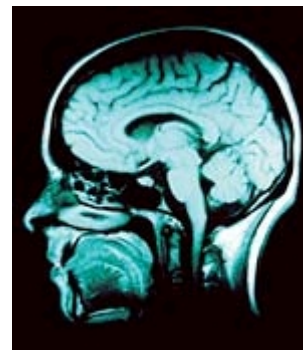
The brain is very “plastic” by nature, with functions shared somewhat by all lobes. The cognitive functions of IQ, attention, and memory are subdivided into four types of each, related primarily to a specific lobe pair. So abstract, emotional, creative, and perceptual IQs are associated with the frontal, temporal, parietal, and occipital lobes, respectively, and consistency, commission, omission, and reaction time measures of attention can be similarly associated. When it comes to memory, primary function resides in the parietal lobes, where immediate, or short-term, memory supports three other types of memory—working, verbal, and visual—that can be associated with the frontal, temporal, and occipital lobes, respectively.

Why is this important? The initial stages of memory decline manifest problems associated with immediate memory. Assessing this earlier, starting at age 40, affords an opportunity to intervene as soon as a deficiency becomes apparent, when better outcomes can be achieved.

### **Holistic Memory Assessment**

Medical conditions rarely exist or are treated effectively in a vacuum. Individual symptoms such as irritable bowel, palpitations, and clammy hands could be addressed with multiple prescriptions from multiple physicians in multiple locations—or one enlightened physician in one office could treat the underlying anxiety responsible for them all. The same holds true with memory.

Numerous illnesses, such as depression, obsessive-compulsive disorder, and diabetes, affect cognitive function.<sup>10-12</sup> Addictions to alcohol, tobacco, and drugs also have been studied for their relation to the brain.<sup>13-15</sup> Coronary bypass surgery and the menstrual cycle affect cognition.<sup>16,17</sup> A temporary anxious moment could cause a “tip-of-the-tongue” short-term memory loss.



The list continues: toxic metal poisoning, menopause, posttraumatic stress, head injuries, chronic fatigue, anemia, kidney failure, pulmonary disease—all affect brain function and thus memory.<sup>18-21</sup> A comprehensive health assessment would identify contributing factors to memory impairment and would provide the necessary information for a global treatment plan. Such an assessment can be administered in the primary care setting, and would include:

- Testing of the four types of attention, using a simple personal computer
- IQ evaluation using standardized written tests
- Psychiatric assessment, using a standardized true/false exam
- Ultrasound to assess carotid arteries
- Blood testing for toxic metal, amino acid, and vitamin levels
- Patient history
- Diet and lifestyle review.

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While how to correct conditions that affect memory is beyond the scope of this article, knowing that other health complaints have a bearing on memory leads to pointed questions that can be directed to a physician so that the contributing factors to, or actual cause of, the memory loss can be address-ed. When indicated, psychiatric counseling or medications, hormone balancing, or chelation could go a long way to slowing, or even reversing, cognitive loss. Once other conditions have been mitigated or eliminated, all effort can be brought to bear on the memory decline itself.

As Dr. Braverman notes, "It doesn't make much sense to pump out your basement if you don't patch the hole in the roof."

A global health assessment that identifies contributing factors to memory loss is what leads to patching that hole. What follows is how to pump out the basement.

#### Preserving Your Memories

Although memory loss can begin earlier, its first signs usually manifest after age 40. At this age, most of us do not suffer with one of the major contributing conditions to memory loss mentioned earlier, yet we may "misplace" things or forget the names of people just introduced to us. This is not a quaint consequence of getting older—it is an early sign of cognitive decline.

Aging affects brain anatomy and physiology. After age 40, our gray matter shrinks: with each succeeding decade, the brain steadily loses some brain cells, called neurons, and some of the surrounding cerebrospinal fluid. Neurons begin to lose some of their chemical firepower, and neuronal connections are short-circuited by a buildup of plaque, a breakdown of the insulating layer that covers neurons, and the aforementioned loss of fluid.<sup>22</sup> These underlying changes that cause cognitive declines have been confirmed by both magnetic resonance imaging (MRI) scans and QEEG. Knowing what is happening to the body leads to effective countermeasures.



The discussion earlier about brain lobe anatomy and function is crucial to the treatment of illness. Associating medications with specific areas of the brain and their specific brain chemicals has produced dramatic advancements in pharmacology. For example, the introduction of selective serotonin reuptake inhibitors (SSRIs), which affect the production of serotonin in the occipital lobes, greatly advanced the treatment of depression. Similarly, sleep medications also address serotonin in the same lobes that are responsible for the restorative function.

It is interesting to note that memories remain stored even when our ability to access them is impaired. A study conducted by Dr. William Penfield showed hidden memories still present in the brain when they were electrically activated in an open skull. Since the nineteenth century, enhancement of the memory function has been attempted and described through the use of hypnosis; individuals have been described as accessing areas of the brain thought lost when they spoke in a language they had not used for decades.

But the memory function starts with the reception of information controlled by the parietal lobes and the acetylcholine neurotransmitter. It is followed closely by the processing of that information in the frontal lobes that are powered by dopamine. Memory decline starts at the beginning: if we cannot receive information, we certainly cannot process or store it.

Life is defined by the electrical activity that takes place in the brain. Chemicals initiate this electrical activity, which is represented by various brainwaves. Assuming that no other contributing conditions discussed earlier are present, diminished electrical activity, which causes diminished cognitive function, is restored by the replacement of the vital neurotransmitters, or brain chemicals. The ways to accomplish this include lifestyle changes and exercise, electrical stimulation, diet and supplements, and medications and hormones. All of these affect brain chemistry incrementally.

#### Lifestyle and Exercise

No one needs another reason to quit smoking, reduce alcohol consumption, and not use illegal drugs. But if you wish to preserve your mental faculties, you will do all three. As mentioned earlier, studies have shown how such habits contribute to cognitive decline. Even if advances in cloning, organ replacement, gene therapies, and nanotechnology extend the life of your body, you will not be able to appreciate it if your brain is not functioning properly.

Physical exercise plays an important role in mental acuity.<sup>23</sup> Exercise promotes general health and minimizes the factors that

contribute to memory loss. Maintaining a healthy cardiovascular system ensures proper blood flow to the brain, supplying the necessary raw ingredients it needs to function properly.

Other prudent recommendations include avoiding toxic metal poisoning by drinking filtered water and reading labels for harmful ingredients. Everyday products such as baking powder, antacids, water softeners, paints, varnishes, and makeup may contain lead, aluminum, or mercury. Electromagnetic fields such as those near power lines, as well as microwave radiation from appliances and cell phones, should be avoided.<sup>24,25</sup>

Just as physical exercise builds and tones muscle, simple mental exercises can build and tone cognition. Crossword puzzles, brainteasers, and trivia games are all ways to flex your mental muscles. Other simple exercises include repeating the significant details of a story immediately after it is read to you, duplicating a drawing or diagram right after viewing it, repeating a series of 10 numbers after seeing or hearing it, or reading a news story and writing the answers to the who, what, when, where, why, and how questions.

None of the recommendations here will reverse a severe case of cognitive decline. But all are part of the first line of defense against a slipping memory, and it is never too early to use them.

## Electrical Stimulation

It has already been shown that electrical stimulation of the vagus nerve by an implanted electrical device similar to a heart pacemaker will reduce or eliminate seizures such as those related to epilepsy. Research now shows that this nerve, located at the base of the skull, also might be the mechanism by which hormonal responses that occur during memorable events travel to the brain.

The introduction of electrical modulation does not have to be so invasive. Research abounds about the external application of gentle direct current via two electrodes attached to a palm-sized cranial electrical stimulation (CES) device.<sup>26</sup> CES is used for 45 minutes when relaxing in the evening, by attaching the electrodes to each ear lobe or to the forehead and wrist.

CES has been proven to have a positive impact on anxiety and insomnia, as well as other conditions.<sup>27,28</sup> It plays a role in keeping cognitive circuits open and functioning. This makes perfect sense: reduce anxiety, one of the conditions that contribute to memory loss, and your memory will improve.



### A DIET TO REMEMBER

While supplementation of choline is recommended, the following foods are good dietary sources of choline:

#### Breakfast

eggs, wheat germ, tofu, blueberries, grape juice, coffee.

#### Lunch

eggs, cheese, peanut butter, chicken, fish, lettuce, soybeans.

#### Dinner

caviar, cod roe, beef liver, beef steak, chicken, fish, cabbage, cauliflower, broccoli, fava beans.

#### Snacks

peanuts, almonds, hazelnuts, peanut butter, celery, hardboiled eggs, blueberries, oranges, raw broccoli or cauliflower, beef chopped liver on whole wheat crackers.

## Diet and Supplements

No matter how one chooses to do so, eating a healthy diet, maintaining healthy weight and cholesterol levels, and exercising regularly ensure that the brain receives adequate nutrition and is not handicapped by other health complaints. But even when all of these are addressed, more has to be done to support cognitive function.

The neurotransmitters, or biochemicals, responsible for brain activity come from the foods we eat and the supplements we take.<sup>29,30</sup> As discussed earlier, memory function starts in the parietal lobes where the neurotransmitter acetylcholine controls brain speed. Boosting acetylcholine naturally when memory first starts to slip is something everyone can do.

Acetylcholine is synthesized by the body from choline, a B vitamin that comes from lecithin in the foods we eat (see sidebar on p. 51, "A Diet to Remember"). Choline is now recognized as so important to cognitive function that the US government requires food manufacturers and processors to supply at least 55 mg per portion to claim "a good source of choline" on their labels. It should be noted, however, that the recommended daily allowance for choline is 550 mg for men, 425 mg for women, and 450 mg and 550 mg for pregnant and lactating women, respectively.

Because the digestive system is inefficient and cannot absorb all of the nutrients available from food before they pass through the body, essential nutrients such as choline must be supplemented. Natural formulations containing choline in any of its many forms, along with other ingredients that support its circulation to and absorption by the brain, are a vital part of a healthy diet.

"There is clinical evidence that acetylcholine and dopamine precursors enhance P300 wave magnitude and latency [speed]," says Kenneth Blum, PhD, adjunct professor in the Department of Biological Sciences at the University of North Texas. Blum is an expert on genetics and brain function, and coauthor of a P300 study.<sup>31</sup> "Blood-flow enhancers like

quercetin and d-phenylalanine, and herbals such as Huperzine, Rhodiola rosea, and ginkgo, have improved memory and focus in Alzheimer's patients," he says.

"Supplements such as Cognitex (a potent source of glycerylphosphoryl-choline and other nutrients for the brain) are as vital to overall health as a daily multivitamin," says Dr. Braverman.

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#### Medications and Hormones

The most serious cases of memory loss require the most powerful remedies, prescribed and monitored by a physician. To complete our discussion of treatments for memory loss, we will briefly mention these prescription medications so that intelligent questions can be asked of a physician who is treating a patient for memory loss.

As noted earlier concerning depression medications addressing occipital lobe serotonin deficiencies, potent prescription medications are available to address parietal lobe acetylcholine deficits.<sup>32-34</sup> These include Aricept® and Exelon®, among others. Regardless of which is prescribed, indications and side effects should be fully explained to the patient or caregiver.

Hormones, too, can be grouped into families associated with brain regions and functions. For example, testosterone, while commonly associated with sex drive, belongs to the frontal lobe/energy group. Hormones associated with the memory function include human growth hormone, vasopressin, DHEA, and pregnenolone. Hormone assessment and balancing should be included in a treatment plan for severe memory impairment.

#### Dollars and Sense

Memory decline can be identified at an early stage by tests administered in a primary care setting.<sup>35</sup> When mild deficits are uncovered at their onset, simple remedies can be used to postpone the ravages of senility.

Early testing and treatment result in a short-term increase in health care expenditures, but the long-term benefits in both dollars saved and human suffering averted are many times more significant. In 1997, 90% of the 2.3 million people diagnosed with Alzheimer's disease were over 60 years of age. In the US alone, treatment of Alzheimer's costs \$100 billion a year. Yet this immense figure spent on Alzheimer's care may come to seem small when the majority of baby boomers turns 65.<sup>36</sup> Coupled with the positive economic impact that a larger number of productive older people can have, the financial ramifications of early treatment of memory decline are irrefutable.

And the value of having loved ones remaining vital and connected to us longer is in itself incalculable.

*The author gratefully acknowledges Eric Braverman, MD, and his PATH Medical Group for contributing research material and quotes used in this article. Dr. Braverman's new book, The Edge Effect: How the Balanced Brain Can Give You an Advantage in Life, will be available from Sterling Publishers this spring.*

#### SOURCES OF P300 TESTING

For information on P300 testing, contact the neurology department of your nearest hospital, or one of these doctors:

Eric Braverman, MD  
New York, NY  
888-231-7284

Ronald Goedeke, MD  
Auckland, NZ  
011-649-479-1199

Roger Nocera, MD  
Scottsdale, AZ  
602-686-4400

Murray Susser, MD  
Los Angeles, CA  
310-966-9194

Richard Delaney, MD  
Milton, MA  
617-698-0715

Eugene Hong, MD  
Singapore  
011-65-8349-718

Titus Parker, MD  
Virginia Beach, VA  
757-226-8880

Robert Thatcher, PhD  
Bay Pines, FL  
727-391-0890

Frank Duffy, MD  
Cambridge, MA  
617-355-7846

Young Chul Lee, MD  
Seoul, South Korea  
82-2-548-4711-2

Andrea Raub, MD  
San Diego, CA  
858-724-1313

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