

The
®
Ageless Concept
Research Summary

Stephen Cherniske, M.Sc.

I. Background:

The Metabolic Model of Aging has created a unified view of the myriad forces and events that cause the aging process. While academicians split hairs trying to differentiate between age-related degeneration and the diseases that result, the average baby boomer is only interested in one thing: “What can I do right now, to maintain health, vitality and wellness?”

To that point, the Metabolic Model describes a seesaw between the regenerative forces inherent in human physiology, and the damage that we experience over time (see *The Metabolic Plan*, Ballantine, 2003). With this understanding, it becomes clear that as the seesaw tips against you (repair fails, damage accumulates), morbidity and mortality follow.

The answer to “What can I do?” is now clear. One must support the body’s natural and remarkable ability to regenerate and at the same time reduce damage as much as possible. Since 1997, the ECONET scientific engine, including full-scale genomics, proteomics, biologic, and biochemical research facilities, has been focused on precisely this task. Natural product compounds derived from its vast medicinal plant library have been formulated and tested for safety and efficacy and used by tens of thousands of people across North America.

Perhaps the most important formulations have been **Ageless[®]** and **AgelessXtra[®]** because they address both sides of the seesaw. These products, distributed by Univera, Inc., have helped people to dramatically alter the way they experience the aging process. Ageless capsules (Table A) were tested in a double-blind, placebo-controlled human clinical trial in 2002. The results, summarized here, were quite significant, leading Univera to create a liquid version known as AgelessXtra in 2003.

Table B lists the ingredient deck for AgelessXtra. To create a ready-to-drink liquid, Univera researchers substituted Cordyceps sinensis for the ginseng in Ageless, added alpha lipoic acid and Ginkgo biloba, and blended the botanical ingredients with concentrates of blueberry, cranberry, grape, black cherry and Aloe vera. The result was even more impactful than Ageless capsules because the damage-reducing effect of these concentrates gave AgelessXtra an ORAC score of 4,500 – the antioxidant equivalent of approximately 12 servings of fruits and vegetables (Table C). Surveys show that the ORAC value of the average American’s ***total dietary intake*** is only 1,200 to 1,700 per day.

Table A **Ageless Capsules formulation**

Ingredients supporting repair and regeneration

- * Vitamin B-6 (as pyridoxal-5-phosphate)
- * Vitamin B-3 (as niacin / niacinamide)

- * Panax ginseng
- * Elutherococcus senticosus (American ginseng)
- * Ornithine alpha-ketoglutarate

Ingredients included to help reduce damage

- * Protectin™ (extract from Scutellaria baicalensis and Acacia catechu)
- * Serenix™ (corn leaf extract)
- * Rhodiola extract
- * Green tea extract

Table B

AgelessXtra formulation

Ingredients supporting repair and regeneration

- * Vitamin B-6 (as pyridoxal-5-phosphate)
- * Vitamin B-3 (as niacin / niacinamide)
- * Ornithine alpha-ketoglutarate
- * Cordyceps sinensis
- * Ginkgo biloba
- * Aloe vera concentrate

Ingredients included to help reduce damage

- * Protectin™ (extract from scutellaria bicalensis and acacia catechu)
- * Serenix™ (corn leaf extract)
- * Rhodiola extract
- * Green tea extract
- * Alpha lipoic acid
- * Concentrates of blueberry, cranberry, black cherry and grape

Table C

Antioxidant potency (ORAC value) of commonly consumed fruits and vegetables:

1.	Red Grapes	730
2.	Cherries	670
3.	Grapefruit	580
4.	Potato	100
5.	Green beans	330
6.	Carrots	250
7.	Banana	220
8.	Mixed Salad	200
9.	Orange Juice	220
10.	Cucumber	180
11.	Tomato	310
12.	Peach	400
	Total:	4190

The Ageless[®] Clinical trial

The emerging scientific discipline known as healthy aging has focused primarily on the protection and repair of the body. New technologies on the horizon include stem cells, gene therapies, nanotechnology and a variety of natural products and pharmaceuticals for maintaining anabolic drive, immunity, and cardiovascular health. Studies show, however, that 40 percent of those reaching age 85 will suffer from significant brain degeneration or senility. It is imperative, therefore, that more attention and research be directed towards protecting and maintaining optimal brain function.

One of the most important advances in this arena was the research of James Joseph and colleagues, published in the *Journal of Neuroscience* in 1998.¹ These scientists demonstrated that oxidative stress is a major factor in age-related neurodegenerative disease, and they showed in a rat model that many of its deleterious effects could be retarded or even reversed by feeding concentrates of anthocyanin-rich fruits, primarily blueberries. The proposed mechanisms of action included effective quenching of free radicals, improved membrane fluidity, and the ultimate restoration of youthful balance, coordination, memory, and learning capacity. Importantly, feeding blueberry concentrate spared vitamin E, so that vitamin E levels in the brain were higher than control animals. This is a significant finding, as increased vitamin E has been associated with decreased risk for Alzheimers disease.²

Beyond the protective and potentially restorative effects of anthocyanin-rich fruits and vegetables, a growing body of research is demonstrating potential benefits from anti-inflammatory agents, stress management, additional free radical quenchers, and bioenergetic nutrients including alpha-ketoglutaric acid, vitamin B-6, B-3, and extracts of *Cordyceps sinensis* and *Rhodiola*.

III Methodology

A. Measuring Brain Function

Until recently, the only reliable assessment tools for measuring brain function were EEG and a variety of functional tests for dementia (eg. MMSE and ADAS-Cog). Unfortunately, these tests were relatively ineffective for identifying early degeneration, and EEG could only be performed in a clinical setting.

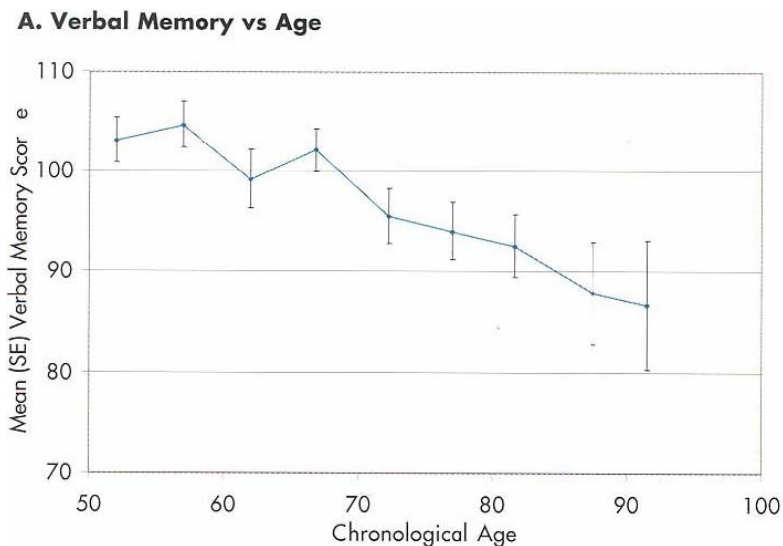
The recent breakthrough in testing mood, memory and cognition came from technology capable of measuring reaction time in milliseconds. Virtually all recently-manufactured computers have this capability. The only remaining hurdle was to develop software to effectively utilize this capability and a central database to compare results to others of the same age and gender. This was accomplished by Cognitive Care, Inc. 2102 Business Center Drive, Suite 130, Irvine, California.

The Cognitive Care system is based on neurocognitive, chronometric assessment technology (NCAT), a proprietary Internet-based assessment tool that measures mental and physical reaction time. NCAT includes computerized cognitive tasks to assess the brain's information-processing (speed and accuracy) across several domains (memory, attention, reasoning).

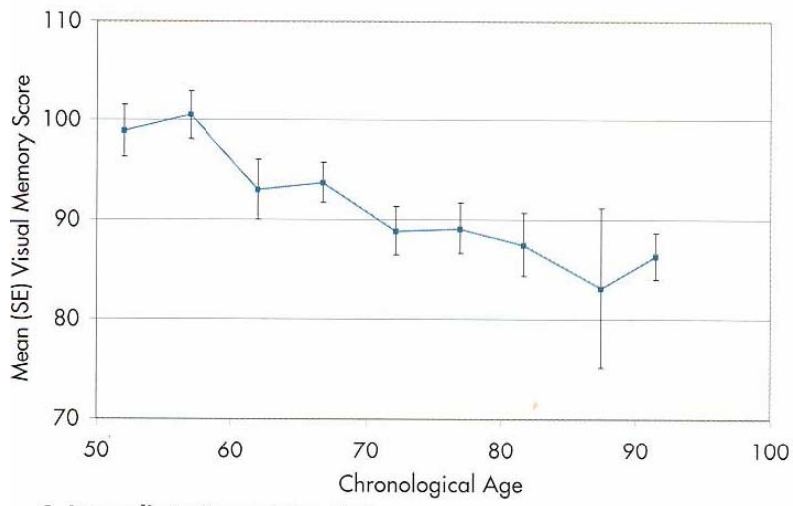
This combination of tests utilizing online brain-processing speed technology has been validated at four major universities and provides instantaneous comparison to an enormous national database. A correlation test performed by our research group showed that information-processing speed measured by the Cognitive Care results differed from a 12-sensor EEG by only two milliseconds.

What does “normal” brain aging look like?

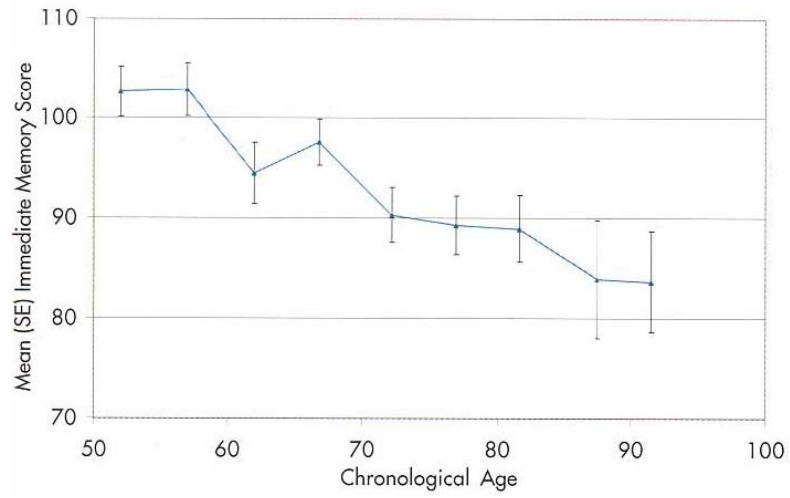
Results presented at the annual conference of the EEG and Clinical Neuroscience Society (ECNS) in September 2002 paint a clear picture of age-related neurodegeneration.³



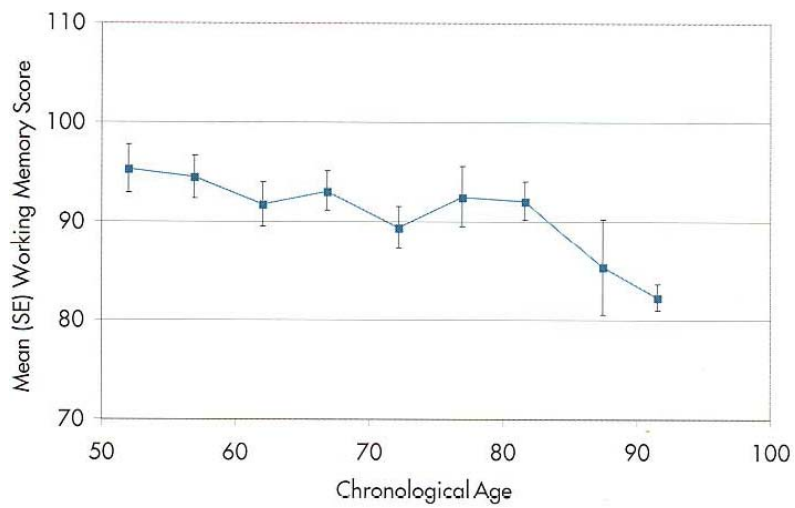
B. Visual Memory vs Age



C. Immediate Memory vs Age

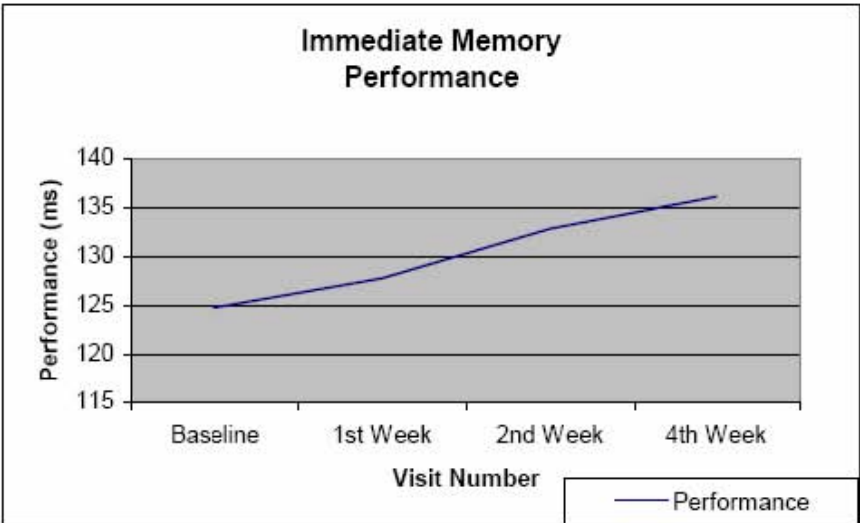
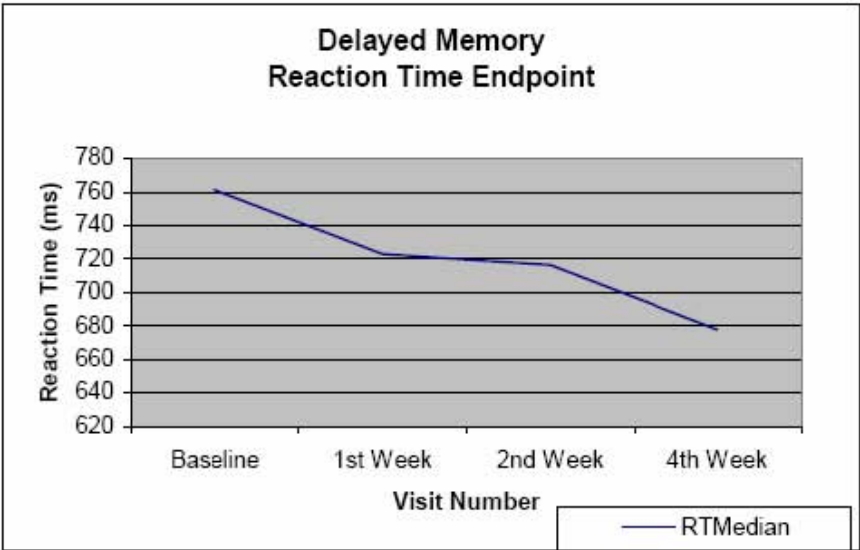
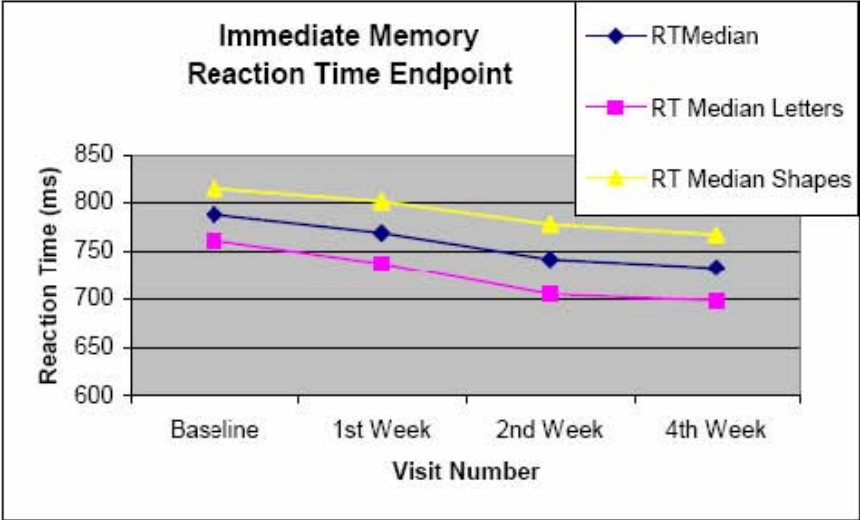


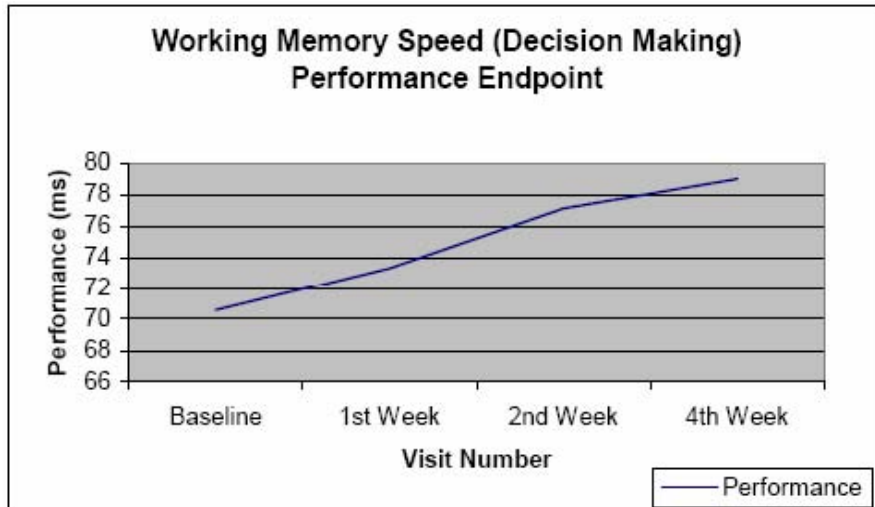
D. Working Memory vs Age



Results

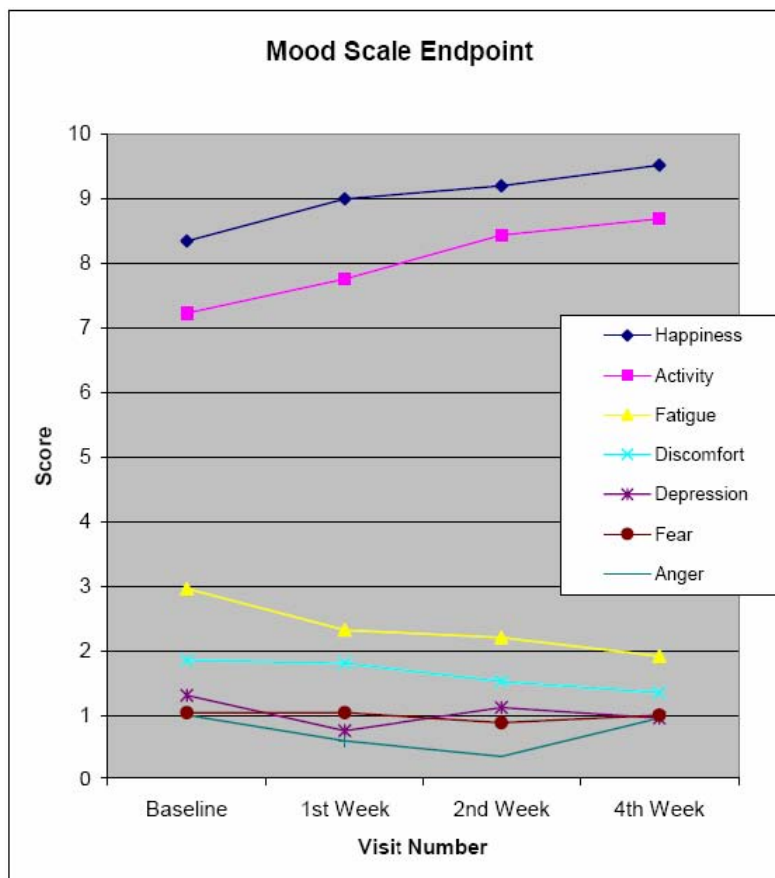
The following are the Cognitive Care results with 44 individuals taking Ageless over a four-week period. These data were not obtained in a clinical setting and must, therefore, be regarded as preliminary and experimental. Subjects were tested once each week at the same time of day, and it is important to note that each testing session is entirely different. Thus improvements were not due to the “practice effect.”





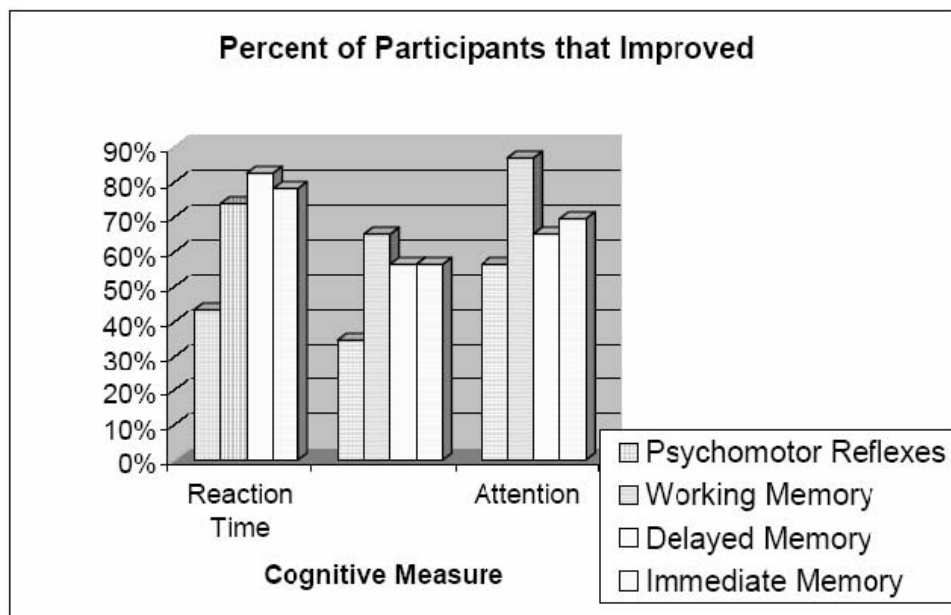
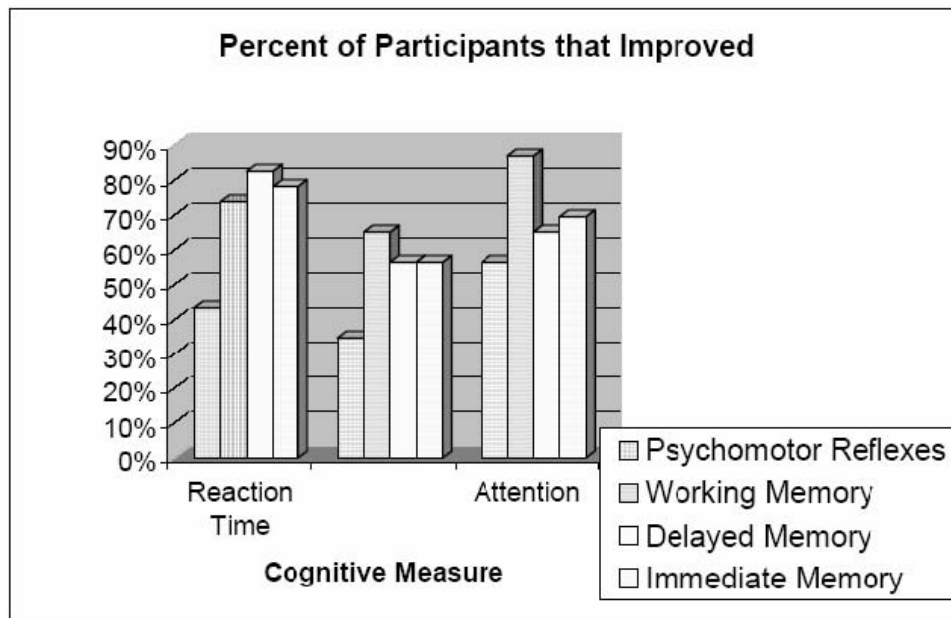
Mood

“Age is a feeling, not a number.” While that makes sense to anyone who has thought about the aging process, it is important to define, as much as possible, what those feelings might be. We used another Cognitive Care program – the same one used by NASA – to measure indicators of happiness, activity, fatigue, discomfort, depression, fear, and anger.



Statistics

It is important to look at statistics with a skeptical eye. Regarding changes reported for a group of subjects, it is useful to know the mean or average improvement, but this must be accompanied by information on the *distribution* of these changes and the degree of change. If the average improvement for the group was due to a remarkable improvement in one subject and only modest or no improvement in the others, the results would be essentially meaningless. To address this, we looked at *the number of people* who improved in each of the above categories, and then looked to see if the improvement was significant.



Notice that the percent of participants who improved was generally extremely high, in the 60 percent to 80 percent range; and the degree of change was also impressive. What if you could improve your working memory by 32 percent or your attention (ability to concentrate) by 38 percent in four weeks? Again, we are not claiming that these results will be obtained by everyone, or that they represent average results for a large population. But the subjects for this study were randomly selected by Cognitive Care from respondents to a newspaper ad. They represent, to the best of our ability, average Americans with an average diet, experiencing the kinds of stress that you and I face.

Ingredient Summary

Serenix™: A proprietary extract from Zea maize (corn leaf). Serenix is a unique extract from corn leaf that helps support healthy mood, positive outlook, and may help maintain normal sexual response and desire.

Energetix™: Energetix is the trade name for the proprietary 3-ginseng blend that is unique to Ageless. Energetix contains:

A. Standardized, ECONET-derived Panax ginseng specially-processed to a highly potent extract.

B. Rhodiola extract from Unigen Pharmaceuticals (a.k.a. Ultrin TG™ or Tibetan ginseng)

C. Siberian ginseng (*Eleutherococcus senticosus*).

Both Panax ginseng and Ultrin TG were studied in an animal model measuring stamina and energy. Both showed a 200 percent improvement after just 4 days of supplementation with no increase in resting cortisol levels. This strongly suggests that the bioenergetic improvement is not derived from increased stress (such as experienced with caffeine and ephedrine) but rather an improvement in cellular energy efficiency.

Protectin™ Protectin is a patented botanical complex developed by the Univera research partner, Unigen Pharmaceuticals, Inc. Protectin has been shown, in genomic, biochemical, and biological studies, in both animals and humans in vitro and in vivo, to have a remarkable ability to improve joint comfort, mobility, and range of motion. It can help reduce the discomforts associated with the aging process.

A 90-day randomized, multi-center, double-blind, placebo-controlled human trial on Protectin was carried out by a licensed research organization in Montreal. Physical function and range of motion were measured by a validated research protocol (WOMAC). At 30 days, Protectin produced statistically significant improvements compared to a placebo.

Ornithine alpha-ketoglutarate (OKG) Ornithine alpha-ketoglutarate (OKG) is a salt formed of two molecules of ornithine and one molecule of alpha-ketoglutaric acid. It possesses significant anabolic and bioenergetic activity in human metabolism, and may play a critical role in cellular detoxification and

antioxidant defense.^{4 5} ,

Alpha-ketoglutarate is a vital component of the Krebs and glucose-alanine cycles. During exercise, there is evidence that this essential nutrient is a rate-limiting factor contributing to fatigue. Mobilization of branched-chain amino acids depends upon adequate levels of alpha-ketoglutarate, and clinical trials with oral supplementation have resulted in enhanced human performance.⁶

Pyridoxal-5-phosphate (P-5-P) Pyridoxal-5-phosphate is the activated coenzyme form of vitamin B6 and is necessary for a myriad of biochemical functions including amino acid absorption and metabolism, energy production, immunity, and brain function. This coenzyme form is easier to absorb and has been the subject of more than 5,000 metabolic studies. Importantly, sub-optimal vitamin B6 intake is quite common in the U.S., and a deficiency of this critical nutrient has been associated with increased psychological stress, impaired energy metabolism, brain degeneration, and increased risk for cardiovascular disease.^{7 8} Recent studies have also shown that vitamin B6 may play an important role in the activation of critical antioxidant defenses.^{9 10 11} , ,

Vitamin B3 as Niacin / niacinamide: Vitamin B3 is necessary for thousands of biochemical reactions in the body, including cell respiration and the release of energy from carbohydrates, fats and proteins. In addition, these forms of vitamin B3 support mental function, including memory.¹² A 6-year evaluation of cognitive function with healthy elderly subjects age 66 to 90 demonstrated a significant association between niacin levels and brain functions related to learning.¹³

Green Tea Extract Traditional Chinese medicine has espoused the use of green tea for centuries, and its beneficial effects have been shown in more than 1,756 Medline studies. Green tea contains antioxidant compounds known as polyphenols, which appear to help protect brain function.^{14 15} In vitro studies have also identified valuable anti-inflammatory effects of green tea polyphenols.¹⁶ Green tea also contains theanine, an amino acid that has been shown to promote relaxation without drowsiness.^{17 18} Animal and human studies suggest that theanine may provide additional protection and support of brain function, including potentiation of receptor sensitivity¹⁹ , neuroprotective effects against ischemia²⁰ , and support of detox/ antioxidant activity.²¹

Conclusion

Data from this study was evaluated by biostatisticians from the University of California, Irvine. Their report includes the following analysis:

Immediate Memory is similar to the classic Sternberg task where a string of stimulus "target" items to be remembered are followed by a "probe" item. The subject must decide yes or no if the probe item was a member of the previous target list. List length can be varied to provide an estimate of the short-term memory capacity of the individual. Both letters and spatial position are examined in this task. In terms of the performance index there was a significant change across weeks of testing ($F(2,38) = 6.801$, ($p = .003$), most noticeable comparing baseline to week 2. In addition, there was a significant improvement in the reaction time mean ($F(2,38) = 5.96$, $p = .0056$) and the standard deviation across the weeks of testing ($F(2,38) = 3.605$, $p = .0368$), again with the most noticeable improvements between baseline and week 2.

Overall the test for immediate memory showed the most robust changes across the weeks of testing, indicating improved immediate memory capacity, faster reaction time, improved sustained attention and more accurate processing of information.

We are excited about this report because information processing speed has recently been found to be a reliable biomarker of aging and perhaps the best early indicator of brain degeneration.²²

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