

HEALTH AND STRESS

The Newsletter of The American Institute of Stress

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Honoring Richard H. Rahe, M.D., 1997 Hans Selye Award Recipient

CALL FOR PAPERS

Sessions on Stress and Health, Evolution of the Holmes-Rahe Scale, Stress and Subtle Energies, Biological Effects of Weak Electromagnetic Fields, Stress and Children, Stress and Auto Accidents, Stress and the Immune System, Naturopathic Approaches to Stress Reduction, etc.

STRESS AND MEMORY LOSS: Some Speculations and Solutions

KEY WORDS: stress, memory, holography, vasopressin, pregnenolone, ginseng, ginkgo, huperzine, adaptogens, acetylcholine, Alzheimer's Disease, insomnia, melatonin

Almost everyone has had the frustrating experience of suddenly not being able to remember a very familiar name or phone number. Other common occurrences are not being able to find your keys, going to the supermarket and forgetting to bring home the main item you originally went for, or the name of an important colleague or customer you bump into, and must introduce to your boss.

Memory loss for recent events is quite common in the elderly, but a 1995 survey of internists and family care practitioners, reveals that such problems are increasingly being seen in middle-aged individuals. Four out of five reported that people 35 years or older experience some trouble with memory or concentration, and 75 percent expected that this trend would worsen over the next decade. The problem is probably even more widespread, since nine out of ten physicians feel that many patients have such difficulties, but never discuss them during office visits. Almost ninety percent cited an increased amount of stress from work or personal pressures as the leading cause of memory loss. Other contributing factors included a diminished blood supply to the brain, lack of sleep, alcohol abuse, and certain prescription drugs.

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*The Newsletter of
The American Institute of Stress*

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Short Term, Long Term, And Other Memory Distinctions

We forget names much faster than faces. In one study, seniors were 90% correct in picking out the pictures of their high school classmates three months after graduation, but could only recall 70% of their names. Some 50 years later, 70% of those faces that were familiar were still remembered, compared to just 20% of the names. Professors were able to identify 85% of their students from a series of photographs 11 days after the semester concluded, but were correct only 35% of the time when asked to recollect the name associated with each picture. This plummeted to 6 percent after one year, and eight years later, not one name could be recalled after looking at the same pictures.

While we tend to think of memory as a distinct "faculty", it is a complex phenomenon involving numerous structures, circuits, and chemical messengers in the brain. It is likely that remembering a list of facts, a poem, the sound of a harp, the smell of honeysuckle, the taste of asparagus, or the color of a sunset, all utilize different pathways.

Remembering recent events appears to involve mechanisms quite different than those responsible for long term memory. Short term memory is used to recall items that we are likely to need, such as certain

names and numbers, and has a more limited capacity. Thus, although it is fairly easy to repeat a 1-800 phone number, most of us would have difficulty with an overseas call or credit card requiring 12 or more numbers. Short term memory also seems to be related to sounds and speech. A series of similarly sounding consonants like C G T P V B, is harder to remember, than a diverse string such as K G R F L W. This is not a function of auditory processing, since the same distinction can be demonstrated when the letters are seen, rather than heard. Likewise, we tend to forget things if they don't stand out. It is more difficult to remember a recipe if you have just read six others, compared to reading just one, along with a similar amount of text dealing with automobile repairs.

Some people have phenomenal, or photographic memories. Alexander Luria, a Russian psychiatrist, described in detail the phenomenal feats of Shereshevsky, who seemed to be able to permanently remember everything he had ever encountered. On one occasion, he was shown a lengthy, complex, and meaningless mathematical formula that had been especially contrived. After looking at it for just a few minutes, Shereshevsky was able to reproduce every precise detail. What was even more amazing, was that when asked to repeat this feat 15 years later, his rendition was perfect, although it had never been seen in the interim. On the other hand, he had problems remembering individuals, and items with which they were associated, which led to difficulties in his personal relationships.

Where Are Memories Stored?

In 1904, a German biologist coined the term *engram*, to refer to the site and substance of the location of memories in the brain. However, the common notion that they are stored in specific areas, like furniture in different rooms of a house, has been difficult to prove. The pioneer neuropsychologist, Karl Lashley, first proposed that learning and memory involve the entire cerebral cortex, and that parts of the brain can substitute for one another in this process. Karl Pribram, a neurosurgeon and brain researcher, found that once experimental animals had learned how to negotiate a complicated maze, he could selectively remove up to 90% of the cerebral cortex, without impairing memory for this task. He and the late Nobel Laureate physicist, David Bohm, have

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suggested that memory is dispersed throughout the brain as a holographic picture, which would thus allow reconstruction of the entire hologram from any of its portions.

The following analogy may be helpful in understanding this. If a rock were dropped into a quiet pond, a series of concentric waves or ripples would start to emanate outward from the spot where it entered the water. Assume you could suddenly freeze the pond and then take a three dimensional photograph of its surface. The picture would show a symmetrical series of circles of increasing diameter, composed of waves that progressively diminished in height. If you snipped out any portion of this picture, you could mathematically reconstruct the entire photograph by analyzing the arc of the circle and the height of the wave. In this analogy, an event will send similar ripples throughout the brain, allowing it to be retrieved from any of these impressions, even though they may be in many different areas.

However, studies of brain damaged patients suggest that different areas may be more involved than others for long and short term memory retention. A blow to the head, or electric shock therapy, results in transient general amnesia, with older memories being the first to be restored. In some instances, events immediately prior to the trauma may never be remembered. Damage to a portion of the left cerebral hemisphere often impairs short term memory, but not long term recall. Injury to the temporal lobes and hippocampus of both hemispheres produces predominantly long term memory deficits. In one middle-aged man with severe epilepsy that could not be controlled with medication, significant portions of these areas had to be removed to eliminate the source of the seizures. The epileptic attacks were significantly reduced, but now, although he could remember new information for a brief period of time, it could not be transferred to long term memory. He was perfectly able to recall things that had happened prior to the surgery, but not what had occurred in the previous 24 hours or week, and lived in a perpetual present, where "every day was alone by itself".

This type of deficit could arise from problems either in learning or retrieval, and the hippocampus appears to be particularly involved in the latter process. The hippocampus progressively atrophies as we grow older, which explains why loss of recent memory,

as well as impaired learning and concentrating skills, are so commonly seen in elderly individuals.

Stress And Memory

Stress also causes the hippocampus to shrink, most likely due to damage from increased cortisol secretion. A recent study of Vietnam veterans suffering from post-traumatic stress disorder, found that the hippocampus was significantly smaller in those with more combat exposure. As one might suspect, since there are different types of memories, and stress can vary so much with respect to its nature, degree, and duration, interrelationships between the two can be complex and confusing. It's easy to forget ordinary events, but those which are life threatening or extremely stressful, seem to stand out forever. This would make sense from an evolutionary viewpoint, since the ability to remember dangerous situations, and how best to respond to them, would obviously have survival value.

The retention of such memories appears to be facilitated by hormones like adrenaline and noradrenaline, that are secreted during acute stress. In one study, volunteers viewed either a boring narrated slide show of a boy visiting a hospital to observe the staff preparing for a routine emergency drill, or a dramatic depiction of him being hit by a car, and transported by ambulance to the hospital Emergency Room. Prior to watching these, volunteers received either a placebo, or a beta blocker drug that blunts the activities of these stress hormones. One week later, all participants completed a questionnaire designed to determine how accurately they remembered the details of both slide shows. There was no difference in memory retention between the placebo and beta blocker groups with respect to the boring emergency drill, or the neutral aspects of the more vivid and provocative offering. However, those receiving beta blockers, were much less able to recall the traumatic portions of the latter presentation, compared to the group whose stress hormone actions had not been blocked.

In addition to long term injurious effects on the hippocampus, cortisol, which is increased during chronic stress, can also acutely diminish short term memory. In one report, healthy older individuals were subjected to a stressful public speaking performance, which they were told was also being videotaped for future presentation to a very large audience.

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Cortisol levels were obtained just prior to this, and periodic measurements over the preceding 3-6 years were also available. A few days later, they were quizzed to determine how much of the text they were able to remember. Those who showed the highest cortisol rises in anticipation of the stressful public speaking performance, had the greatest difficulty in recalling the content of their presentation. In addition, those whose cortisol levels had increased significantly over the previous three to six years, also tended to have poorer memories, compared to those whose values showed little change. This deficiency was presumably the result of hippocampal damage.

Elevated cortisol concentrations are quite commonly seen in patients who are chronically depressed. Such individuals also often complain of frequent forgetfulness, and difficulty in concentration. Following successful treatment with antidepressant medications, these symptoms usually improve as cortisol levels return to normal, further suggesting a causal relationship.

Medications To Improve Memory

Antidepressants have also been shown to improve memory and learning skills in experimental animals, and further exploration of this relationship could lead to more effective medications for preventing and treating memory loss. Mice begin to show impairment of recent or "working" memory when they are about 16 months old, as assessed by a food finding test. However, in those who received AIT-082, a new antidepressant analog in their drinking water, memory deficits did not appear until at least 3 months later, which would correspond to five to ten years for humans. Indeed, half the mice still showed normal memories at 21 months of age, and clinical studies in humans are now being planned.

Estrogen can improve or prevent memory loss in post menopausal women, including some with Alzheimer's disease. Testosterone has been reported to provide similar benefits in older men, and dehydroepiandrosterone (DHEA) may be effective in both sexes. Experimental drugs that increase levels of corticotrophin releasing factor (CRF), a stress related hormone that is deficient in Alzheimer's disease, have been found to increase memory and learning in rats, and are scheduled for clinical trials. Vasopressin, a hormone stored in the posterior pituitary gland, also

increases short term memory in laboratory animals, and has become popular with college students who must cram for examinations.

One of the most effective hormones appears to be pregnenolone sulfate, a steroid precursor for both male and female hormones. Pregnenolone has been classified as a neurosteroid, since it has been shown to facilitate communication between brain cells, and recent research has demonstrated its efficacy in promoting regeneration in damaged peripheral nerves. In one experiment, rats were released into a complex maze, and received mild electric shocks to their paws whenever they took the wrong path to the exit. On average, they generally learned the correct route to avoid the shocks after four successive attempts. Once this had been mastered, various steroids, and a control solution of saline were injected into specific regions of the brain. One week later, the experiment was repeated, noting how many trials it took for the animals to successfully escape the shocks in five consecutive attempts. The most potent steroid proved to be pregnenolone. Researchers found that as little as 15 to 145 molecules injected into the amygdala could impressively improve their memory for correctly traversing the maze. This observation is significant, since the amygdala has close connections with the hippocampus, which processes sensations of fear, as well as the retrieval of memories.

Obtaining adequate sleep is important, since this can influence the levels of various hormones and neurohumoral agencies that may be required to maintain memory. Most people think the brain is at rest while they are sleeping. In reality, it is very active in processing and organizing information that has accumulated during the day, so that it can be filed for future retrieval. As a consequence, sleep deprived individuals have an impaired ability to move information from temporary to long term storage. Students who cram for an examination the night before can score good grades, but the information will soon be forgotten, compared to those who study for shorter periods, but do so on a regular basis.

Ritalin, Cylert, and other stimulants like caffeine and nicotine, have been reported to improve short term memory in some experiments, but do nothing for long term recall. The various compounds noted above, including pregnenolone, which seem so impressive in animal studies have thus far shown no

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benefits in humans. Tacrine, the only medication presently approved for Alzheimer's disease, has similarly not demonstrated any consistent or significant memory boosting powers. Theoretically, drugs that reduce stress or promote sleep should be beneficial. However, benzodiazepines, which are among the most popular and powerful tranquilizers (Valium), and sleeping pills (Halcion), can actually cause memory loss. Numerous other prescription drugs, as well as anesthetics and alcohol, which many rely on to relax, can also interfere with memory.

Naturopathic Stress Reduction And Memory Enhancement

All of this has spurred a search for non-drug approaches to improve memory, and this is an area with tremendous potential. A survey of over 100 Alzheimer disease caregivers, revealed that more than half had tried at least one alternative therapy to improve memory, including vitamins (84%), herbal medicines (11%), "smart pills" (9%) and home remedies (7%). In almost all instances, these were eventually discontinued because of lack of benefit. For healthy people who have difficulty in remembering things, avoiding alcohol or other drugs that can impair memory is an obvious first step, as is getting adequate rest. Most people recognize that stress is a major contributor to insomnia, but do not appreciate that this can precipitate a vicious cycle, since sleep deprivation frequently causes emotional and mental stress. In a recent poll, 40% said that lack of sleep affected them more mentally than physically, usually manifesting itself by increased irritability, forgetfulness, and mistakes, shortened tempers and diminished productivity. This seemed to be much more common in females (51%), compared to males (29%). While there are a variety of naturopathic products used to promote sleep, only a few appear to reduce stress or improve memory.

A standardized extract of *Ginkgo biloba*, has been the subject of more than 200 scientific studies, including 40 double blind human trials, that confirm its efficacy in improving memory and concentrating abilities. It is the leading herbal prescribed in Europe, (over 1 million per month) and the most popular over-the-counter medication in Germany. It contains a unique combination of terpenoids and flavonoids known as ginkgolides, which are found nowhere else

in nature. One of the characteristic signs of aging, "benign senescent forgetfulness", which refers to memory loss for very recent events, is due to progressive atherosclerotic obstruction of blood vessels, which decreases the supply of oxygen rich blood to the brain. Ginkgolides decrease blood stickiness due to platelet clumping, increase the elasticity of tiny blood vessels, and also have potent antioxidant properties that block free radical damage to cells. Each of these activities can be beneficial in improving blood flow in the brain via different mechanisms, and their combination seems to produce a synergistic effect. A recent double blind study reported that ginkgo even improved memory in patients with early Alzheimer's disease. In the laboratory, it has been shown to block the damaging effects of stress on the hippocampus, and to prevent the atrophic changes associated with aging. However, under current labeling and advertising regulations, manufacturers must strictly avoid any mention of possible anti-stress or anti-aging properties.

The transmission of nerve signals in the brain requires acetylcholine, a neurotransmitter which is destroyed by the enzyme acetylcholinesterase. Consequently, recent attempts to improve memory function have focused on ways to either increase acetylcholine production, or inhibit cholinesterase activity. Drugs like scopolamine, which impair memory or induce amnesia, increase acetylcholinesterase, thus making less acetylcholine available. Huperzine A, a compound found in certain Chinese plants, appears to reverse or prevent this. When rats were trained to successfully navigate a maze in return for a reward, scopolamine significantly impaired their ability to complete the course. However, treatment with huperzine A quickly restored their memory. Giving huperzine for one week prior to the administration of scopolamine was equally effective in preventing memory loss. Because of its ability to inhibit cholinesterase, huperzine also reduces pesticide and nerve gas damage, and could provide important protection for troops and populations threatened by chemical warfare. A recent experiment examined its effects in one hundred patients with normal age related memory impairment. At the onset of the study, none of the patients were within the normal range of memory function, based on several measurement criteria. Benefits were often evident after only two weeks, and by the end of the four week trial, memory scores in

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over 70% had increased to normal values. In another study of 111 patients with advanced Alzheimer's disease, huperzine resulted in a 10% improvement in memory and a significant increase in other measurements of cognitive skills.

One of the most versatile of all the nutritional supplements is ginseng, which is widely used as a tonic and aphrodisiac, but has also been shown to improve memory and learning skills in mice. Large doses have also been advocated as an anti-stress preparation. Allegedly, 50 mg/kg of ginseng is equivalent to 1mg/kg of Valium, and there appear to be no side effects or toxicity from taking even much greater amounts.

Nature's Answer To Stress is the title of a recent article about the "adaptogens". This term was coined to describe any natural product that satisfies the following criteria:

- it must be totally safe and non-toxic with respect to long term use in humans.
- it must be able to provide protection from a broad range of emotional, mental and physical stressors, such as trauma, chemicals, free radicals, extremes of temperature, physical exertion, and infection.
- it should be able to show a tendency to restore cell and organ homeostasis.

There are some two thousand studies of various adaptogenic herbs and plants, like *Eleutherococcus senticosus* and *Glycyrrhiza uralensis*, that have these characteristics. Most of the research has been conducted by scores of scientists in the former Soviet Union, at a cost of approximately \$700 million. Adaptogens have been used by their Olympic athletes, cosmonauts, military elite, as well as top dancers and chess players. Little was known about them in the West until recently, when a special formulation containing seven of the top adaptogens was introduced in the U.S. The Russian Olympic Committee contracted to use this preparation for four of their ten teams in the 1994 Winter Games in Lillehammer, Norway.

These four teams won *all* of Russia's eleven gold medals, more than any other country, and attributed their outstanding success to this product. Some of the testimonials are impressive. The winner of the 3000 meter women's speed skating had never succeeded in a major competition before she started on the adaptogen

formulation. The 21 year old who won the Gold Medal in the 500 meter speed skating event set a new Olympic record. Before taking adaptogens, he had never won any medals in numerous international competitions. Combinations of various herbals would appear to offer particular promise, because of the possibility of similar synergistic potentiation. A combined preparation of ginkgo and ginseng was shown in one study to decrease blood pressure and heart rate significantly more than giving either separately in much larger doses. Perhaps combining these with various adaptogens might provide even greater benefits.

There are numerous other nutritional supplements, such as vitamin E and carnitine, that have been demonstrated to mitigate stress or improve memory in laboratory animals. Valerian extracts are approved in Germany for "states of excitation", and "difficulty in falling asleep due to nervousness". Chamomile tea, and certain scents, such as lavender, and a variety of homeopathic preparations allegedly have stress reduction properties and can enhance memory, but there are few scientific studies to support such anecdotal claims.

Other Tips To Improve Memory And Reduce Stress

In addition to adequate sleep, regular exercise and proper nutrition can help reduce stress and forgetfulness. One effective memory aid is associating the name of a person you want to remember with a mental picture of something that it rhymes with, or signifies (belly for Kelly, Xmas tree for Noel), or a song (Sweet Sue for Susan). Another useful tip is to pick a specific spot to put things that you frequently misplace, like keys.

Plan ahead! When you need to attend a function where you are apt to run into people whose names may be difficult to recall, try to anticipate who will be there, and write their names down in advance. If you do have a conversation, especially with someone new, make a practice of repeating their name often, like "Isn't this a good party George?", or "Where are you from, George".

Writing things down can help to improve your memory in other situations, like remembering the punch line to a joke. Having such memory aids

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readily available in a small notebook is helpful, and frequently, just writing something down makes you remember it better.

Use it or lose it! All structures and organs in the body atrophy if they are not used, and the brain is no exception. Brain cells can grow and multiply well into the later decades of life, and stimulating mental activity promotes this. Reading, traveling, writing, doing crossword puzzles, or getting involved in anything that interests you will invigorate your brain cells. Keep your blood pressure under control. Recent studies show that hypertensive patients are much more apt to suffer memory loss in later life.

Reduce stress! Stress accelerates the aging process by increasing the production of free radicals, and hormones like cortisol that damage brain structures responsible for memory. Take periodic breaks to do something you enjoy, like watching a movie, reading, fishing, or engaging in an enjoyable sport or hobby. Meditation, yoga, and listening to music are also good ways to relax. Strong social support is a very powerful stress buster. Touching, hugging, and having a close relationship with someone can provide unusually rewarding benefits.

Although stress is different for each of us, and no stress reduction strategy works for everyone, the suggestions noted above have been helpful for many individuals. The feeling of having little control over situations is always distressful, but often results from faulty perceptions. Anything you can do to correct this, or to gain a sense of greater control in your life, will not only reduce your stress level, but quite likely also help to improve your memory.

Paul J. Rosch, M.D., F.A.C.P.
Editor

A man's real possession is his memory. In nothing else is he rich, in nothing else is he poor.

Alexander Smith

Memory is the thing you forget with.

Alexander Chase

The things we remember best are often those that are best forgotten.

Anonymous

Low Blood Pressure And Depression

Lower than normal blood pressure is not an uncommon finding in apparently healthy young females. In the U.S., it is rarely treated, and some believe it may actually be associated with longevity. In Europe, however, chronic hypotension is viewed as an illness that causes fatigue and depression, and various medications and/or tonics are prescribed. Epidemiologic studies do confirm that low blood pressure tends to occur most often in females, who also have higher rates of depression and emotional problems, but it is not clear whether this is cause or effect, or gender related.

In one report, researchers studied 900 men between the age of 60 and 89, to determine if there might be any correlation between symptoms of depression and blood pressure levels. They found that those with low diastolic pressures did have higher depression rating scores, and more fatigue, pessimism, sadness, insomnia, and loss of appetite. This link was independent of age, weight loss, or evidence of any illness.

Although these findings confirm an association between low blood pressure and depression, it is still not clear which came first. Nevertheless, patients with low blood pressure, who also complain of significant fatigue, loss of appetite, or other depressive symptoms, might benefit from antidepressant medication. Since these drugs generally lower blood pressure, if they also restored low values to normal, it would suggest that depression comes first. Conversely, it would be of considerable interest to learn whether correcting low blood pressure could significantly improve associated symptoms of depression.

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Book Reviews • Meetings and Items of Interest

Book Review

Measuring Stress: A Guide for Health and Social Scientists, Cohen, S., Kessler, R.C., and Gordon, L.U., eds., Oxford University Press, New York, 236 pgs. \$39.95

The purpose of this volume is to provide a "resource for state-of-the-art assessment of stress", a somewhat Herculean task, since it is difficult to define stress, much less measure it. Part of the problem is that the term is frequently used to describe both stimulus and response, and the editors have been careful to avoid these and other semantic pitfalls. The book is divided into four parts, the first of which discusses various definitions of stress, and putative pathways that are possibly involved in producing stress related illnesses. It includes a comprehensive review of the evolution of the stress concept, and the numerous objections, criticisms, and attempts to reconcile opposing views. Part II, The Environmental Perspective, discusses various check list measurements of stressful life events, and contains chapters dealing with interview measurements of stressful life events daily, and within day event measurements, such as the Hassles scale, and various approaches to the measurement of chronic stressors. Part III, The Psychological Perspective, deals with how stressors are perceived, and strategies for measuring the appraisal process, and affective responses. Surprisingly, no mention was made of Spielberger's well validated scales for state and trait measures of anxiety and anger, nor do any of these terms appear in the index. Part IV, The Biological Perspective, has chapters devoted to the

measurement of stress hormones, as well as cardiovascular, and immune system responses.

This book should prove to be a valuable resource for all individuals interested in any aspect of stress research. The job content questionnaire citations should be updated, but the voluminous literature on stress is increasing so rapidly that it is impossible to encompass everything, especially in a volume of this size. The authors are to be commended for even considering such an ambitious undertaking.

Meetings and Items of Interest

Aug. 28-30 Conference on The Emotions in Health and Disease, Tilburg University in The Netherlands, conference chair Dr. Ad J.J.M. Vingerhoets, fax: 011-31-13-466-2370

Sept. 13-15 Music and Miracles: Healing with Spirit and Sound, Rowe Camp & Conference Center, Rowe, MA, call (413) 339-4216

Sept. 20-22 Aroma '96, Conference and Trade Show, National Association for Holistic Aromatherapy, San Francisco, CA, call (415) 731-4634

Sept. 27-Oct. 6 Office of CME-UCLA School of Medicine and The American Academy of Medical Acupuncture will be sponsoring Unit 3: Clinical Experience, Bethesda, MD, call for info (310) 794-2620

Oct. 3-6 Third World Congress of Psycho-Oncology, New York Vista Hotel, New York, NY, for more information, call the Congress Secretariat in Georgia at (770) 751-7332

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