As science explores the brain ever more deeply, new information is coming to light about how our lifestyle affects brain function. How does the brain react to relaxation and mental exercise? Can we heighten cognition and brain function to achieve the most heightened awareness and consciousness? In the following essay, Dr. Gary Small, director of the UCLA Memory and Aging Research Center and author of several books, most recently *The Longevity Bible: Eight Essential Strategies for Keeping Your Mind Sharp and Your Body Young*, reviews a study conducted to determine the effects of a healthy longevity lifestyle program on cognition and cerebral metabolism in people with age-related complaints. Our ability to pursue spiritual practice is inextricably linked to our brain's ability to function and achieve full awareness; as this study concludes, a healthier lifestyle may be a big step toward maintaining and even improving brain function.

Effects of a Fourteen-Day Healthy Longevity Lifestyle Program on Cognition and Brain Function

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Many elements contribute to a better quality of life, a heightened awareness, and a more fulfilling day-to-day experience. Expanding the scientific frontier of cognition and brain metabolism in an effort to improve memory and brain function is a valuable step in the journey toward achieving long-term health, happiness, and even spirituality as it is defined: "the quality or state of being." In the following article are the findings of a longevity lifestyle program in relation to brain function that reveals how our lifestyle may, within a relatively

short time period, have an impact on both our brain function and memory ability. Through studies like these, it is possible for us to improve our memories, and ultimately our long-term quality of life.

As people age, their risk for cognitive decline increases. An estimated 40 percent of people sixty-five years and older have age-associated memory impairment characterized by self-perception of memory loss and a standardized memory test score demonstrating lower objective memory performance compared with young adults.[1, 2] Such mild age-related memory changes are often relatively stable over time. In contrast, patients with mild cognitive impairment, characterized by greater cognitive decline without impairment in the activities of daily living, are at risk for progressing to Alzheimer disease at a rate approximating 15 percent each year.[3] The MacArthur study of successful aging[4] found that certain lifestyle habits are associated with health and vitality as people age and, for the average individual, such nongenetic influences can account for a higher proportion of cognitive and physical health than genetic factors. Epidemiologic, laboratory, and clinical evidence point to several lifestyle behaviors that may maintain brain health and lower the risk for dementia, including mental and physical activity, diet, and response to stressful stimuli.[5–7] These and other lifestyle habits are not only associated with better health status, but also to increased longevity.[4, 8]

Studies of rodents in enriched environments have found more neurons in their hippocampal memory centers than in rodents living in ordinary laboratory cages.[9] Research in humans has shown that the risk for developing Alzheimer disease is lower in people who have been mentally active.[10] People with advanced educational and professional accomplishments tend to have greater density of neuronal connections in brain areas involved in complex reasoning.[11] Other studies of specific

memory techniques, including visualization, elaboration, and association, have been shown to improve objective memory performance scores.[12] These discoveries support the conclusion that mental stimulation and cognitive training may not only improve memory performance, but also stave off future cognitive decline.

When laboratory animals exercise regularly, they develop new neurons in the hippocampus, whereas inactive animals do not.[13] The physical exercise may increase cerebral blood flow, which in turn promotes neural growth. Studies of physically active people show that they have a lower risk for Alzheimer disease compared with inactive individuals.[14] A study of healthy older adults found that mental tasks involving executive control improved in a group that was prescribed a cardiovascular conditioning program but not in a control group that was prescribed only stretching and toning.[15] Excess body fat increases an individual's risk for such illnesses as diabetes and hypertension, which can increase the risk for dementia, cerebrovascular disease, and cognitive decline.[16]

Epidemiologic studies have found lower rates of dementia in geographic areas where populations eat diets low in animal fats.[17] Diets high in omega-3 fats from olive oil or fish,[18] as well as those rich in antioxidant fruits and vegetables,[19] are associated with less age-related cognitive decline. In addition, diets that avoid processed and refined foods and emphasize low glycemic index carbohydrates may reduce the risk for type 2 diabetes, stroke, and vascular dementia.[20, 21] Studies of laboratory animals show that prolonged exposure to stress hormones has an adverse effect on the hippocampus, a brain region involved in memory and learning.[22] Human investigations[23] indicate that several days of exposure to high levels of the stress hormone cortisol can impair memory. Proneness to psychologic distress also is associated with an increased risk for Alzheimer disease.[24]

Data from controlled clinical trials on the short-term benefits of many of these lifestyle strategies are limited. Moreover, cognitive and brain function effects of combining several strategies together are not known. To this end, we studied a fourteen-day program that combined healthy lifestyle behaviors associated with a lower risk for dementia—mental and physical exercises, healthy diet, and stress reduction techniques—on cognitive ability and brain function.

METHODS

Subjects and Clinical Assessments: We studied seventeen right-handed white adults who were selected from a pool of 344 potential volunteers recruited through advertisements, media coverage, and referrals from physicians and families. After telephone screening, forty-nine individuals were seen for clinical evaluation. We excluded volunteers who had major medical or neuropsychiatric illnesses that could affect cognitive status as well as those who were unwilling to make a commitment to undergo the study procedures as described. To be included in the study, volunteers needed to have objective cognitive performance scores that were normal for their age group. All subjects had mild age-related memory complaints, which is present in nearly half of individuals age 50 and older.[2] All subjects had neurologic and psychiatric evaluations, routine screening laboratory tests, and magnetic resonance imaging scans to rule out reversible causes of cognitive impairment,[25] and volunteers meeting diagnostic criteria for dementia[26] or mild cognitive impairment[3] were excluded. All subjects were given a Mini-Mental State Examination[27] and Hamilton Rating Scale for Depression.[28] Volunteers were excluded if they were taking drugs that could influence cognition (e.g., cholinesterase inhibitors, sedative-hypnotics) or supplements (e.g., phosphatidyl serine, ginkgo biloba) that could have such effects. Volunteers with a history

of excessive alcohol, caffeine, or tobacco use were also excluded from participation.

At baseline and follow up (within one week after completing the fourteen-day program), subjects received objective cognitive assessments, including a multitrial verbal learning and memory test[29] and a word-generation (letter-fluency) test.[30] Subjects also completed a standardized measure of self-awareness of memory ability, the Memory Functioning Questionnaire (MFQ).[31] The MFQ is a sixty-four-item instrument that provides four-unit weight factor scores measuring frequency of forgetting, seriousness of forgetting, retrospective functioning (changes in current memory ability relative to earlier life), and mnemonics use. Higher scores indicate higher levels of perceived memory functioning (e.g., fewer forgetting incidents, less frequent mnemonic use). For a sample of 639 adults aged 16 to 89 years, Cronbach alpha internal consistency alphas ranged from 0.82 to 0.93 for different scales on the MFQ, and test-retest reliabilities, over a three-year period, ranged from 0.22 to 0.64.[32]

All scanning procedures were performed within two weeks of clinical assessments. Informed consent was obtained in accordance with the recommendations and requirements of the Radiation Safety Committee and the Institutional Review Board of the University of California, Los Angeles, Healthy Lifestyle Program. After baseline assessments and scanning procedures were completed, each subject in the intervention group received a notebook with the fourteen-day healthy longevity lifestyle program, which is detailed elsewhere.[33] This program provides simple instructions so that subjects were able to readily follow several healthy lifestyle strategies—memory training, physical conditioning, relaxation techniques, and diet—that are associated with a lower risk for dementia.[7–10, 12, 14–21, 23, 24] The conceptual basis of the program involved developing a usable guide to initiating lifestyle and behavior strategies associated

with improved cognitive abilities and a lower risk for cognitive decline. The exercises build gradually over a fourteen-day period so they are readily learned and integrated into the volunteer's daily schedule. In addition to brain teasers and mental puzzles, the program provides daily exercises that teach memory techniques to help focus attention and improve visualization and association skills for better retention and recall.

These memory techniques begin at a basic level and increase in complexity over the two-week period. For example, the first day, subjects are given an exercise to focus attention to improve learning and concentration (e.g., subjects are instructed to concentrate on two random details of the clothing or accessories on a family member). After attention skills improve the first few days, exercises are introduced to improve visualization and association skills for better mnemonic techniques. Cardiovascular conditioning exercises such as brisk walks are recommended each day. Daily brief relaxation exercises are designed to lower stress and help subjects to focus their attention. Suggested shopping lists and menus guide subjects to follow a healthy diet plan, including five daily meals emphasizing antioxidant fruits and vegetables, omega-3 fats, and low glycemic index carbohydrates. The brief fourteen-day period was chosen so that volunteers would not be daunted by a requirement for an extensive commitment. Moreover, it was predicted that the time period would be adequate for participants to adapt to and feel comfortable with the lifestyle changes so they would continue them beyond the initial two-week period. Exercises and suggested menus were described in simple terms and the amount of time needed to follow the exercises totals from 30 to 45 minutes each day. Before initiating the program, a research nurse reviewed the daily instructions with each subject. The research nurse monitored self-reports of compliance through participants' daily notes and post-treatment interviews to ensure that volunteers were

able to follow the recommended program exercises and diet. The volunteers in the control group were instructed to continue their usual lifestyle habits during the two-week period between clinical and brain imaging procedures.

RESULTS

Subjects were on average middle-aged (overall mean age: fifty-three years; standard deviation: 10; range: 35 to 69 years) and college-educated, and did not have evidence of cognitive impairment or depression. The intervention and control groups did not differ significantly in mean age or years of educational achievement, proportion of females, or in mean baseline scores on the Mini-Mental State Examination and Hamilton Rating Scale for Depression.

Mean baseline subjective and objective cognitive measures did not differ significantly between the intervention and control groups. Changes in cognitive measures were not significantly different between the intervention and control groups. However, for the objective measures, the intervention group improved significantly in verbal fluency, whereas the control group did not. Subjects in the intervention group showed a 5 percent decrease in left dorsolateral prefrontal activity compared with baseline (Z 3.30, p control group showed no significant change in brain metabolism, and direct statistical comparison of the two therapy arms demonstrated that the decline in this region, involving a stretch of prefrontal cortex in the vicinity of Brodmann's areas 8, 9, and 10, was significantly greater in the intervention group than in the control group.

DISCUSSION

To our knowledge, this is the first study to show that combining several healthy lifestyle strategies will change measures of cognitive and brain function in a relatively brief time period.

The results suggest that a program combining mental and physical exercise, stress reduction, and healthy diet can have significant short-term effects on brain metabolism and cognitive performance.

The Statistical Parametric Mapping (SPM) analysis identified a change in cerebral activity in the intervention group in a brain region that modulates several mental functions relevant to the lifestyle intervention. Previous studies have demonstrated that working memory, the ability to retain information for brief periods, requires an intact dorsolateral prefrontal cortex.[34] A study using functional MRI found that semantic organizational strategies engage this same region.[35] The dorsolateral prefrontal cortex also mediates anxiety symptoms, and this regional metabolic reduction may in part have resulted from the intervention's relaxation exercises.[36] The significant change observed in the left hemisphere is also consistent with the verbal emphasis in the program's memory training exercises.

Moreover, the observations that the intervention group experienced both improved objective verbal fluency and significant change in left dorsolateral prefrontal metabolism are consistent with previous work showing that verbal fluency is associated with activation in this same brain region.[37] Future studies will determine specific effects of individual components of the program and whether a combination of healthy lifestyle strategies produces a greater effect than individual strategies.

The finding that the intervention reduced regional cerebral metabolic rates could correspond to subjects developing greater cognitive efficiency during mental rest, and previous studies are consistent with this hypothesis. PET scans of volunteers playing a computer game for the first time show high cerebral glucose metabolic rates, but after several months of practice, when the volunteers become proficient at the game, their scans display significantly lower rates of glucose metabolism.[38] This lower brain activity with improved mental performance suggests

that with time, practice, and familiarity, our brains can essentially adapt themselves to achieve comparable performance levels with less work. The present study suggests that such an improvement in brain efficiency may occur over relatively brief periods of intervention.

In a previous functional MRI study,[39] our group found that middle-aged and older adults with a genetic risk for Alzheimer disease had greater MR signal activity in the dorsolateral prefrontal cortex during a memory task compared with those without such a genetic risk. Moreover, higher MR signals at baseline correlated with lower verbal memory scores two years later. Future studies may determine whether such apparent neural compensatory responses to genetic risk would change after a lifestyle intervention such as the one used in the present study.

We did not find significant changes in subjective cognitive measures in the intervention group, which could reflect the small sample size as well as the insensitivity of the MFQ to measure short-term changes in memory self-awareness (several items in the questionnaire focus on longer-term memory abilities). Self-awareness of cognitive improvement is helpful in encouraging individuals to continue a healthy life style beyond a two-week period. By contrast, worry and concern about memory performance has been associated with worse objective memory performance scores.[40] The current study combined several different lifestyle approaches. Previous research indicates that combining different kinds of interventions can augment the overall effect on age-related health outcomes. For example, investigators have combined a healthy diet with regular physical exercise to reduce the risk for developing type 2 diabetes.[41] A strategy combining stress reduction with physical activity has been found to lower the risk for ischemic chest pain in cardiac patients, compared with exercise alone.[42]

Several methodological issues deserve comment. The small sample size and relatively brief intervention period limits how much any conclusions from these results can be generalized. Because volunteers were living in the community and not strictly monitored on how closely they followed the healthy lifestyle program, compliance would be expected to be lower than in a closely monitored, residential intervention program. Moreover, without objective measures of physical activity, dietary intake, or degree of compliance with memory and relaxation exercises, the actual lifestyle behavior changes in the intervention group are not known. The research nurse monitored activity self-reports, but recall bias could have influenced these reports. Thus, the observed changes in outcome measures may have reflected nonspecific or placebo effects of being given a program that participants were only claiming to have followed.

The nature of the cerebral metabolic results, however, would argue against such a possibility, because the brain region showing highly significant results was not a random region, but rather one that controls brain functions that were specific targets of the program (e.g., working memory, verbal fluency). Although we recruited a convenience sample of volunteers who may have already been following a healthy lifestyle regimen, such a convenience sample would be expected to reduce any differences between groups rather than exaggerate them. Our significant findings, despite such methodological limitations, suggest that people may be able to enjoy the benefits of healthy lifestyle programs when they follow them on their own without the assistance of a professional staff.

In summary, a fourteen-day healthy lifestyle program improved measures of verbal fluency and reduced left dorsolateral prefrontal cortical metabolism, suggesting that such a program may result in greater cognitive efficiency of a brain

region involved in working memory functions. Future longitudinal studies will determine the long-term effects of such combined interventions and whether they eventually lower the risk for developing dementia.

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