

Brain Exercises Fail to Increase Cognitive Power

VITALS

Major Finding: Improvements seen in “brain training” tasks translated poorly to performance on benchmarking tests that used similar cognitive functions (effect sizes, 0.01-0.22).

Data Source: A 6-week trial of brain training exercises in 11,430 participants

Disclosures: The authors reported having no financial conflicts of interest.

BY LEANNE SULLIVAN

“Brain training” does not improve general cognitive function, according to a 6-week trial of more than 11,000 participants.

The study results “provide no evidence for any generalized improvements in cognitive function following brain training in a large sample of healthy adults,” Adrian M. Owen and his colleagues reported.

The participants were divided into three groups: the experimental group 1 (4,678 subjects), which did six tasks emphasizing reasoning, planning, and problem solving; experimental group 2 (4,014 subjects), which practiced six tasks focusing on short-term memory, attention, visuospatial processing, and mathematics; and a control group (2,738 subjects), which answered various research questions using the Internet. The groups were matched in size initially, but more of the control group members dropped out before the final assessment. The participants were recruited from among viewers of a British science television show (Nature

2010 Apr. 20 [doi:10.1038/nature09042]).

The tasks given to group 2 were considered to be most like those of commercially available “brain training” programs, said Mr. Owen of the Medical Research Council Cognition and Brain Sciences Unit, Cambridge, England, and his colleagues.

The participants were assessed before and after the intervention using benchmarking tests that measured reasoning, verbal short-term memory, spatial working memory, and paired-associates learning. These validated cognitive

assessment tools (at www.cambridge-brainsciences.com) were chosen for their proven sensitivity to small cognitive changes because of disease or neuropharmacologic therapy.

Participants completed an average of 24 training sessions over the 6-week period (range, 1-188). The tasks were performed for a minimum of 10 minutes a day, three times a week. All three groups improved on the tasks they had been assigned to practice during the trial (effect sizes: group 1, 0.73-1.63; group 2, 0.72-0.97; controls, 0.33). However, postintervention improvements on the benchmarking tests were much smaller (effect sizes, 0.01-0.22 for all groups).

The control group improved slightly more than the experimental groups on two measures.

The groups were similar in age (average, 39-40 years) and gender (each group had 4-5 times as many female participants). No relationship was seen between number of training sessions performed or age of participants and postintervention benchmarking test scores. The scores on two tests reflected small gender differences.

Although participants improved at their assigned tasks, “training-related improvements may not even generalize to other tasks that use similar cognitive functions,” the researchers said. ■

Credible Study Addresses a Complex Question

MY TAKE

The notion of exercising the mind to reduce its deterioration is popular in the world of Alzheimer’s disease: Do crossword puzzles and you will slow the progression of dementia. But is it true? Epidemiological studies have shown mixed results, possibly reflecting presymptomatic-stage disease, confounding medical issues, and medications influencing outcomes.

Most people “exercise” their brain during their daily activities whether or not they conceptualize it in this way. The term “brain training” implies some kind of special activity that the term “practice” lacks, but acquiring any new skill requires en-

hanced attention, and with increasing task familiarity comes greater automaticity and increasing dexterity. Functional brain imaging studies show activation of prefrontal cortices during the early attentional practice stage that diminishes and vanishes as any skill becomes automatic (Proc. Natl. Acad. Sci. USA 1998;95:853-60).

Cognitive tasks rely on the integration of multiple brain regions that are geographically distant and serve different functions. Because a related, nonidentical task might use this network, it is conceivable that related tasks may be performed with greater facility and dexterity.

Given the effort required to achieve even a “simple” practice effect, studies such as that of Mr. Owen and his colleagues that fail to show any major translational skill differences after a mere 6 weeks of “brain exercises” that sound far less grueling than the practice of professional musicians and athletes are certainly credible.

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IVIIG Slows Brain Atrophy in Mild to Moderate Alzheimer’s

VITALS

Major Finding: Treatment with a range of doses of IVIG for 18 months resulted in a mean increase of 6.7% in lateral ventricular volume, which was significantly lower than the 12.3% increase observed with placebo.

Data Source: A double-blind, placebo-controlled, randomized phase II trial of 24 patients with mild-to-moderate Alzheimer’s disease.

Disclosures: Baxter Healthcare, which produces Gamma-gard, the IVIG product used by the investigators, sponsored the study, with additional support from the Citigroup Foundation and the National Institutes of Health. Dr. Relkin reported receiving a research grant from Baxter Healthcare.

BY JEFF EVANS

TORONTO — Intravenous immunoglobulin therapy reduced brain atrophy in patients with mild to moderate Alzheimer’s disease in a small phase II trial. The finding suggests that specific IgG antibody components found in the blood product might be treatment candidates for the disease.

“Relative to what we have available right now [to treat Alzheimer’s], this is a very promising outcome, and it’s associated with a reduction in the

rate of brain atrophy comparable to age-matched normals,” Dr. Norman Relkin said during a poster presentation at the annual meeting of the American Academy of Neurology. Enlargement of the cerebral lateral ventricles is known to occur as a consequence of brain atrophy in AD. This increase in ventricular volume is correlated with cognitive decline and increases in Alzheimer’s disease neuropathology.

Dr. Relkin, who is the director of the Memory Disorders Program at New York-Presby-

terian Hospital/Weill Cornell Medical Center, and his colleagues compared intravenous immunoglobulin (IVIIG) therapy against placebo in a 6-month, double-blind, randomized study of 24 patients with mild to moderate AD.

In a 12-month extension phase of the study, 16 patients who originally were randomized to IVIG continued to receive the same doses of IVIG, whereas 8 placebo-treated patients were re-randomized to one of four doses of IVIG.

IVIIG exhibited a dose-dependent effect on brain atrophy in which higher doses resulted in less atrophy. Among 14 IVIG-treated patients who underwent volumetric MRI at baseline and after 18 months, the yearly increase in lateral ventricle volume measured with volumetric MRI was lowest in patients treated with 0.4 mg/kg every 2 weeks (2.4%) and highest in those treated with 0.2 mg/kg every 2 weeks (11.2%).

The doses of IVIG that were given to patients ranged from 0.2 mg/kg every 2 weeks to 0.8 mg/kg every 4 weeks.

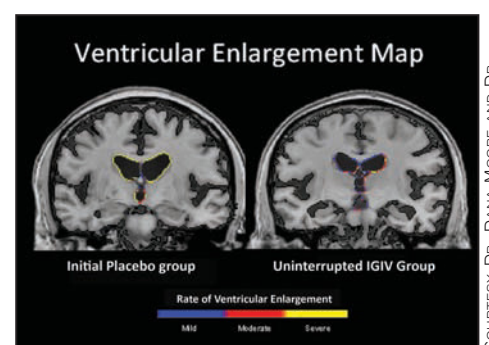
The volume of the lateral ventricles increased by a mean of 6.7% per year during treatment with IVIG (all doses combined), which was significantly lower than the 12.3% annual rate of increase observed in six placebo-treated patients.

The reduction in brain atrophy was significantly correlated with improvement in clinical outcomes at 18 months on the Clinical Global Impression of Change and the cognitive subscale of the Alzheimer’s Disease Assessment Scale. Baseline characteristics of the patients were not correlated with volumetric MRI outcomes.

“We are not encouraging people to use [IVIIG] off-label for Alzheimer’s disease, even

though it has been safe and well tolerated in these small studies,” Dr. Relkin said in an interview. “It has never been studied in the Alzheimer’s population before.”

“This is a ‘kitchen sink’ approach, so the next step is to find what is in [IVIIG] that is causing the therapeutic effect. ... We know that it has a fairly good complement of anti-amyloid antibodies. Those are prime candidates, but we don’t know for sure yet that those are the ones responsible for a therapeutic effect,” he said. ■



The ventricular enlargement rate was greater with placebo (left) than with IVIG (right).