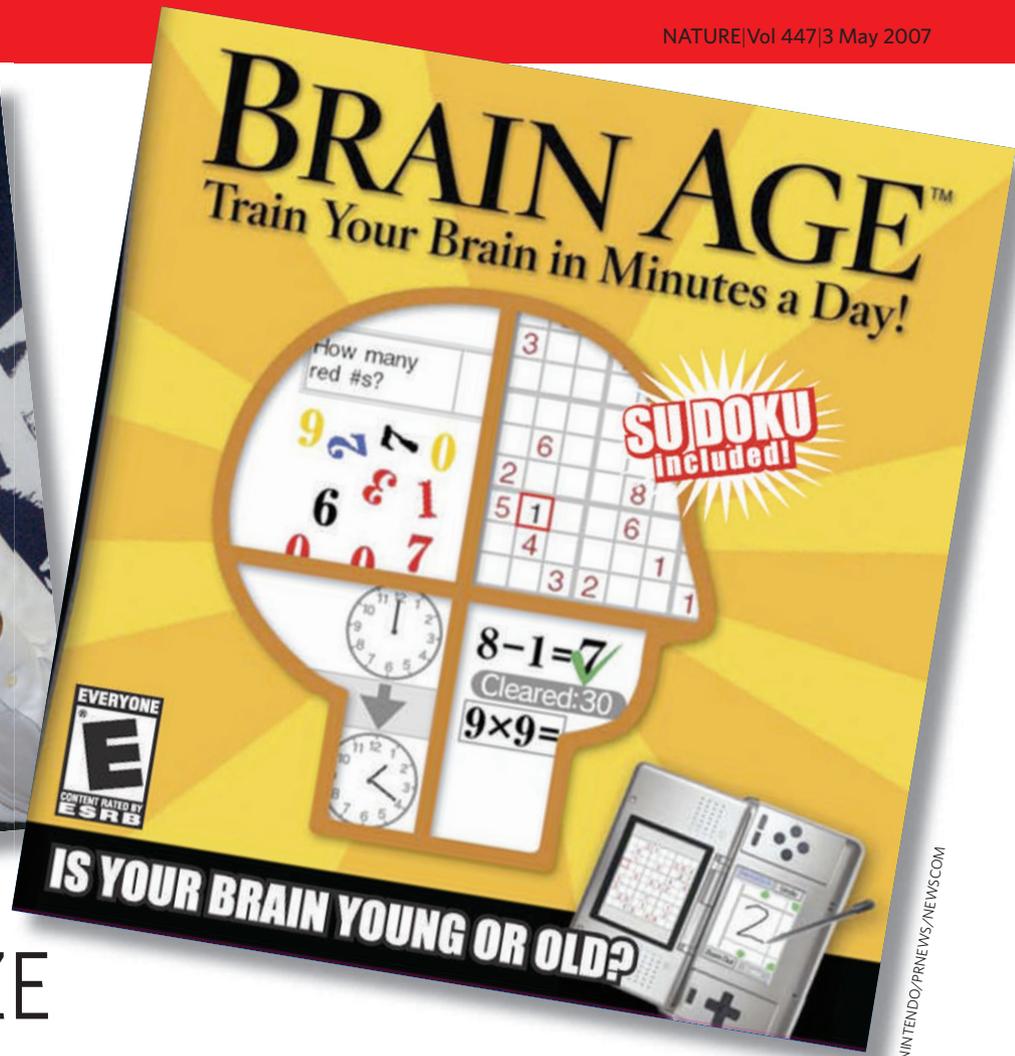




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BRAIN CRAZE

Neuroscientist Ryuta Kawashima promotes the idea that computer games can boost the ageing brain — but others in the field remain sceptical. **Ichiko Fuyuno** investigates.

On a chilly, rainy day last November, Ikuyo Narawa climbed on a tour bus in Tokyo in the hope of revitalizing her brain. She knew that she drank too much and never exercised, and she thought that her memory was weakening. So, along with 40 companions, she travelled to the scenic Tateshina highland in Nagano Prefecture, where she tried hiking and handicrafts, ate organic meals and bathed in hot springs.

At the start of the tour, the 37-year-old dental assistant took several simple computer tests, such as clicking a mouse as soon as a lamp lit red, and was surprised to be told that her 'brain age' was 61 years. After two days of activities, she took the test again and found that her result was, disappointingly, unchanged. But on her fifth time, attempting the test at home, her brain age dropped to 20. "I was very relieved," she says.

The brain-train tour, organized by the region's local chamber of commerce and a travel agency, is the latest example of a brain-exercise boom that is consuming Japan and spreading across the globe. In Japan, TV quizzes aimed at boosting the brain are popular, and fashion magazines run rejuvenating advice for the mind

alongside that for the skin. And throughout the world, a proliferation of books, websites and software is available claiming to preserve our mental capabilities.

At the centre of this craze is a ragingly popular video game developed by Japanese video game maker Nintendo and based on the research of Ryuta Kawashima (pictured above), a neuroscientist who specializes in brain imaging at Tohoku University in Sendai. Players of the game — called 'Brain Age' in the United States and 'Dr Kawashima's Brain Training' in Europe — use a console to complete simple tasks such as reading aloud, multiplication and memorizing words. In promotional material for the game, Kawashima says that daily training on these activities can "help to prevent a decrease in brain function". He promotes the idea that these types of activity enhance blood flow to the brain's prefrontal cortex — the region of the brain that regulates aspects of memory, reasoning and some of the other complex behaviours that deteriorate with age.

Many neuroscientists and gerontologists are sceptical of the claims made for Brain Age and similar games, saying that there is scant evidence that any type of brain exercise can halt

mental ageing. Kawashima has published a paper¹ suggesting that the type of mental activities in the game can help elderly people with dementia, but critics say that these findings do not necessarily apply to healthy adults. A player's score could well improve with practice, but whether that translates into an improvement in other mental tasks or everyday life skills remains unknown. "That's what I think is a big question," says Timothy Salthouse, a researcher of cognitive ageing at the University of Virginia, Charlottesville. "I don't think there is scientific evidence that the improvements after mental exercise can be generalized beyond what you have trained on."

In a rapidly ageing population, people are understandably keen to live a long life with their mental capacities intact. Neuroscientists think that from as young as 30, changes in the chemistry and connections between nerve cells cause some cognitive functions to decline. Brain-training programmes typically claim to slow this mental descent or even to recover some lost ground. Some studies have shown that physical exercise can prevent some of the brain's deterioration (see 'Body and mind'), and the idea that simple mental activities could do the same is enticing.

Brain training has already earned Kawashima celebrity status in Japan. He studied to be a

"People are paying for Brain Age. They deserve to know whether it really works"

— Dorothy Bishop

physician but, after learning about imaging techniques at Sweden's Karolinska Institute in Stockholm, he became one of the first to pursue brain-imaging research in Japan. Using techniques such as functional magnetic resonance imaging (fMRI), he showed that blood flow to the brain's prefrontal cortex increases when people are calculating sums quickly or reading aloud. He has published more than 100 drill books with such exercises for adults.

Mental work-outs

In 2001, Kawashima won a coveted ¥60-million (US\$500,000) grant from the Japan Science and Technology Agency in Saitama to study whether mental exercises improve cognitive function in elderly people. He and his team investigated 32 individuals who had been diagnosed with Alzheimer's dementia in Eiju-no-sato nursing home, Fukuoka. Over six months, half of the people were asked to do simple calculations and language tests, such as arithmetic division or reading fairy tales aloud; the other half received no training. Kawashima's team measured their cognitive status before and after the training with two widely used tests to diagnose dementia — the Mini-Mental State Examination (MMSE) and the Frontal Assessment Battery (FAB). The tests included questions such as "What day of the week is it?" and "What do bananas and oranges have in common?"

People in the training group improved their FAB score, maintained their MMSE score and became more communicative and independent



The Brain Age game claims that its cognitive exercises can help the ageing brain.

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than they had been before the training. The control group, however, showed no change in FAB score and a decline in the MMSE score¹. In addition, a 75-year-old man in the treatment group regained his ability to go to the toilet by himself, and a 77-year-old woman who used to come to the learning centre in her pajamas started to arrive fully dressed.

Kawashima and the other authors acknowledge the study's limitations. They could not

tell whether the cognitive improvements were attributable to the training itself, or to the extra attention and social interaction the individuals received from the experimenters and nursing staff. But Kawashima thinks that the method may have stimulated the prefrontal cortex, causing improvements in general cognitive functions such as communication. He called the method 'learning therapy', and it has now been introduced at 300 nursing homes across Japan at a monthly cost of ¥1,575 per user. Kawashima has conducted two more unpublished studies of the same training on elderly people with and without dementia and says that the training improved their MMSE scores.

Body and mind

Physical activity is already heralded for warding off cardiovascular disease and various other conditions. A growing body of evidence suggests that it can improve mental health too.

In a recent study, 11 young people were given a 12-week aerobic exercise programme. Afterwards, the participants performed better at memory tests. The exercise also promoted blood flow to the dentate gyrus, a region of the brain important in memory and cognitive ageing, and the authors suggest that it promoted the birth of new neurons there (A. C. Pereira *et al. Proc. Natl Acad. Sci. USA* **104**, 5638–5643; 2007). But researchers are not sure

exactly how physical exercise benefits the brain, or how much exercise is best for brain function.

Everyday life requires numerous skills, points out Warner Schaie, a psychologist studying cognitive development at Pennsylvania State University in Philadelphia. So elderly people should continue to do intellectually stimulating activities and to interact with other people, he says. The activities can be tailored to individuals' taste — from volunteer work to square dancing and travelling.

Many experts say that leading a generally healthy lifestyle — including physical



exercise, a good diet and mental and social activity — is probably the surest route to cognitive health. "The hypothesis we have is that mental and physical activities, social engagement and lowering vascular risks can lessen your chances of a decline in cognition," says Marilyn Albert, from Johns Hopkins School of Medicine in Baltimore, Maryland. "But we have a long way to go to understand that." I.F.

Adult entertainment

At the end of 2004, Kawashima was contacted by Nintendo. The company thought that his drill books could be turned into a stimulating game that would attract those adults who usually shy away from conventional video games.

Working with Nintendo to develop the game, Kawashima says that he studied 120 Japanese people aged from their 20s to their 70s. He used a technique called optical coherence tomography to examine blood flow in their brain while they tackled dozens of exercises, such as adding up numbers and memorizing Chinese characters. The tomography technique is not as accurate as fMRI, but Kawashima says that he used it because it was quicker and easier for the volunteers. He and his research team selected 15 tasks that boosted blood flow to the prefrontal cortex and calculated an average score for each age, which they used as a basis for the Brain Age game.

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The video game debuted in Japan in May 2005. Sales of the ¥2,800 product, together with its sequel, have reached more than 3 million units in Japan — in a market in which 1 million units is considered a hit. The game was introduced in the United States, Europe and Australia in 2006 and in South Korea earlier this year. Kawashima says that he uses all of the royalties from Nintendo and other companies — more than ¥400 million in 2006 — on his research, including construction of a new laboratory near his office.

Lost in translation

Other neuroscientists, many of whom say that they respect Kawashima's work, express discomfort with his Brain Age concept. Although the game could work in principle, they question whether simple mathematics and reading tests of the type in Brain Age are any more effective than other cognitive tasks at boosting blood flow to the prefrontal cortex. And they say that there is little evidence that a brief boost in blood flow would improve brain processes or the everyday skills that decline in normal ageing adults. "I see no reason to believe that Brain Age gains will transfer to other kinds of cognition, or to real-world function," says Michael Marsiske, who also studies interventions to improve cognitive performance, at the University of Florida, Gainesville.

Earlier this year, 41-year-old Marsiske played the game himself. He says the game was entertaining and fun and that his brain age dropped from 78 to 26 after three days. But much of the improvement could be attributed to practice, he says. "Users may get the illusion of huge gains when starting with Brain Age, but these have more to do with learning the device than actual mental improvements."

Marsiske and other neuroscientists say that they would like to see well-controlled, published studies to show that Brain Age benefits those who are buying it. "People are paying for it. They deserve to know whether it really works," says Dorothy Bishop, a neuroscientist at the University of Oxford, UK. Kawashima is indifferent to this criticism and says that he does not intend to conduct more detailed studies on the game's effects because his earlier study on those with dementia, and his additional unpublished work, demonstrated that his learning therapy works. "I am sure it works because all the data we obtained so far have been showing positive



Grey gaming: researchers are testing whether computer exercises can improve elderly people's skills.

results," he says. "The most important thing is that behaviours of older people have got better with our training method." Yasuhiro Minagawa, a spokesman for Nintendo, says that the company is not in a position to comment on the scientific evidence behind the game, and the company is confident that Brain Age provides high-quality entertainment.

Other scientists are eager to test more rigorously whether mental work-outs can enhance the ageing brain. "A lot of people are interested in this area and are working hard to see whether or not this kind of short-term training has a long-term benefit," says Marilyn Albert, an expert on Alzheimer's disease at Johns Hopkins School of Medicine in Baltimore, Maryland.

A firm called Posit Science in San Francisco, California, is conducting research into Brain Fitness Program, its best-selling computer-based exercise (costing from \$395), in which users distinguish similar sounds, reconstruct sequences of words and do other mental exercises. A team led by Michael Merzenich, the company's chief scientific officer and a researcher on cortical plasticity at the University of California, San Francisco,

assigned 182 participants aged over 60 to one of three groups. The first group performed brain exercises on a computer, the second watched and listened to educational DVDs on their computers and the third had no computer time. After the 8–10 weeks of the study, the training group had improved at the tasks in the program and in other standardized assessments of memory it had not been trained in², whereas those in the control groups showed no improvements.



"I see no reason to believe that Brain Age gains will transfer to real-world function."
— Michael Marsiske

Perhaps the best study on mental training so far, Albert says, was that published by a team including Marsiske late last year³. It suggested that healthy elderly people given a cognitive work-out can gain long-lasting mental benefits, which may have transferred into improvements in their daily living activities. More than 2,800 mentally healthy adults aged over 65 were randomly assigned to receive ten hour-long training sessions over five weeks or to a control group that received no training. The team found that the training groups had improved cognitive ability for the specific tasks they had trained on, and that the benefit lasted for as long as five years. And compared with the untrained controls, participants in one of the training groups reported that they had less difficulty in performing routine tasks, such as preparing meals and using the telephone.

Many neuroscientists are optimistic that brain training will have proven benefits. And they see no more harm in doing computer exercises than in completing brain teasers such as crosswords or sudoku, and can at least give a warm glow of accomplishment. At the Eijuno-sato nursing home, those with dementia are given basic exercises in reading and calculation for 15–20 minutes a day. Head of the nursing home Ritsumi Yamasaki says that this schedule has improved patients' behaviour more than therapies she had tried before, such as gardening and karaoke, and it helps their interaction with carers.

"I tell people to do it if it's enjoyable," agrees Salthouse. "There's little evidence that it's damaging or harmful, and we may eventually find out there are some benefits."

Ichiko Fuyuno is a reporter for Nature in Tokyo.

1. Kawashima, R. *et al. J. Gerontol. A* **60**, 380–384 (2005).
2. Mahncke, H. W. *et al. Proc. Natl Acad. Sci. USA* **103**, 12523–12528 (2006).
3. Willis, S. L. *et al. J. Am. Med. Assoc.* **296**, 2805–2814 (2006).