Cognitive Shields

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Novelist Terry Pratchett once noted that because aging baby boomers will spend more years as senior citizens than any previous generation, they will “run right into the dementia firing range.”

Indeed, dementia afflicts an estimated 35.6 million people across the globe, according to the World Health Organization, and that number is projected to double in the next 15 years. Pratchett himself suffers from an atypical form of Alzheimer’s disease.

Unfortunately, cures for various types of dementia remain elusive, making rising life expectancies look like a curse as much as a blessing.

But psychological researchers and other scientists are closely investigating some apparent cognitive shields against age-related impairment. In doing so, they have discovered that several protective factors appear to operate even in brains that have all the molecular signs of dementia. A 2006 study from Rush University, for instance, found that about a third of post-mortem brains with telltale features of dementia — protein tangles or miniature strokes — came from people who never exhibited symptoms during life. How is it that the cellular pathologies so seemingly intertwined with Alzheimer’s and other forms of dementia don’t always produce illness?

According to psychological scientist Barbara B. Bendlin, Alzheimer's investigator at the University of Wisconsin–Madison, certain individuals may build buffers over their lifetimes, a phenomenon called *cognitive reserve*.

"What's interesting is that there are several protective factors against developing dementia, including higher education, and higher physical and possibly mental fitness," Bendlin explains. "Some individuals remain cognitively healthy even in the face of increasing burdens of brain pathology."

If that's true — if cognitive reserve can help protect against the onset of dementia — the next question is obvious: How do we develop more of it?

Energizing the Mind

Over the last couple of decades, researchers have found evidence that various behavioral therapies can strengthen mental buffers and help people maintain memory later in life, often at a fraction of the cost required for large-scale drug development. These therapies — cognitive training, exercise, and a healthy diet, for instance — are the same factors that ward off other chronic diseases, and psychological scientists are investigating them in earnest as a means to offset a dementia epidemic.

To date, most studies examining lifestyle factors and dementia have been retrospective and correlational, with researchers relying on participants to report how frequently they engaged in certain activities and when their symptoms began to emerge. That kind of research is valuable for tracking trends, but only a few studies have actually examined lifestyle factors in an experimental context, directly pitting one set of activities against another to see which produces the greatest cognitive benefits.

One study published in *Psychological Science* did just that, examining how actively engaging the brain can actually boost older adults' recall power.

In this experiment, Past APS Board Member Denise C. Park and colleagues at the University of Texas at Dallas randomly assigned more than 200 older adults (ages 60–90) to engage in a particular type of activity for 15 hours a week over the course of 3 months. Some participants learned skills that required significant cognitive investment, like digital photography or quilting. Other participants were asked to take part in more leisurely activities — say, listening to classical music or completing word puzzles. Park wanted these activities to mirror the types of activities people might engage in anyway, rather than using obscure memory-training tasks.

"I think it's very important to understand the types of everyday tasks or hobbies that maintain or improve cognitive health," she explains. At the end of 3 months, Park and her colleagues tested the participants' overall cognitive abilities.

As it turned out, the participants who engaged in digital photography or quilting showed a significant improvement in memory compared with those who took part in the leisure activities. Importantly, the researchers accounted for participants' overall social contact throughout the 3-month period, which allowed them to conclude that it was the psychological challenge, and not social interaction, that was critical for bolstering participants' cognitive performance.

Another recent study from the University of California, San Francisco, revealed similarly encouraging results. In this experiment, led by psychological scientists Adam Gazzaley and Joaquin A. Anguera, 16 older adults were recruited to play a videogame called “Neuroracer.” In the game, participants attempted to drive a car down a virtual road, keeping constant speed and lane position. While doing so, they also had to pay attention to sporadically appearing shapes, pressing a button whenever they observed a green circle. As participants improved, the game became increasingly more challenging, ensuring that it was always difficult enough to be mentally engaging.

For comparison, another 15 participants played an easier version of the game, requiring that they drive *or* pay attention to the shapes, but not both. Fifteen more participants didn’t play Neuroracer at all. After 1 month, the researchers brought all the participants back to complete several cognitive tests.

The results indicated that those who played the difficult version of Neuroracer were much better at multitasking *within* the game, and they also scored better on unrelated cognitive tests. This kind of transfer — with improvement on one task leading to a more general boost in cognitive functioning — has been notoriously elusive in studies of so-called “brain games,” making the Neuroracer results particularly intriguing. Brain imaging with EEG revealed noticeable differences at the neural level: Participants who played the difficult version of the game showed more coherent activation patterns in cognitive control networks, including the prefrontal cortex.

And the benefits seemed to last: Adults who played the difficult game maintained the cognitive gains 6 months later.

Although these results are promising, it’s not clear how these particular cognitive improvements would actually play out in the daily lives of older adults, much less whether they might aid in curbing full-blown dementia; larger, longitudinal experiments will be required to answer these questions. As Park points out, such studies might address a crucial gap between animal and human dementia research.

“The animal literature suggests that without continued engagement in a stimulating activity, gains for engaging in cognitive challenges are quickly lost,” she says. Just like booster shots, periodically revisiting the challenging activities may be necessary to buffer against later dementia.

Still, these experiments reveal that it’s never too late to challenge the mind, and that even short stints of training can produce tangible benefits.

Moving to Protect the Brain

Continuing to exercise the mind in the later years of life is important, but research suggests that physical exercise is equally critical. According to Art Kramer, APS Fellow and director of the Beckman Institute for Advanced Science and Technology at the University of Illinois at Urbana–Champaign, both the mind and brain thrive when the body is in motion.

Kramer and colleagues have designed numerous randomized experimental studies to identify the types of exercise that are most effective at boosting cognition later in life.

In one study, Kramer randomly assigned 120 older adults to either an aerobic fitness routine — about 40

minutes of brisk walking 3 days a week — or a less intense stretching routine for the same amount of time. Both groups stuck to their respective routines for about a year, and Kramer used MRI to assess any change in the structure and size of participants' brains over time.

In doing so, he and his colleagues hoped to determine whether demonstrated changes in memory map onto specific changes in the brain. That is, is there evidence for "brain reserve" that can be linked to cognitive reserve?

Their findings suggest so. Participants in the stretching group — who didn't undergo aerobic exercise over that year — showed a typical age-related decrease in volume of the hippocampus, a brain region crucially involved in memory. Participants in the aerobic group, on the other hand, exhibited *increases* in hippocampal volume, effectively offsetting 1–2 years' worth of volume loss.

Together, the findings suggest that aerobic fitness produced increased hippocampal volume, which in turn was directly related to improvements on memory tests in the walking (aerobic training) group. Because of these potential neuroprotective effects, Kramer and his coauthors stress the importance of squeezing in an exercise routine at any stage in life and especially as we age.

Other studies support these findings. Stephen Rao, professor at the Schey Center for Cognitive Neuroimaging at the Cleveland Clinic, was interested in whether exercise can grant neuroprotective effects in people who are at genetic risk for Alzheimer's. Alzheimer's is considered a heritable disease, and a variation in one particular gene, APOE, confers an elevated risk. For this investigation, Rao and his colleagues studied about 100 older adults, many of whom carried the APOE gene. The participants explained their normal exercise habits and had their brains scanned twice over a period of 18 months.

By comparing the first and second brain scans, Rao and his colleagues found evidence suggesting that exercise was critically important for the at-risk group: People with the APOE gene who didn't routinely exercise exhibited about a 3% decrease in hippocampal volume over time. By contrast, those carrying the gene who did incorporate exercise into their lives — more than 15 minutes of moderate exercise at least 3 days a week — didn't show any decreases in hippocampal volume. People without the risk gene did not show a decrease in hippocampal volume, whether they were sedentary or exercised regularly. This finding suggests that the neuroprotective effects of exercise may be specific to persons at risk for Alzheimer's.

Although the study doesn't point to a specific mechanism linking exercise and brain volume, Rao and colleagues have some hypotheses: for example, staying active might reduce inflammation in the brain and promote neuronal growth in the hippocampus, effectively building up cognitive reserve *and* brain reserve in people at risk for developing Alzheimer's.

The Language Buffer

Although studies have identified the hippocampus as one area of the brain linked with cognitive reserve and brain reserve, other studies suggest an important role for networks involved in executive control. Investigations of bilingual people have shown that the networks we use for language — and the executive control required for learning new languages — are the same networks that seem to deteriorate with dementia.

The first hints that bilingualism might promote cognitive reserve came from epidemiological research. Two investigations led by APS Fellow Ellen Bialystok and APS William James Fellow Fergus I. M. Craik, psychological scientists from the Rotman Research Institute at Baycrest, Canada, indicated that older adults who regularly used at least two languages for most of their lives were, on average, diagnosed with dementia 4 years later than their monolingual counterparts. And that held true even when the researchers accounted for potentially related factors like education, cognitive skills, occupation history, and immigration status.

Bialystok and Craik believe that because using two languages requires the recruitment of many higher order cognitive abilities, bilingualism may delay dementia in the same ways as other cognitive challenges. The ability to learn diverse grammatical rules, suppress one language in favor of another, and quickly switch sentence styles is difficult, and difficult tasks have the potential to strengthen cognitive reserve.

Several dementia-research studies have provided neural evidence in support of the protective effects of bilingualism. In one investigation, Tom Schweizer from the University of Toronto, Canada, used CT scans to measure brain atrophy in 40 older adults with probable Alzheimer's disease, some of whom were bilingual and some of whom were monolingual. Crucially, the researchers ensured that both groups exhibited the same level of dementia symptoms; that way, any differences in the brain could not be accounted for by dementia severity.

Compared to monolingual individuals, patients who spoke two languages exhibited more atrophy in regions most associated with Alzheimer's disease decline.

These findings may seem paradoxical at first blush, but they are actually directly predicted by the cognitive reserve hypothesis.

As Schweizer and colleagues hypothesized, a lifetime of speaking two languages may build stronger shields *against* the effects of brain atrophy — which may explain why bilinguals' symptoms of dementia weren't worse than their monolingual counterparts, despite the greater degree of atrophy. In effect, it's as if the bilingual individuals were cognitively "younger" than one would predict by simply looking at the deterioration in their brains.

In another recent study, Gigi Luk of Harvard University, along with Craik, Bialystok, and Cheryl Grady of the University of Toronto, discovered that bilingual older adults had more robust white matter tracts than did monolingual participants. This suggests that the myelin on axons in these nerve bundles is more intact (less degraded), which would help to maintain efficient transmission of nerve signals. Ultimately, preservation of white matter among bilinguals may help to buffer against age-related changes in the size and structure of critical areas of the brain.

Mark Antoniou, a psychological scientist from the Chinese University of Hong Kong, is especially convinced by these findings and has suggested that language training later in life might be a useful method for reducing rates of dementia.

"The end result of foreign language learning may be that language function is promoted, the integrity of brain structures involved is maintained, and a greater number of potential neural circuits could be

available that allow for compensation of age-related cognitive declines," write Antoniou and his colleagues.

Just as with physical exercise and other cognitive training techniques, however, moving from principle to practice is not so straightforward.

"Motivation also plays a larger role in determining language-learning success in older adults," Antoniou suggests. "Therefore, it is crucial to identify the optimal learning method for older learners, namely by ensuring that older learners are motivated, that the material has immediate practical value, and is personally rewarding."

From Cortex to Community

The results of these studies are exciting, but translating the science of cognitive reserve into healthier people is another problem entirely.

Research has shown, for example, that although people may have a vague understanding that they can shield themselves against age-related memory decline, they're fuzzy on the details. Funded by the US Centers for Disease Control,
a collaborative research effort among nine universities found that most people recognize the link between exercise and cognitive health, but they're unsure about how much exercise they should be getting and what types of exercise are most effective. That is, they have difficulty translating what they *should* do into actual healthy actions.

Kristen Felten, a social worker and dementia specialist in the Wisconsin Department of Health Services, believes fixing this problem is of paramount importance.

"You can have a good quality of life, you can mitigate the symptoms of the disease, you can affect the trajectory of its progression with lifestyle changes," Felten explains. "Often, people don't realize they can take control."

As the research suggests, it's crucial that early symptoms be taken seriously. Some symptoms simply reflect the quotidian annoyances of an aging brain, but, in other cases, they may be early signs of dementia.

And this issue underlies perhaps the most critical policy measure societies can take: early dementia screening. Studies have shown that detecting signs of cognitive impairment early and targeting intervention programs appropriately can provide significant government savings in the long run. Furthermore, it can reduce the time patients spend in severe stages of the illness, leading to reduced emotional stress for families.

To address these dementia challenges, state and local authorities are beginning to develop strategic plans using the most recent scientific evidence. In her home state of Wisconsin, Felten has worked tirelessly to construct a systematic response to what is most certainly a large-scale problem, including building public awareness campaigns, disseminating evidence-based educational materials, and conducting outreach with rural and minority populations.

Perhaps most importantly, Felten and others are developing “dementia-capable” communities.

“We work with local businesses, grocery stores, pharmacies, banks, and restaurants — anywhere someone with dementia might go as part of their daily life,” she says. “It’s important that older individuals stay socially active and engaged, and communities need to be ready and willing to have that happen.”

These opportunities for community engagement, she adds, may promote cognitive reserve.

Helping people make lifestyle changes that boost cognitive reserve is an important component of addressing the dementia epidemic, but there is no magic bullet. Invariably, there will be people who exercise, stay mentally fit, and keep an eye out for the early symptoms, but still develop dementia. These cases reinforce the notion that the onset of cognitive impairment is governed by a complex mix of biological and environmental risks, and there is much about the ailment that scientists don’t yet know. Detaching dementia from aging will be an important part of ensuring that well-being increases alongside human longevity. œ

A symposium on “Game-Based Cognitive Training for the Aging Brain” will be held at the inaugural International Convention of Psychological Science, March 12–14, 2015, in Amsterdam, the Netherlands.

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