



## Exercising the Body *and* the Mind

Improved physical fitness is a common New Year's resolution. Might it have more benefits for our patients than we thought?

**W**e missed Grammy this year. Like me, Grammy is married into a remarkably extended family that converges on South Florida over the Thanksgiving holiday each fall. But when you're 96 years old and don't show up for the family reunion, everyone expects the worst. In this case, the news—though not good—wasn't as bad as it could be. She had sustained a compression fracture in her osteoporotic spine and was in too much pain to tolerate the long trip from Illinois to Florida. We were all reassured, however, that Grammy remained “as sharp as a tack.”

Grammy could be the poster child for successful cognitive aging. Through her 95th year (when I most recently saw her) she remained fully engaged in the world, thirsty to know more about everyone she met, and expressing her unique blend of feistiness and charm that endears her to nearly everybody who knows her. She is more mentally and physically active than many of members of her childrens' generation who gather to celebrate Thanksgiving with the clan. If I asked her about why she stays so active, I'm sure her answer would be something like, “Being 95 is no reason to slow down.”

She's probably onto something there. There has been a lot of interest in the impact of mentally and physically active lifestyles on cognition over the last few years. When the electronic medical information service Medscape sent me their “Top Neurology & Neurosurgery News of 2006” list by e-mail at the end of the year, two of the 10 articles addressed relationships between physical activity

and cognition in older adults. (In fact, six of the referenced articles covered the impact of lifestyle choices, like diet and fitness, on cognition or dementia risk; this would have been unheard of just 10 years ago).

One of the studies, by Ian Deary and colleagues from the University of Edinburgh, examined the relationship between school-based intelligence testing at age 11, repeat testing at age 79, and several measures of physical fitness in a cohort of 460 individuals born in Scotland in 1921.<sup>1</sup> They found that general physical fitness was the best predictor of successful cognitive aging on IQ testing separated by nearly seven decades. The pattern of their findings also led them to conclude that the observed effect was not simply the result of smarter people staying more fit. That's all well and good, you might think, and fits in well with Grammy's story, but what about those of us whose lifestyle has reflected a more sedentary bent? Is there hope for us?

That's where the second “Top Ten” study comes in. Gary Small and colleagues at UCLA randomly assigned eight nondemented people, ranging in age from 35-69, to participate in a two-week program of combined dietary, relaxation, physical conditioning, and mental exercise interventions.<sup>2</sup> They were compared with nine matched control subjects who were randomly assigned to maintain their usual lifestyle. All participants had normal age-related memory complaints, but no dementia or other illnesses known to be causing their complaints. After only two weeks, the intervention group showed improvements in

word list generation and a five percent decrease in left dorsolateral prefrontal cortex activity on FDG-PET scans. The authors concluded that the decrease in cortical metabolic activity reflected improved “cognitive efficiency.” While hardly overwhelming, these results at least suggest that the “better late than never” philosophy might apply to mental sharpness, too. (The Small et al study also makes me think I might have to drag the treadmill out of the storage room. Looking at the rest of their intervention approach—and always in search of efficiency—I wonder if I could implement the other parts of the program by relaxing while learning how to cook healthier meals during my exercise time!)

### Calisthenics and the Cortex

So how does fitness work as a tonic for cognition? Hypotheses about how lifestyle, including physical fitness and social contact, influences cognitive aging abound, but no single mechanism has emerged to explain the phenomenon.<sup>3,4</sup> Many of the constructs focus on the idea of brain reserve, whereby physical activity stimulates growth of new neurons or synapses through enhanced release of neurotrophic factors. In these models, having more neurons or, more likely, synapses not only improves function, but also protects against decline by providing more back-up processing power in the face of pathologies that kill off those synapses and neurons. Other mechanisms may act concomitantly, such as improved cerebrovascular function and oxygen delivery, or reduction in the adverse effects of insulin resistance on neuronal function and viability. Exercise

also has stress-reduction properties which is important because physiologic markers of stress appear to be associated with reduced neuronal viability, especially in the hippocampus.

It is likely that these mechanisms interact with background genetic factors as well. We can look, for instance, at apolipoprotein E (ApoE). The  $\epsilon 4$  allele of ApoE is a commonly recognized risk factor for Alzheimer's disease and the relationship between poor cognitive performance and low levels of exercise appears to be strongest in men who possess the ApoE  $\epsilon 4$  allele.<sup>5</sup> The issue of genetic background is also pertinent to another important 2006 paper (which didn't make the "Top 10" list) showing that memory function in healthy adults varies based on specific allelic variation in a gene called KIBRA.<sup>6</sup>

There are likely to be other subtle genetic factors that link exercise, mental stimulation, cognition, and risk of Alzheimer's disease. Transgenic mice, engineered to develop AD-like pathology, that were exposed to an enriched environment that included ample opportunities for mental stimulation and physical activity increased activity for multiple genes associated with learning and memory, neurogenesis and cell survival.<sup>7</sup> Polymorphisms in any of those genes have the potential for facilitating or diminishing the impact of environmental enrichment on the expression of Alzheimer's disease.

What does this mean for us and our patients? There is already plenty of evidence out there that a healthy lifestyle, including hefty doses of regular exercise, is good for people, with well-recognized and prominent effects on vascular disease and diabetes. It's hard to imagine that the growing evidence for cognitive preservation or even a slight reduction in dementia risk will have a big impact on most people's lifestyles.

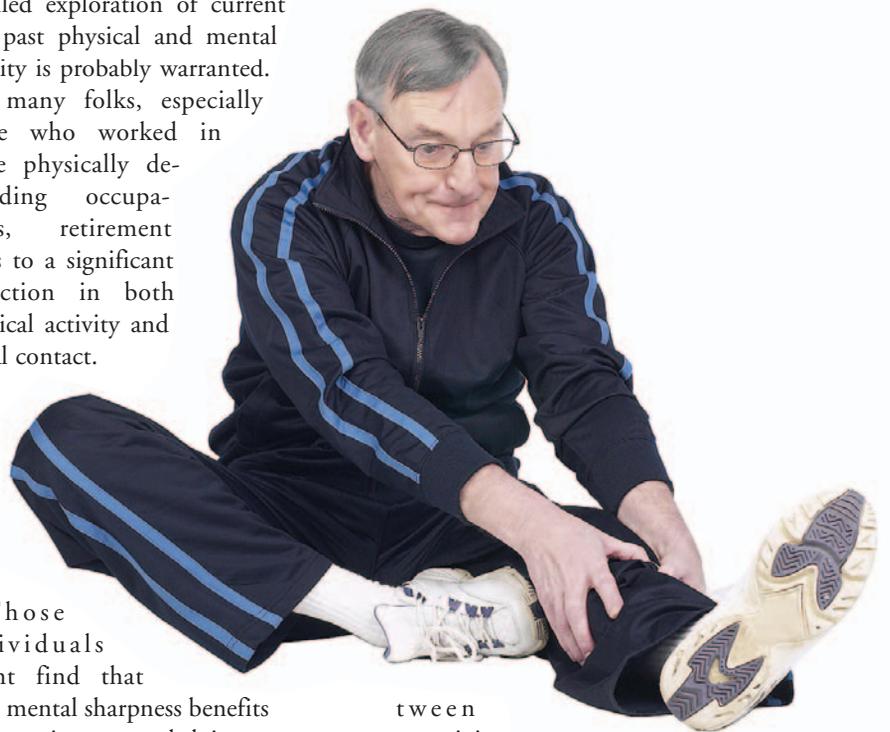
However, when that next older person comes in the office complaining of some

mild memory problems, a more detailed exploration of current and past physical and mental activity is probably warranted. For many folks, especially those who worked in more physically demanding occupations, retirement leads to a significant reduction in both physical activity and social contact.

Those individuals might find that their mental sharpness benefits from getting out and doing more, especially if it involves some parallel social stimulation. Ideas for them include walking groups at the local shopping mall, or exercise programs at the senior center or YMCA. If physical problems, like Grammy's, are preventing more activity, physical therapy can be a great way of getting them out and moving. In that situation, I'll often request at the time of referral that the therapist develop an exercise program for the patient to continue after formal therapy.

We know less about the impact of activity-based interventions in people who already have Alzheimer's, but the social withdrawal and apathy that are common early in the disease are likely contributors to reduced physical activity. Both patient and caregiver might benefit from patient participation in exercise programs or daycare activities, if for no other reasons than socialization and stress reduction.

There is much more yet to be learned about these complex interactions be-



tween cognitive aging, fitness and activity, and dementia, but Grammy's example of not slowing down certainly seems to be pointing us in the right direction. **PN**

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