Overweight and hypertension are major risk factors for cardiovascular morbidity and mortality\textsuperscript{1,2}; both are associated with decline in cognitive performance.\textsuperscript{3,4} We know that exercise is associated with modest reductions in blood pressure (BP) and that weight loss results in even larger, clinically important reductions in BP.\textsuperscript{5} What we did not know, before a report\textsuperscript{6} in this issue of Hypertension, is whether reductions in BP in association with diet and exercise (or diet alone) are associated with improvement in cognitive functioning. With publication of this article, we have evidence supporting an association of diet and exercise and diet alone with a concordant decline in BP and improvement in cognition.\textsuperscript{6} These are important findings given a recent meta-analysis of clinical trials of antihypertensive medications that indicated no improvements in cognitive performance associated with decline in BP.\textsuperscript{7} Two important issues are raised in this editorial comment: are the Smith et al\textsuperscript{6} findings important clinically, and where should this line of research go from here?

Using a sample of 124 overweight and prehypertensive or moderately (stage 1) hypertensive adults, Smith et al\textsuperscript{6} examined the association between 2 interventions and a control on cognitive performance for 3 groups: (1) diet alone (Dietary Approaches to Stop Hypertension [DASH]-alone [A]), n=38; (2) diet and exercise (DASH+weight management [WM]), n=43; and (3) usual care control (UC), n=43. The UC group maintained their usual lifestyles.

After 4 months of treatment, participants randomly assigned to the DASH-A group improved with respect to psychomotor speed as compared with persons assigned to the UC group. Persons randomly assigned to DASH+WM improved on a composite of cognitive tests reflecting executive performance (eg, planning, organization, and shifting set) and learning-memory and also improved on psychomotor speed as compared with persons in the UC group. Power limitations precluded a comparison of DASH-A and DASH+WM groups. Importantly, the improvement was not remedial, because none of the groups exhibited clinically important deficits in cognition before the first assessment.

No reductions in weight or BP were seen for the controls; however, relative to the controls, impressive reductions in average systolic and diastolic BPs were observed for the DASH+WM group (14 and 10 mm Hg) and the DASH-A group (10 and 8 mm Hg). Weight decreased and peak oxygen consumption improved in the DASH+WM group as compared with the UC group. DASH-A participants did not differ from the UC group in maximum oxygen consumption or weight. Clearly, diet plus weight management, including exercise, was effective with regard to lowering BP.

Improvements in cognitive performance with DASH+WM were modest, \textasciitilde0.08 SD units for an executive functioning/learning-memory composite. Participants in the DASH-A diet showed essentially no change. Participants in the DASH+WM diet performed at an average level before diet and exercise, but modest improvement is an important finding for 2 reasons: hypertension-related cognitive deficits are cumulative over the life span,\textsuperscript{4} and modest decrements in cognition in midlife increase the risk for dementia in later life.\textsuperscript{8} Improvements in cognition for any reason lead to increased cognitive reserve and prolong cognitive performance across the life span.

Some members of the Seventh Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of Hypertension were initially concerned over premature treatment with antihypertensive medication.\textsuperscript{1} The Smith et al article\textsuperscript{6} offers support for supervised diet and exercise as an alternative treatment for mild hypertension with a positive outcome with respect to cognitive functioning. Moreover, the Smith et al article and its companion publication\textsuperscript{5,6} clearly specify the protocol for a demonstrably effective diet and weight management program.

Smith et al\textsuperscript{6} advocate further work with elderly adults, patients on antihypertensive drugs, more severely hypertensive individuals, individuals with more severe cognitive impairment, and those in the preclinical phase of dementia. These are admirable and appropriate goals, but the number of exclusions required to select a sample with young, prehypertensive, and stage 1 individuals in their initial investigation\textsuperscript{6} forewarns of many methodological challenges to the work proposed. We see the most practicable and useful next step as a larger trial or trials, ideally including an exercise-only group and specifically targeted at individuals diagnosed with prehypertension. With the exception of secondary hypertension and hypertension-related complications requiring prescribed medication or surgical intervention, it seems logical to argue that prehypertensive patients, especially those who are over-
weight, are most likely to profit from diet and exercise intervention as early in life as possible. Prehypertension begets hypertension at an alarming rate and heralds cardiovascular disease events many years later; therefore, an ounce of prevention is worth a pound of cure in terms of hypertension-related mortality and morbidity and preservation of cognitive ability over the life span. A search of PubMed for the years 2000–2010, using diet/exercise as descriptors, revealed only 5 studies of diet and exercise in prehypertensive individuals; none involved cognition.

The unanswered question in the Smith et al study is as follows: what mechanisms, aside from peak oxygen consumption, intervene among diet and exercise, BP, and cognition? The Figure illustrates models for the studies addressing this question using path analysis as the statistical approach. We have observable variables (rectangles) in Figure A (epidemiological model) and observable and latent variables or unspecified mechanisms (ovals) in Figure B (biological model). Arrows represent paths from one variable to another variable. As research progresses, the latent variables (labeled “mechanisms”) will be filled in with observable variables. Peak oxygen consumption is a candidate variable on the basis of the Smith et al study. A review of the expanding literature on changes in brain structure and function triggered by chronic exercise in humans and animals is beyond this commentary, but it is noteworthy that many of these alterations occur in the hippocampus and other structures involved in executive performance, learning, and memory. Insulin resistance, changes in cerebral blood flow, and lowered levels of noradrenalin in central and peripheral nervous system tissue are just some among the important candidate mechanisms that may explain not only how diet and exercise may influence cognition but also how BP modulates their relationships, as well as how BP directly affects cognition.

Mediation regression analysis by Smith et al indicated that adjustment for BP does attenuate the relations between diet+exercise and cognition. Our personal view, reinforced by the Smith et al and McGuinness et al studies, is as follows. Treatment does not directly mitigate the effects of hypertension on cognition but affords protection against rise in BP over time and further brain injury. This is an arguable point subject to further investigation. Regardless of whether lowering of BP and improvement in cognition are simply coincidental phenomena, the Smith et al data strongly encourage consideration of diet combined with exercise as a means to protect and better serve our patients.

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References

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