Intensive intervention and cognitive impairment

Are lifestyle changes enough for a good brain?

Richard Camicioli, MDCM, FRCP(C)
Ira Drisoll, PhD

Correspondence to Dr. Camicioli: rcamicio@ualberta.ca

Neurology® 2017;88:1–2

The Look AHEAD (Action for Health in Diabetes) study examined how a lifestyle intervention (diet and exercise), compared to diabetes support and education, may help to improve function in a population at high risk for cognitive decline—people with excess weight or obesity and type 2 diabetes.[1] Lifestyle is a complex construct that includes behaviors such as cognitive and social engagement as well as diet choices and exercise. There is no clear consensus regarding the nature of the ideal choices and who gets to benefit by adhering. Much data regarding lifestyle come from observational studies, which by design cannot absolutely prove causation and might not motivate behavioral change. There are no proven pharmacologic interventions that prevent or treat cognitive decline, though modifiable risk factors might account for a substantial proportion of the risk for cognitive decline.[2]

Some recent epidemiologic studies suggest that dementia incidence may be decreasing, possibly due to better control of vascular risk factors and improved lifestyle in Western populations.[3,4] In contrast, a recent study suggested an increase in dementia incidence in the Netherlands.[5] The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) study, which targeted people at risk for cognitive decline, suggested that a multifaceted lifestyle intervention prevented cognitive decline.[6] Investment of resources may thus be best targeted to high-risk populations, who may be most likely to benefit. Diabetes and being overweight are acknowledged risk factors for cognitive decline and dementia worldwide.[7]

Overall, the Look AHEAD study suggests potential benefits for lower weight patients and possible harm in higher weight patients. Results of short-term follow-up and an imaging substudy were previously reported, and are consistent with the larger trial. There is some evidence that weight loss in midlife might be associated with an increase in dementia and dementia-related mortality, albeit at a cost of other health risk,[8] and lower BMI might be associated with increased amyloid burden.[9]

Does this study suggest that lifestyle interventions, diet and exercise in particular, are not worthwhile? While the intervention in the Look AHEAD study did not result in a reduced risk of cognitive decline, the study population is clearly defined as American patients with type 2 diabetes and who are overweight or obese, albeit with reasonable control of glucose, blood pressure, and lipids; it is unknown, therefore, whether we can generalize to other populations. Randomization in a clinical trial serves to balance known and unknown factors between groups. In the Look AHEAD cohort, while there were no major imbalances between groups when they were compared directly, there were some differences in baseline cognitive function, with more of the most obese patients in the lowest quartile of cognitive function at baseline. The intensity of the intervention that aimed to make people meet caloric and exercise targets decreased over the study, as did the resulting effects on weight and physical activity. Blinding of participants with behavioral interventions was not possible, though there was a comparison group. Assessment staff were blind to the participants' group and the measurements were objective.

An algorithmic approach was employed for classification of cognitive outcomes, using the Modified Mini-Mental Status Examination (3MS) to identify cognitive impairment and the Functional Assessment Questionnaire to identify functional problems. While the 3MS test is not highly sensitive to dementia, it is likely to identify clear-cut cases. Maintenance was not perfect; 26% of participants could not be followed up at 11 years and there were some differences in baseline characteristics between those who did and did not continue. This drop out weakens the power of the study to make confident conclusions.

The Baltimore Longitudinal Study of Aging (BLSA) suggests that obesity may be an important modifier of brain atrophy in individuals who are developing cognitive impairment and dementia, with little effect on structural brain integrity in older adults without dementia.[10] The prevalence of cognitive impairment and dementia was relatively low in the

See page XXX

From Medicine (Neurology) (R.C.), University of Alberta, Edmonton, Canada; and Psychology Department (I.D.), University of Wisconsin-Milwaukee.

Go to Neurology.org for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the editorial.

Look AHEAD sample and the sensitivity of global cognitive performance as an outcome simply may not be on par with measures of brain integrity closer to a neural substrate. Moreover, the BLSA also suggests that a different pattern of results can emerge from the same data based on statistical modeling and whether cutoff points were used to define obesity and overweight or whether trajectories of change were examined across a range of values; thus, the choice of statistical models may be yet another consideration in evaluating the generalizability of the results.

Why should this be of interest to neurologists and other clinicians managing people with cognitive decline? Neurologists are often involved in the care of patients who have the consequences of diabetes, overweight, and obesity, including neuropathy and vascular events. Similarly, cognitive decline is common in people with such risk factors. The prevalence of diabetes in adults is high: 9.1% of the US population and 25.9% of seniors over age 65 years (who.int/diabetes/global-report/en/) have diabetes, with overweight (70%) and obesity (35%) as common coexisting factors. Obesity may potentiate the effect of diabetes in the development of neurologic complications.

The limitations of this study do not negate the possibility that earlier or longer-term intervention might provide important benefits or that there may be benefits as the study population ages further. The interaction suggesting that the most obese individuals might do worse and that the lower weight group did better also cannot be concluded with confidence. It remains to be seen whether different types of lifestyle interventions (such as different types or duration of exercise, for example) confer similar benefits or the lack thereof. Nonetheless, the authors should be applauded for conducting a challenging study that might provide a basis for future work. To be practical, such interventions should be readily incorporated into everyday life—a major challenge.

STUDY FUNDING

No targeted funding reported.

DISCLOSURE

The authors report no disclosures relevant to the manuscript. Go to Neurology.org for full disclosures.

REFERENCES

1. Espeland MA, Luchsinger JA, Baker LD, et al. Effect of a long-term intensive lifestyle intervention on prevalence of cognitive impairment. Neurology 2017;88:xx–xx.
2. Norton S, Matthews FE, Barnes DE, Yaffe K, Brayne C. Potential for primary prevention of Alzheimer's disease: an analysis of population-based data. Lancet Neurol 2014;13:788–794.
3. Wu YT, Fratiglioni L, Matthews FE, et al. Dementia in western Europe: epidemiological evidence and implications for policy making. Lancet Neurol 2016;15:116–124.
4. Satizabal CL, Beiser AS, Chouraki V, et al. Incidence of dementia over three decades in the Framingham Heart Study. N Engl J Med 2016;374:523–532.
5. van Bussel EF, Richard E, Arts DL, et al. Dementia incidence trend over 1992–2014 in The Netherlands: analysis of primary care data. PLoS Med 2017;14:e1002235.
6. Ngandu T, Lehtisalo J, Solomon A, et al. A 2-year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomized controlled trial. Lancet 2015;385:2255–2263.
7. Ng TP, Feng L, Nyunt MS, et al. Metabolic syndrome and the risk of mild cognitive impairment and progression to dementia: follow-up of the Singapore Longitudinal Ageing Study Cohort. JAMA Neurol 2016;73:456–463.
8. Strand BH, Wills AK, Langballe EM, et al. Weight change in midlife and risk of mortality from dementia up to 35 years later. J Gerontol A Biol Sci Med Sci Epub 2016 Aug 10.
9. Hsu DC, Mormino EC, Schultz AP, et al. Harvard Aging Brain Study: lower late-life body-mass index is associated with higher cortical amyloid burden in clinically normal elderly. J Alzheimers Dis 2016;53:1097–1105.
10. Driscoll I, Beydoun MA, An Y, et al. Midlife obesity and trajectories of brain volume changes in older adults. Hum Brain Mapp 2012;33:2204–2210.