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Long-term impact of intensive lifestyle intervention on cognitive function assessed with the National Institutes of Health Toolbox: The Look AHEAD study

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Abstract

Introduction: This study sought to determine whether 10 years of assignment to intensive lifestyle intervention (ILI) relative to diabetes support and education leads to better cognition. We examine intervention effects overall and among clinical subgroups, and report correlations between computer-administered and interviewer-administered cognitive batteries.

Methods: The Action for Health in Diabetes (Look AHEAD) was a 16-site randomized controlled trial with overweight/obese individuals (aged 45–76) who had type 2 diabetes. The NIH Toolbox Cognition Battery tests developed to measure cognition across the lifespan were used to evaluate cognition. Results were compared with standard paper-and-pencil tests. The Toolbox and paper-and-pencil tests were administered an average of 10.9 years after randomization to 1002 participants.

Results: Toolbox measures significantly correlated with interviewer-administered measures, with the strongest correlations between the Toolbox Fluid Cognition Composite and Trails B ($r = -0.64$, $P < .0001$) and Digit Symbol Coding ($r = 0.63$, $P < .0001$), and between the Toolbox Dimensional Change Card Sort ($r = 0.55$, $P < .0001$) and the Digit Symbol Coding test. Overall, ILI and diabetes support and education groups had similar adjusted mean cognitive outcomes ($P > .05$ for all). Subgroup analyses identified different intervention effects within baseline body mass index groups for Picture Sequence Memory ($P = .01$), within baseline cardiovascular disease groups for Picture Vocabulary ($P = .01$) and Fluid Cognition Composite ($P = .02$) measures, and within baseline age groups for Picture Vocabulary ($P = .02$).

Discussion: Correlations between Toolbox and interviewer-administered outcomes provide a measure of internal validity. Findings suggest no overall effect of the intervention on cognition and

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that an ILI resulting in weight loss may have negative implications for cognition in individuals aged ≥60, with previous history of cardiovascular disease, and those with body mass index ≥40.

Keywords: Diabetes mellitus; Obesity; Cognition; Body mass index; Randomized controlled trial; Weight loss; Neuropsychological tests; Aged

1. Introduction

Midlife obesity is associated with an increased risk for cognitive deficits in later life [1–3], whereas midlife physical activity is associated with less cognitive decline [4,5]. Behavioral interventions targeting weight loss and increased physical activity may reduce risk of cognitive impairment [6,7]. However, evidence that weight loss will prevent cognitive decline is lacking. Moreover, late life weight loss can be a sign of increased risk for dementia [1], and midlife weight change in either direction may be associated with greater risk for dementia later in life [8,9].

Type 2 diabetes mellitus is also associated with increased risk for cognitive deficits in later life [10–12]. Many pathologic processes may lead to this outcome, including reduced vascular function, increased inflammation, impaired glucose metabolism, and concomitant disorders, such as hypertension and depression [13]. Weight loss through reduced caloric intake and increased physical activity has the potential to improve each of these conditions [13,14]. Adults with type 2 diabetes may thus be particularly sensitive to any cognitive benefits of behavioral intervention for weight loss.

The Action for Health in Diabetes (Look AHEAD) study was a randomized controlled clinical trial that compared 10 years of intensive lifestyle intervention (ILI) targeting weight loss and increased physical activity to a diabetes support and education (DSE) control among overweight or obese adults with type 2 diabetes [14,15]. Although no cognitive assessment was conducted at baseline, earlier cross-sectional analyses of Look AHEAD participants at year 8 showed that there were no differences in overall cognitive function between the ILI and the DSE based on a standardized interviewer-administered battery of cognitive tests [16,17].

The computer-administered NIH Cognitive Toolbox has been designed to provide greater precision in cognitive assessments, particularly for domains related to processing speed and executive function [18,19]. There are three primary objectives of this report. We examine whether 10 years of random assignment to ILI relative to a control condition leads to better performance on cognitive measures. We examine the consistency of any intervention effects among previously examined baseline clinical subgroups in Look AHEAD including those with higher body mass index (BMI) and previous history of cardiovascular disease (CVD) [17]. We also report correlations between computer-administered and interviewer-administered cognitive test batteries to provide support for the use of the NIH Toolbox in cognitive research.

2. Methods

The design and methods of Look AHEAD have been previously described [14]. Look AHEAD was a 16-site randomized controlled trial that recruited 5145 individuals (from 2001 to 2004) who were overweight or obese and had type 2 diabetes. Participants were aged 45 to 76 years and had a BMI of >25 kg/m^2 (or >27 kg/m^2 if on insulin), glycated hemoglobin (HbA1c) <11%, systolic/diastolic blood pressure <160/<100 mm Hg, and triglycerides <600 mg/dL. All participants completed a maximal treadmill test. All Participants provided informed consent and were randomly assigned (1:1) to ILI or DSE. Local institutional review boards approved the protocol. The present study involved six Look AHEAD sites (including Baton Rouge, Denver, Memphis, Philadelphia, Pittsburgh, and Providence) that implemented two ancillary studies, the Look AHEAD Movement and Memory study and the Look AHEAD Brain study. All active participants at these sites who were willing to participate and free of contraindications (e.g., for magnetic resonance imaging [MRI] studies) were invited to participate. Although there were no baseline cognitive assessments in Look AHEAD, both of these ancillary studies administered paper-and-pencil tests in addition to the NIH Toolbox cognitive assessments an average of 10.9 years after randomization. The study sample comprised 1002 participants at those sites who completed both the NIH Toolbox and the face-to-face cognitive assessment (described subsequently). We attempted to administer both batteries on the same day whenever possible.

2.1. Interventions

ILI participants received dietary and physical activity goals for weight loss, and were seen weekly by study staff for 6 months and subsequently three times per month for 6 months, using a combination of group and individual contact. Thereafter, ILI participants were offered two contacts per month plus optional group meetings and refreshers, and national campaign materials [15]. DSE participants were invited to attend three group sessions per year for the first 4 years, and one session per year thereafter [14].

In September 2012, the study's sponsor (National Institute of Diabetes and Digestive and Kidney Diseases) terminated interventions based on recommendations from the