Effects of Exercise and Nutrition on Memory in Japanese Americans With Impaired Glucose Tolerance

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Type 2 diabetes, impaired glucose tolerance (IGT), and associated hyperinsulinemia increase the risk for impaired verbal memory (1–3). In rodents, insulin resistance adversely affects brain structures that support memory (4). In humans, pharmacologic management of diabetes improves cognitive functioning (5,6). Weight loss and exercise decrease the incidence of diabetes (7,8). This study examined whether endurance exercise and dietary fat restriction would improve cognition in Japanese American adults who have a high risk for IGT and type 2 diabetes (9).

RESEARCH DESIGN AND METHODS

— Adults with IGT were recruited from the Japanese American Community Diabetes Study. Screening and diagnostic procedures have been described previously (10). Participants (15 active and 13 control) completed cognitive testing at baseline and at 6 and 12 months. Treatment was randomly assigned, and groups were equivalent with respect to baseline age ([mean ± SD] active 58.0 ± 9.7 and control 60.6 ± 9.0 years), BMI (active 24.7 ± 3.2 and control 26.7 ± 4.3 kg/m^2), $V\text{O}_{2max}$ (active 29.5 ± 7.1 and control 27.4 ± 5.6 ml · kg^{-1} · min^{-1}), and 2-h oral glucose tolerance test (OGTT) glucose levels (active 9.4 ± 1.1 and control 9.4 ± 0.9 mmol/l).

Active participants followed an American Heart Association step 2 eucaloric diet (total calories <30% fat, <7% saturated fat, 55% carbohydrate, and 15% protein). An exercise physiologist supervised walking or jogging on a treadmill three times weekly for 1 h. Over 12 weeks, effort was increased from 50% of heart rate reserve (0.5 × [maximal heart rate − resting heart rate] + resting heart rate) to 70%. Control participants performed supervised stretching three times weekly for 1 h and followed an American Heart Association step 1 diet (total calories 30% fat, 50% carbohydrate, and 20% protein). After 6 months, exercise and diet were home based without supervision.

$V\text{O}_{2max}$ and computed tomography intra-abdominal fat (IAF) measures were acquired at baseline and 6 months. BMI and OGTT were acquired at baseline and at 6 and 12 months.

Cognitive testing included measures of memory (story recall and Benton Visual Retention Test) and selective attention (Trail Making Test and Stroop interference test). Equivalent forms were administered in counterbalanced order. Story recall consisted of two brief narratives, with recall elicited immediately after each story presentation and after a 10-min delay. We followed standard administration for other cognitive measures (11).

Statistical analyses

Baseline differences were evaluated with χ^2 and *t* tests. Treatment effects were evaluated with repeated-measures ANCOVA with time of testing (baseline, month 6, and month 12) as a within-subject factor and group (active and control) as a between-subject factor. For story recall, delay (immediate recall and delayed recall) was a within-subject factor. Change in IAF volume (6-month values adjusted for baseline) was included as a covariate because of its well-established role in exercise-mediated changes in insulin sensitivity. Effect sizes were calculated as f^2 (small, medium, and large = 0.02, 0.15, and 0.35, respectively).

RESULTS

— At month 6, we observed treatment-related improvements in $V\text{O}_{2max}$ [active 33.8 ± 6.3 and control 27.3 ± 5.5 ml · kg^{-1} · min^{-1}; $F(1,26) = 10.10$, $P = 0.004$, $f^2 = 0.39$] and BMI [active 23.6 ± 2.9 and control 26.4 ± 4.1 kg/m^2; $F(1,26) = 7.18$, $P = 0.013$, $f^2 = 0.28$]. This effect did not persist at month 12 for BMI. After 6 months, story recall performance was related to treatment assignment, delay, and change in IAF [$F(1,24) = 7.63$, $P = 0.011$, $f^2 = 0.32$] (Fig. 1*A*). For the active group, the relative amount of information retained following a delay increased, independent of change in IAF (Fig. 1*A*) [$F(1,13) = 9.13$, $P = 0.010$, $f^2 = 0.70$]. For the control group, the relative amount of information retained over a delay increased as IAF decreased ($r = -0.62$, $P = 0.024$), showing that IAF loss was associated with improved memory. No story recall effects were observed at month 12 for either group. In the active group, this may reflect suboptimal compliance during self-monitoring, since BMI increased between months 6 and 12. No effects were observed for other cognitive measures at 6 or 12 months.

Given that hyperinsulinemia has been associated with memory impairment, we next examined the relationship of delayed

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Abbreviations: IAF, intra-abdominal fat; IGT, impaired glucose tolerance; OGTT, oral glucose tolerance test.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

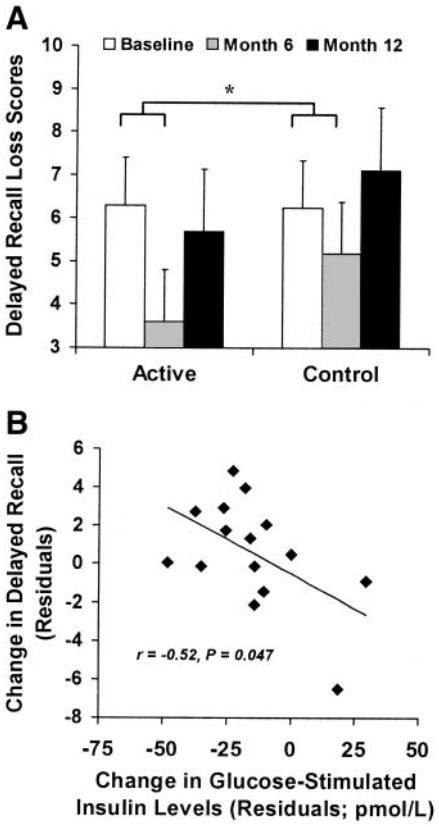

Figure 1—*Lifestyle modification and story recall.* A*: Delayed recall loss scores (immediate recall – delayed recall) reflect the loss of information during a delay. Therefore, a lower score is indicative of greater retention over time. At month 6, the active treatment group lost significantly less information due to a delay* (P = *0.01*). B*: Delayed recall residuals reflect 6-month delayed recall adjusted for baseline immediate recall, baseline delayed recall, and 6-month immediate recall. Insulin residuals (2-h postglucose during OGTT) reflect 6-month plasma insulin levels adjusted for baseline. For the active treatment group, delayed recall improved as 120-min glucose-stimulated plasma insulin levels decreased, suggesting that reduced insulin elevations are associated with better delayed memory.*

recall to glucose-stimulated plasma insulin levels. Adjusted 2-h OGTT insulin levels (residual score: month 6 adjusted for baseline levels) were significantly lower for active than for control participants [active -107 ± 36 and control 123 ± 92 pmol/l; $t(26) = -2.44$, $P = 0.0216$]. Lower adjusted insulin levels, signifying treatment-related decreases, were correlated with greater increases in delayed recall for the active group (Fig. 1*B*) ($r = -0.52$, $P = 0.047$) but not for the control group ($r = 0.02$, $P = 0.946$).

CONCLUSIONS — Endurance exercise and dietary fat restriction improved metabolic parameters and verbal memory. These lifestyle interventions likely influence memory through several central nervous system mechanisms, related in part to improved insulin regulation (12). In the present study, the relative amount of story information retained after a delay increased as glucose-stimulated insulin levels decreased in the active treatment group. We note that our sample was small and that replication in a larger sample would strengthen this finding. Furthermore, diet and exercise may influence neurotrophic factors and plasticity in brain regions directly relevant to memory. In rats, exercise increases hippocampal brain-derived neurotrophic factor protein and mRNA levels and enhances cell proliferation in the dentate gyrus (13).

In conclusion, exercise and nutrition may facilitate memory for older adults at high risk for developing type 2 diabetes. Thus, lifestyle modification constitutes an effective and accessible strategy to improve quality of life for older adults by preventing type 2 diabetes and preserving cognitive functions.

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