Abstract

Introduction: Association between healthy diet and better cognition is well established, but evidence is limited to evaluate the effect of dietary changes adopted in older age.

Methods: We investigated the role of dietary changes in the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) with 1260 at-risk participants (60–77 years) who were randomized to intensive multidomain intervention (including dietary counseling) or regular health advice for 2 years. Parallel process latent growth curves of adherence to dietary recommendations and cognitive performance were analyzed.

Results: Adherence to healthy diet at baseline predicted improvement in global cognition, regardless of intervention allocation ($P = .003$). Dietary improvement was associated with beneficial changes in executive function, especially in the intervention group ($P = .008$; $P = .051$ for groups combined).

Discussion: Dietary changes initiated during the intervention were related to changes in executive function in 2 years. Long-term diet appeared more influential for global cognition.

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Keywords: Diet; Cognitive performance; Prevention; Older adults; Growth curve analysis
1. Introduction

Numerous observational studies have linked healthier dietary patterns such as the Mediterranean diet with less cognitive decline or lower risk for Alzheimer’s disease [1–3]. Also protective role of many foods and nutrients has been identified, for example, fish and fish-derived fatty acids, vegetables, and fruits [4–6]. Evidence linking overall healthy diet with better brain health appears convincing, but most studies have been cross-sectional, or they have measured subsequent cognitive performance following a single dietary evaluation. Data relating dietary changes to cognitive changes in older age are scarce, hindering possibilities to evaluate if dietary modification actually is an effective way to delay cognitive decline.

Early nutritional interventions in dementia prevention most often tested dietary supplements, and they had virtually no effects [7]. Food-based dietary intervention trials primarily targeting cognitive performance are lacking, but secondary analyses of trials that comprised dietary guidance suggest cognitive benefits [8,9]. Furthermore, modifying a single factor like one nutrient might be insufficient, and multidomain interventions are suggested to tackle the dementia epidemic [10].

The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) was the first study to demonstrate beneficial effect of a 2-year multidomain intervention for cognitive performance [11], in a heterogeneous population of older adults [12]. The dietary component of the FINGER intervention also proved successful in promoting healthy dietary changes [13]. Here, our aim is to investigate how dietary changes are associated with cognitive changes over 2 years in both the multidomain intervention group and in the control group.

2. Methods

2.1. Study design and participants

Participants in the FINGER comprise a population-based sample identified from earlier national health surveys in six areas in Finland. They were invited based on age (60–77 years at the beginning of the study) and elevated risk for dementia identified with a risk score [14]. Cognitive performance measured with the Consortium to Establish a Registry for Alzheimer’s Disease (CERAD) neuropsychological test battery had to be at the mean level or slightly lower than expected for age at the screening visit. The sample was described in detail previously together with description of all interventions [15,16]. Flowchart is included as Supplementary Fig. 1.

Participants were randomized to multidomain lifestyle intervention or control group (1:1). Before randomization, all participants received an oral mini-intervention from the study nurse, and after randomization, the intervention group was offered dietary counseling, physical exercise program, cognitive training, and management of metabolic and vascular risk factors for 2 years. The control group received regular health advice.

2.2. Dietary intervention

A detailed dietary intervention protocol has been published [13]. Briefly, goals of the intervention were based on the Finnish nutrition recommendations [17], which were translated into food consumption goals comprising consumption of fruits and vegetables above 400 g/d; whole-grain cereal products instead of refined ones; low-fat options in milk and meat products; sucrose intake to less than 50 g/day; vegetable margarine and rapeseed oil instead of butter or butter-oil mixtures; and fish consumption of at least two portions per week. Need for weight loss was always considered individually after taking into account BMI, health status, age, and diet of the participant. Minimum of 10 μg supplemental vitamin D was recommended daily throughout the year for all participants (including the control group) according to national recommendations.

Dietary intervention was combination of individual counseling (3 sessions) and group meetings (6 sessions), mainly during the first year. At the individual sessions, the study nutritionist considered personal adjustments of the individuals’ diet and facilitated individual goal setting. During group sessions food-related themes were discussed, and peer support and group activities were exploited to facilitate lifestyle changes. Examples of the themes include, for example, how to read and interpret package labels, how to modify recipes into a healthier direction, or how to deal with cravings.

2.3. Other components of multi-intervention

In addition to dietary intervention, everyone in the intervention group was offered also physical exercise program, cognitive training, and management of metabolic and vascular risk factors [15]. Exercise training program consisted of individually tailored programs for progressive muscle strength training (1–3 times per week) and aerobic exercise (2–5 times per week), and exercises to improve postural balance. Cognitive training included group sessions (6 sessions) and individual computer-based training sessions (2–3 times per week, total of 144 sessions). Management of metabolic and vascular risk factors was based on national guidelines and included discussions with a study nurse and a physician and feedback on personal risk factors. Study physicians did not prescribe medications but recommended contact to participants’ own physician if needed.

The control group received regular health advice and feedback on their vascular risk factors measured during study visits. They also met the study physician in the beginning and at the end of the study. Group allocation was not
actively communicated to participants, and opportunities for between-group interactions were restricted as much as possible.

This study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures were approved by the Coordinating Ethics Committee of the Hospital District of Helsinki and Uusimaa, and written informed consent was obtained from all subjects. This trial is registered with ClinicalTrials.gov (number NCT01041989).

2.4. Cognition assessment

Trained study psychologists performed an extended and modified version of the neuropsychological test battery annually [18]. A composite score reflecting global cognition was calculated as an average of 14 tests standardized to Z scores using baseline mean and SD, higher scores indicating better performance (opposite numbers were used when better results were indicated by lower scores such as in tests measuring time). Secondary outcomes included cognitive domain Z scores for executive function (Category fluency test, Digit span, Concept shifting test condition C, Trail making test shifting score B−A, and Stroop test interference score); processing speed (Letter digit substitution test, Concept shifting test condition A and Stroop test condition 2); and memory domain (Visual paired associates test, immediate and delayed recall; Logical memory immediate and delayed recall from Wechsler Memory Scale-Revised/III; and word list learning and delayed recall).

2.5. Diet assessment

Participants completed 3-day food records close to annual visits. They received written instructions to record all foods and beverages they had consumed, including type, brand, and preparation method, and amount with household measures. Trained nutritionists recorded dietary data with a software program developed at the National Institute for Health and Welfare, and data were analyzed with the food composition database Fineli [19] (www.fineli.fi). The program allows modification of standard recipes, and personal recipes were used when available (e.g., the type of fat used in cooking). Nutrient intakes only from food were included in these analyses.

Main outcome of the dietary intervention was a composite score measuring adherence to national dietary recommendations that were also targets of the dietary intervention [13]. The adherence score reflects the dietary intervention targets with nine distinct goals: proportion of energy from saturated plus trans fatty acids <10% of total energy intake (E%), polysaturated fatty acids 5–10E%, sucrose <10E%, protein 10–20 E%, alcohol <5 E%, intake of dietary fiber >3 g/MJ of energy, consumption of vegetables >200 g/d, fruit and berries >200 g/d, and fish (any consumption during 3 days). Participants received 1 point for each goal when achieving the predefined level of intake, and zero otherwise (range 0–9).

2.6. Covariates

Annual study visit comprised anthropometric measurements, blood samples, and questionnaires about background, lifestyles, and general health. Education data were not available for 14 participants, and mean value (9 years of education) was assigned to them. Participants reported physical activity with a questionnaire covering previous 12 months, from which we calculated the average frequency of moderate to vigorous activities including sedate walking, brisk walking, Nordic walking, jogging, cross-country skiing, cycling, swimming, skating, rowing, golf, ball games, dancing, bowling, aerobics, gymnastics, and exercise at the gym (duration >10 minutes at once). Cognitive and social activity (referred to as cognitive activity) was reported with a 12-question questionnaire, and the total amount of activities per week was calculated including reading, cross-words, writing, games, listening or playing music, communal activities or participation in societies, studying, handicrafts, gardening, cleaning, baby-sitting, and voluntary work. Average activity during 2 years was calculated for physical and cognitive activity, respectively, and categorized at tertiles. Those with no physical or cognitive activity data from any round were excluded from the adjusted analysis (model B; n = 19 for physical and n = 8 for cognitive activity, n = 24 for either one).

2.7. Statistical methods

Background characteristics between groups and participants versus nonparticipants were compared using $\chi^2$ or t-test as appropriate.

We applied parallel process latent growth curve analysis for estimating the association between diet and cognition throughout the study [20,21]. General level (latent intercept) and change (latent slope) of both diet and cognition over the study period (baseline, the 1st and the 2nd year) were estimated, and their associations were investigated using structural equation modeling. Graphical presentation of the model is included as Supplementary Fig. 2. Based on better model fit in univariate models, adjustments for age and education were applied for latent variables, and for sex and study center for observed variables (model A). The second model additionally included average physical and cognitive activities as covariates for observed cognition and diet scores (model B). Latent intercept, i.e., the general level, is referred to as the baseline level in the text and tables, and latent slope as the change.

Analyses were initiated with hypothetical full path model (model 0) where all parameters were estimated for the intervention and control groups as unequal, as if there were two separate models. Parameters were constrained as equal one
at a time, each model tested against the full model as described in Supplement 1. If all constraints were allowed, the final model treated groups as equal, as if there was only one group (model 6). We also present an intermediate model without any constrains on paths between the latent variables (model 3), to describe associations between diet and cognition in the two groups separately, which is of interest in the intervention setting.

Main analyses included those with baseline and at least one of the follow-up measures available for both cognition and diet (modified intention-to-treat approach). Sensitivity analyses were run for all participants with at least one measurement for both and for those with all three measures available (complete case approach). All analyses were executed with Stata SE 15.1 for Windows (StataCorp LP).

### 3. Results

Among the 1260 randomized participants, applicable dietary data were available for 1163; cognitive data for 1190; and both for 1155 participants (modified intention-to-treat population). Baseline characteristics of intervention and control groups were similar (Table 1). Compared with the whole sample, those included in the modified intention-to-treat approach had higher baseline cognitive performance ($P = .020$) and indication of healthier baseline diet ($P = .065$). As previously reported, cognitive performance among all participants improved, but in the intervention group, improvement was significantly greater in global cognition and in executive function and processing speed domains [11]. Dietary quality remained unchanged in the control group over 2 years, whereas in the intervention group, it improved [13].

#### 3.1. Diet and global cognition

Baseline dietary adherence score and global cognitive performance were nonassociated, but in both intervention and control groups, healthier baseline diet predicted more improvement in global cognition over 2 years (Table 2). Changes in dietary adherence score were not related to changes in global cognition during 2 years.

#### 3.2. Diet and cognitive domains

Association between diet and cognition varied across cognitive domains (Table 3). Healthier baseline diet predicted favorable change in executive function in the control group (model 3), but not when intervention and control groups were combined (model 6). Changes in diet had a

<table>
<thead>
<tr>
<th>Path</th>
<th>Model A</th>
<th>Model B</th>
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<tr>
<td></td>
<td>Path coefficient (Standard error)</td>
<td>$P$ value</td>
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<tr>
<td>Global cognition</td>
<td></td>
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<td>Baseline diet $\rightarrow$ baseline cognition</td>
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<tr>
<td>Intervention</td>
<td>$0.005 (0.018)$</td>
<td>.780</td>
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<tr>
<td>Control</td>
<td>$0.011 (0.018)$</td>
<td>.530</td>
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<tr>
<td>Combined</td>
<td>$0.011 (0.018)$</td>
<td>.561</td>
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<tr>
<td>Baseline diet $\rightarrow$ cognitive change</td>
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<tr>
<td>Intervention</td>
<td>$0.046 (0.019)$</td>
<td>.014</td>
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<tr>
<td>Control</td>
<td>$0.051 (0.019)$</td>
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<tr>
<td>Combined</td>
<td>$0.046 (0.016)$</td>
<td>.003</td>
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<tr>
<td>Dietary change $\rightarrow$ cognitive change</td>
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<tr>
<td>Intervention</td>
<td>$0.125 (0.094)$</td>
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<tr>
<td>Control</td>
<td>$-0.043 (0.113)$</td>
<td>.707</td>
</tr>
<tr>
<td>Combined</td>
<td>$0.052 (0.102)$</td>
<td>.608</td>
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NOTE. Baseline refers to latent intercept, and change refers to latent slope estimated with parallel growth curves.

*Model A adjusted for age, education (latent variables), and study area and sex (observed variables).

*Model B additionally adjusted for physical and cognitive activities (observed variables).

*Model 3 where all model parameters except from associations between latent variables are estimated as equal between groups (see Supplement 1.2. for details).

*Model 6 where all parameters are estimated as equal, as if there was only one group of participants (see Supplement 1.2. for details).
linear association with changes in executive function in the intervention group (model 3). This association was borderline significant in analysis with intervention and control groups combined (model 6).

Healthier baseline diet predicted improvements in memory domain in the intervention group (model 3) and in analysis with intervention and control groups combined (model 6). Processing speed showed no associations with cognition in the main analysis, and none of the cognitive domains showed cross-sectional association with diet at baseline.

3.3. Additional analyses

When path between change in diet and change in cognition was dropped from the model (model 7, intervention and control combined), path between baseline diet and change in cognition became significant also in executive function (path coefficient $0.053; P = .004$) and processing speed (path coefficient $0.043; P = .022$). Results were similar with and without adjustment for physical and cognitive activities, but model fit deteriorated in memory domain (still acceptable with Root Mean Square Error of
Approximation < 0.05 and Comparative Fit Index > 0.998). Sensitivity analyses with all participants or complete cases showed virtually the same results as presented in Tables 2 and 3 (results not shown).

Model comparison for the parallel process latent growth curve model appeared best with all associations estimated as equal between groups for all outcomes (Supplementary Tables 1 and 3). Differences between models were small for all cognitive outcomes, as shown for global cognition in Supplementary Table 2, and fit of all models was good (Supplementary Tables 1 and 3).

4. Discussion

These results show that adherence to dietary guidelines predicts subsequent improvement in global cognitive performance among older adults. Improvement in diet during the intervention is associated with favorable changes in executive function over 2 years, but not with changes in memory performance or processing speed, and consequently not with changes in global cognition.

Based on model comparison, the associations between diet and cognition were similar in intervention and control groups. Although similar effects can be expected for some dietary factors with or without an intervention, there were on average no dietary changes in the control group and diet improved only in the intervention group [13]. Therefore, the observed association between changes in diet and executive function in the intervention group indicates that cognitive benefits require intensive dietary changes.

Although better baseline diet predicted more cognitive improvement in all cognitive domains, changes in diet were only related to changes in executive function. To influence other domains, alternative dietary approaches or longer follow-up time may be needed. Executive functions could be more sensitive for lifestyle modification because they are suggested as one of the first cognitive changes observed in preclinical dementia [22], even before memory symptoms. The executive function domain score included tests measuring cognitive flexibility, complex attention, and working memory, which rely on frontal lobe functions and decline first also in normal aging.

Impairments in executive functions are also related to vascular cognitive impairment [23]. The national dietary recommendations underlying our diet adherence score are mainly based on evidence linking diet to cardiovascular health, and hence, the effect of dietary changes for changes in executive function could be mediated through vascular factors.

To our knowledge, this is the first study relating dietary changes during an intervention to simultaneous changes in cognition. In fact, dietary changes in relation to changes in any outcomes have rarely been investigated in epidemiological studies. Results from our control group provide a possible explanation for lack of such studies: without an intervention, dietary changes are likely to be so small that measuring general level is preferable. Still, understanding the effects of long-term diet versus dietary changes in older age in relation to health outcomes is crucial for planning evidence-based health promotion practices targeted for aging populations.

Previous evidence of the effect of dietary interventions for cognitive outcomes comes mainly from secondary analyses of previous trials. A cardiovascular disease prevention trial has suggested cognitive benefit of Mediterranean guidance supplemented with extra-virgin olive oil after 4 years [8], or with either extra-virgin olive oil or nuts after 6 years [24]. Also a 4-month dietary approach to stop hypertension (DASH) intervention improved psychomotor speed [9], yet it remains unclear if weight loss and blood pressure mediated these benefits. One small Mediterranean diet trial that primarily targeted cognitive performance reported no difference between groups after 6 months [25]. Also a multidomain trial with dietary advice showed no effect on cognition with multidomain intervention alone or in combination with omega-3 supplement in 3 years [26]. This lifestyle intervention was less intensive than in the FINGER. A pilot trial of goal setting for exercise and diet suggested cognitive benefits after 1 year [27], and a trial testing medical food Souvenaid reported better functional status in prodromal Alzheimer’s disease over 2 years [28]. Smaller-scale studies show promising but weak evidence of dietary intervention efficacy in prevention of cognitive impairment [29].

Our results showing association between composite dietary score, founded on national dietary recommendations, and subsequent changes in cognitive performance are in accordance with observational studies relating a healthy diet measured with indexes such as Mediterranean diet [2], DASH [30], both of them [31,32], and Healthy Eating Index [33] with better prospective changes in cognition. Also the recently introduced brain-specific dietary index Mediterranean-Dietary Approaches to Stop Hypertension (MIND) has been associated with less cognitive decline over time [29,34]. Many items such as increased intake of vegetables, fruits, and fish are common to all these indexes, and quality of dietary fat and carbohydrate are included too either as consumption of foods, such as, butter, red meat, and whole grain, or as nutrients yielded from them.

Contradictory to our findings, most previous prospective studies reported also a cross-sectional association at baseline. Lack of such association in our study may be due to participant selection: during screening process, those with either low or high cognitive performance were excluded, and hypothetically, they could also have been those with extreme diet qualities. Furthermore, in an older population at risk for dementia, some participants are likely to have underlying neurodegenerative changes (preclinical dementia) that may confound cross-sectional relationships, as diet may have changed as a consequence of the disease process and before manifestation of cognitive symptoms. For example, intakes of fish, fruits, and vegetables have been shown to decrease before dementia diagnosis, which suggests reverse causality [35].
The strengths of this study include population-driven sample, well-described population, detailed dietary data, comprehensive cognitive assessment, low dropout rate, and sophisticated statistical methods. As limitations of this study, we must first address that association between two time-dependent variables and changes in them is complicated and with only three measurements statistical power may be limited to detect significant associations. Two years is a relatively short period of time; and some associations could require latency period, and analysis of simultaneous changes would not be optimal. Second, the multidomain nature of the intervention can never be fully accounted for in analyses focusing on single exposure of interest, and speculation of the role of other lifestyle changes remains. We adjusted for self-reported physical and cognitive activities, but not for actual intervention participation, which can only be measured for the intervention group. Intervention participation may also affect self-reports of diet [36]. Third, the prespecified, guideline-based diet score used in our analyses may not be optimal for brain health in terms of chosen components and especially the cutoffs that were dichotomous and hence insensitive for change.

We conclude that improvements in diet in old age appear beneficial especially for executive function. The clear protective effect of healthy baseline diet for the subsequent changes in cognition underlines the importance of healthy diet throughout life. Other studies clarifying the role of both long-term diet and dietary changes in older age would be of utmost importance.

Acknowledgments

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Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jalz.2018.10.001.

RESEARCH IN CONTEXT

1. Systematic review: The authors searched PubMed for studies that investigated dietary patterns and changes in cognitive performance in clinical trials or in prospective observational studies. Association between healthy dietary patterns and less cognitive decline appears relatively well established, but no observational studies have measured dietary changes over time. Secondary analyses of a few trials have suggested benefit of dietary interventions, but evidence is inconclusive. These studies are appropriately cited in the article.

2. Interpretation: Our findings support the existing data linking healthy dietary patterns with more favorable cognitive changes. The findings relating dietary changes over 2 years with simultaneous changes in executive function are novel and suggest that dietary improvement in older age is beneficial for brain health.

3. Future directions: Our results indicate that dietary intervention contributes to the beneficial cognitive effect of multidomain intervention in a population of older adults at risk of dementia. Future lifestyle intervention trials should include longer-term dietary interventions and collect dietary intake data to better identify dietary factors to focus on in older age, compared with those that would require intervention already at midlife.

References


