Sodium intake and physical activity impact cognitive maintenance in older adults: the NuAge Study

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Abstract

This study examines the association between sodium intake and its interaction with physical activity on cognitive function over 3 years in older adults residing in Québec, Canada. We analyzed a subgroup from the NuAge cohort (aged 67–84 years) with nutrient intake data, including sodium, from a food frequency questionnaire administered at baseline. Baseline physical activity was assessed using the Physical Activity Scale for the Elderly (PASE; high-low). Modified Mini Mental State Examination (3MS) was administered at baseline and annually for 3 additional years. Controlling for age, sex, education, waist circumference, diabetes, and dietary intakes, analyses showed an association between sodium intake and cognitive change over time in the low PASE group only. Specifically, in the low PASE group, elders in the low sodium intake tertile displayed better cognitive performance over time (mean decline in 3MS over years: mean [M] / H11005/H11002 0.57, standard error [SE] / H11005 0.002) compared with the highest (M / H11005/H11002 1.72, SE / H11005 0.01) and mid sodium intake (M / H11005/H11002 2.07, SE / H11005 0.01) groups. This finding may have significant public health implications, emphasizing the importance of addressing multiple lifestyle factors rather than a single domain effect on brain health.

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1. Introduction

Sodium intake is of great interest due to its association with blood pressure regulation and heart disease. Heart disease is a major cause of mortality and disability, especially in individuals 60 years and older (Mathers and Loncar, 2006; Woloshin et al., 2008). Animal and human studies have shown that high sodium intake is associated with increased blood pressure and cardiovascular disease (Cook, 2008; Denton et al., 1995; Stamler, 1997). Based on robust findings, national and international groups, including the World Health Organization (WHO), have set out to promote reductions in sodium intake at the population level to reduce the incidence of cardiovascular disease (Institute of Medicine, 2010; Minister of Health, 2007; WHO, 2007).

While lowering sodium consumption is associated with reduced blood pressure and risk of heart disease (Cutler, 1991), less is known about the effect of sodium intake on cognitive function. With population aging, there is both a rise in cardiovascular events and a projected expansion of dementia cases in late life (Brookmeyer et al., 1998). Furthermore, risk factors for cardiovascular disease, including hypertension, are also common risk factors for dementia...
Hypertension at midlife is reportedly associated with worse cognitive function in late life (Kloppenborg et al., 2008). Studies show that hypertension may mediate adverse effects on brain function through a number of mechanisms, including altered cerebral endothelium, vascular remodeling, impaired cerebral autoregulation, cerebral microbleeds, white matter hyperintensities (WMH), unrecognized lacunar infarcts, and Alzheimer-like changes such as amyloid angiopathy and cerebral atrophy (Manolio et al., 2003). However, according to a Cochrane systematic review, there is no convincing evidence that lowering blood pressure in older adults prevents the development of cognitive impairment or dementia (McGuinness et al., 2009).

Although there is a paucity of research that examines the impact of sodium intake on brain health, research has increasingly examined the link between diet and cognitive function in late life. Research shows that adherence to a Mediterranean diet, which is high in fruits and vegetables, reduces the rate of cognitive decline with age (Tangney et al., 2011). Furthermore, dietary fat intake has been found to associate with cognitive function. Specifically, fatty fish and omega-3 fatty acids are associated with good cognitive health, whereas saturated fat intake is associated with impaired cognitive function in late life (Annweiler et al., 2010; Morris et al., 2007; Usoro and Mousa, 2010). In a small cross-sectional study that assessed the relationship between nutrient intake and cognitive performance in people at risk of dementia, it was found that cholesterol and sodium intakes differentiated middle-aged adults who scored within the normal range on a test of global cognitive function compared with those who scored below the normal cutoff (Salerno-Kennedy and Cashman, 2007).

In addition to reductions in sodium intake, research has shown that physical activity may improve both cardiovascular and cognitive health (Brown et al., 2010; Eskes et al., 2010; Jedrzewski et al., 2010; Kelley and Kelley, 2008; Kramer et al., 2006; Maiorana et al., 2011). Furthermore, an additive effect of reduction in sodium intake and physical exercise has been reported in hypertensive adults. In a randomized controlled trial that assessed the effect of a reduced sodium diet (Dietary Approaches to Stop Hypertension; DASH) and exercise program on neurocognitive function in sedentary, overweight hypertensive adults, it was found that individuals in the combined DASH plus exercise group showed the most pronounced improvement in cognitive function, compared with individuals in the DASH diet alone. It was also reported that the greatest neurocognitive improvement was observed in those with the highest level of systolic blood pressure (Smith et al., 2010). The present study assessed the association between sodium intake and global cognitive function over 3 years of follow-up in older adults. Specifically, the present study examined 3 questions: (1) is there a direct association between sodium intake and cognitive function?; (2) does hypertension moderate the association between sodium intake and cognitive function?; and (3) is there an additive impact of sodium intake and physical activity on cognitive function?. To this end, it is hypothesized that higher sodium intake will associate with lower cognitive function over time and this relationship will be moderated by the presence of hypertension. Further, based on the DASH report (Smith et al., 2010), it is hypothesized that low sodium intake and high physical activity will impose an additive positive effect on cognitive function in older adults.

2. Methods

2.1. Study Population

We examined a subgroup of participants from the Québec Longitudinal Study on Nutrition and Successful Aging (NuAge Study), a 5-year prospective study of 1793 cognitively intact and functionally independent elders aged 67–84 years upon recruitment, described in more detail elsewhere (Bouchard et al., 2007; Gaudreau et al., 2007). Participants in the original cohort were randomly selected from the Québec Medicare database and were stratified by age and sex. They were tested annually at the Institut Universitaire de Gériatrie de Montréal or the Institut Universitaire de Gériatrie de Sherbrooke. All participants signed an informed consent approved by the ethics committee at each institution.

The study subgroup (n = 1262, Nutrition et Cognition; NutCog) included participants who reported plausible energy intakes (see below) on their Food Frequency Questionnaire (FFQ) dietary assessment (n = 1602 from the parent sample). Individuals were further excluded if they reported the presence of, or had missing information on, cerebral vascular disease, Parkinson’s disease, epilepsy, and/or muscular dystrophy (n = 340). These particular neurological diseases were excluded a priori due to their potential negative impact on brain health (e.g., white matter lesions) that may mask the association between sodium intake and cognitive function.

2.2. Materials

2.2.1. Baseline demographic and health factors

Demographic factors included age, sex, and self-reported years of education. Health characteristics included self-report of current smoking status (yes or no) and measurements of waist circumference, body mass index (BMI) as calculated from measured height and weight, and systolic and diastolic blood pressure. Depressive symptoms were assessed using the Geriatric Depression Scale (GDS; Yesavage et al., 1982). Presence of hypertension (self-report or...
medication usage or blood pressure > 140/90) and type-2 diabetes (self-report or medication usage or fasting plasma glucose ≥ 7.0 mmol/L) were determined. Activity level was measured using the Physical Activity Scale for the Elderly (PASE; Washburn et al., 1999), with higher scores indicating greater level of activity. The PASE is a reliable and valid self-report measure suitable for epidemiological studies, comprised of work-related activities (e.g., during the past 7 days did you work for pay or as a volunteer?), household activities (e.g., during the last 7 days, have you done any heavy housework or chores such as vacuuming, scrubbing floors, washing windows, or carrying wood?), and leisure time activity items (e.g., over the past 7 days, how often did you do any exercises specifically to increase muscle strength and endurance, such as lifting weights or pushups, etc?), during a 1-week period (Washburn et al., 1993). The total PASE sum score is computed by multiplying the amount of time spent on each activity (in hours per week) by the empirically-derived item weights and summing over all activities (Washburn et al., 1999).

2.2.2. Measurement of sodium intake
Energy and nutrient intakes, including sodium intake (mg/day), were estimated from a validated 78-item semiquantitative FFQ that captures usual food consumption over the previous 12 months (Shatenstein et al., 2003, 2005). Daily nutrient intakes were calculated from frequency category and portion size, using the then-current Canadian Nutrient File 2001b (Health Canada, 1982). Briefly, the FFQ was developed using a database approach (Block et al., 1986). Information on background consumption frequency and portion size were derived from population-based food consumption data, extracted from a nutrition survey of adults in Québec (Santé Québec and L, 1995) and were used to build the nutrient database using the Canadian Nutrient File (Health Canada, 1982). The FFQ was developed, pre-tested, and validated in both English and French in several adult populations, including older adults (Shatenstein et al., 2003, 2005). Validation studies indicate that the FFQ is a valid instrument for determining usual diet in the adult Canadian population.

Plausibility of the FFQ data were determined by a set of established criteria (Shatenstein et al., 2009). Implausible FFQ scores were defined as those with 1 or more full blank pages, 10% or more foods with missing answers for frequency and/or portion size, or energy intakes lower than 800 or greater than 4000 kcal. Participants with an implausible FFQ score were excluded from the current analysis.

The Canadian Healthy Eating Index (C-HEI), an indicator of global diet quality (Shatenstein et al., 2005), was calculated from FFQ dietary and nutrient data. Possible scores on the C-HEI range from 0 to 100, with 100 points referring to a “perfect” diet quality and lower scores indicating poorer adherence to the recommended intakes.

2.2.3. Cognition
The Modified Mini Mental State Examination (3MS), a measure of global cognitive function, was administered at years 1 (baseline), 2, 3, and 4. The 3MS is an expanded version of Folstein’s Mini Mental State Examination, with possible scores ranging from 0 to 100, and is reportedly more sensitive for the detection of cognitive impairment (Bassuk and Murphy, 2003; Grace et al., 1995). Components including orientation, concentration, language, praxis, and immediate and delayed memory are evaluated, with higher scores indicating better cognitive function. All participants were cognitively intact at baseline, with a 3MS score ≥ 79, used as a cutoff to identify cognitive impairment (note the standard cutoff for impairment is a score below 75).

2.3. Statistical analyses
Given the positively skewed distribution of sodium intake, which is common with nutrient intake data, tertiles were created for sodium intake. Tertiles were computed by using tertiles of sodium intake tertile and baseline factors were determined using χ² for categorical variables or analyses of variance for continuous variables. Variables that statistically differed among sodium intake tertiles (p < 0.1) were considered covariates for subsequent analyses.

Generalized Estimating Equation models were conducted to determine if sodium intake tertile was associated with baseline 3MS and rate of change in 3MS over 3 years (i.e., slope). Models included random intercepts and slopes for change in cognitive score over time. Sodium intake tertile and covariates were entered as fixed effect predictors and participants were specified as a random effects factor. A variable indicating time between first and subsequent visit was entered into the model to specify that slopes over time are associated with an individual and are random. Tests were considered statistically significant at p < 0.05. Two adjusted models were tested: the first adjusted for age, sex, education, waist circumference, and presence of diabetes, the second adjusting for all aforementioned variables and adding total energy, cholesterol, calcium, and total C-HEI score.

Two tests of interaction were performed. To determine whether hypertension moderates the relationship between sodium intake and cognitive function, a sodium intake tertile-by-hypertension interaction was assessed. To determine whether physical activity moderates the relationship between sodium intake and cognitive function, a sodium intake tertile-by-physical activity interaction was assessed. Significant interactions (p < 0.10) resulted in subsequent stratified analyses; analyses would be stratified by either hypertension (yes or no) and/or physical activity (high or low), determined by calculating the median split on total
PASE score. Stratified analyses were considered statistically significant at \( p < 0.05 \). All analyses were conducted using STATA version 10 (StataCorp).

### 3. Results

#### 3.1. Baseline characteristics

Among 1262 participants, 420 fell into the low sodium intake tertile group (median \( M = 1791 \) mg/day, standard error \( SE = 15 \)), 421 fell into the mid tertile group (\( M = 2648 \) mg/day, \( SE = 11 \)) and 421 fell into the high tertile group (\( M = 3919 \) mg/day, \( SE = 36 \)) (for median and range values, see Table 1). Tertile groups differed on total energy, cholesterol, and calcium intake, and total C-HEI score (\( p < 0.001 \)). Baseline characteristics including sex, waist circumference, physical activity, and diabetes, differed among sodium intake tertile groups. All other characteristics were similar across groups (Table 2).

Compared with participants who were included in the study, excluded participants were older (\( M_{\text{excluded}} = 75.00, \ SE_{\text{excluded}} = 0.19 \) vs. \( M_{\text{included}} = 74.20, \ SE_{\text{included}} = 0.12; \ p = 0.004 \), scored higher on the GDS (\( M = 5.70, \ SE = 0.19 \) vs. \( M = 4.70, \ SE = 0.11; \ p < 0.0001 \)), scored lower on the PASE \( (M = 93.20, \ SE = 2.20 \) vs. \( M = 103.20, \ SE = 1.50; \ p = 0.0002 \)), scored lower on the 3MS \( (M = 93.00, \ SE = 0.20 \) vs. \( M = 94.10, \ SE = 0.12; \ p < 0.0001 \)), and reported lower energy (kcal/day) levels (\( M = 1752.30, \ SE = 26.50 \) vs. \( M = 1832.80, \ SE = 15.50; \ p = 0.015 \)).

#### 3.2. Sodium intake and cognitive function

Unadjusted analyses found no association between sodium intake tertile and baseline cognitive function (low tertile: \( M = 93.74, \ SE = 0.002 \); mid tertile: \( M = 94.05, \ SE = 0.003 \); high tertile: \( M = 93.44, \ SE = 0.003; \ p = 0.21 \)) or change in cognitive function over years (low tertile: \( M = -1.18, \ SE = 0.03 \); mid tertile: \( M = -1.83, \ SE = 0.003 \); high tertile: \( M = -1.53, \ SE = 0.004; \ p = 0.11 \)). Results did not change after adjusting for age, sex, education, waist circumference, physical activity, and diabetes; \( ps > 0.05 \). Additional adjustments of total energy, cholesterol, calcium, and total C-HEI score, did not change our findings; \( ps > 0.05 \).

#### 3.3. Tests of interaction

##### 3.3.1. Sodium intake tertile-by-hypertension

No sodium-by-hypertension interaction was observed for baseline \( (p = 0.80) \) or change \( (p = 0.28) \) in 3MS score over years.

##### 3.3.2. Sodium intake tertile-by-physical activity

Test of interaction showed that the association between sodium intake and change in cognitive function was dependent on the level of physical activity \( (p = \)
3.4. Sodium intake and cognitive function stratified by physical activity

Subsequent stratified analyses, adjusting for age, sex, education, waist circumference, physical activity, and diabetes, showed the association between sodium intake and change in cognitive function was significant in the low PASE group (p = 0.0004) but not in the high PASE group (p = 0.41) (Table 1). In the low PASE group, those in the low sodium intake tertile show less decline over follow-up compared with both mid (p < 0.001) and high (p = 0.001) tertile groups. Mid and high sodium intake groups did not differ (p = 0.85).

Additional adjustments were made for intakes of energy, calcium, cholesterol, and total lipids, and total C-HEI score. These adjustments did not change our findings (Table 1).

4. Discussion

Worldwide sodium reduction strategies are being recommended with a focus on reducing heart disease. It is estimated that a reduction in sodium intake may result in major annual savings in medical care costs and physician visits related to hypertension (Joffres et al., 2007). Sodium intake reduction has been reported to be especially beneficial in older populations (Alam and Johnson, 1999; Cappuccio et al., 1997). This study suggests that sodium intake reduction, especially in low physical activity older adults, may further improve brain health in late life. Importantly, the present findings suggest that the impact of sodium intake on cognitive function may be dependent on level of physical activity.

This is the first study to extend the benefits of low sodium intake to brain health in healthy older adults. Specifically, in individuals with low activity levels, low sodium intake is associated with cognitive maintenance over 3 years. Thus, the combination of low levels of physical activity and high levels of sodium intake is particularly detrimental to cognitive health. Importantly, this association was independent of hypertension and global diet quality. The independent effect of sodium intake from other nutrient intakes, including energy and lipids, suggest that sodium intake alone may affect cognitive function in sedentary older adults above and beyond the effects of overall diet.

Based on previous research, a potential mechanism underlying the association between sodium intake and cognition is via blood pressure levels, which are associated with white matter lesions observed in dementia patients (Bowen et al., 1990; Scheltens et al., 1992; Skoog et al., 1996). However, the present findings do not support this hypothesis due to the independent effect of sodium intake on cognitive function from hypertension. Although a cohort effect may be speculated, another explanation is that sodium intake impacts brain health via alternative pathways, such as compromising integrity of the blood-brain barrier (Kanoski et al., 2010), or via function of the hypothalamic paraventricular nucleus (PVN). Animal research shows that increases in brain sodium concentration affect cardiovascular...
and renal function, which is mediated by the PVN (Frithiof et al., 2009). While the PVN is an important regulator of cardiovascular function, it also regulates the secretion of hormones that may impact learning centers of the brain (e.g., glucocortidoids in hippocampal function). Indeed, future research is required to delineate underlying mechanisms in the relationship between sodium intake and cognitive vitality.

The observed interaction between sodium intake and physical activity is important. While a positive additive effect of physical activity and low sodium intake on cognitive function was expected, sodium intake was not found to impact cognitive function in the high activity group. A potential explanation for this finding is that the effect of exercise on the vasculature system outweighs the impact of sodium intake. Further, as exercise may have independent effects on vasculature, it is postulated that the observed association in the low activity group teases out an independent effect of sodium intake on brain health. Importantly, it should be noted that only the low tertile sodium group fell below the recommended upper limit of sodium intake (2300 mg/day), which may explain the absence of a dose effect.

No significant association between sodium intake and cognitive function at baseline was observed in either the high- or low-physical activity groups. A possible explanation for this null effect is selection of the sample. At time of recruitment, participants had to be in good general health with no subsequent exclusions for health reasons, be free of disabilities in activities of daily living, and show no signs of cognitive impairment. This relatively high health status of the group may have diminished the sensitivity of the associations at baseline.

Strengths of the study include the availability of data from a large cohort of elderly men and women over 3 years of follow-up and accessibility to a wide range of measures, including baseline demographic, health, and nutrient intakes. While the present findings are informative and meaningful, it is important to note that groups who declined in global cognitive function over time displayed normal age-related decline and did not display clinically significant rates of decline, defined as a 5-point decline per year on the 3MS (Kuller et al., 2003). Furthermore, we excluded individuals with a diagnosed neurological disorder, thus the current findings are not generalizable to older adults diagnosed with cerebral vascular disease, Parkinson’s disease, epilepsy, or muscular dystrophy. However, these are preliminary results that require further examination in other research. Future studies should address some of the limitations in this study. While self-report sodium intake can be informative, the addition of 24-hour urinary sodium levels would enhance research findings and its interpretation. Longer follow-up time may be required to truly capture the effects of sodium intake on cognitive change and risk of dementia in late life. Finally, multiple measurements of sodium intake and physical activity would improve analyses by allowing for the assessment of change in these baseline factors over the observation period, which may better explain study findings.

As government bodies and private foundations promote lifestyle-based risk reduction strategies, it is important to recognize the compounding effects of adverse lifestyle characteristics and the need for broad lifestyle changes rather than focusing on a single domain in order to effectively prevent or delay cognitive impairment in late life.

Disclosure statement

None of the authors report any conflict of interest.

The protocol was approved by the REB of the institutions involved in the study: Institut Universitaire de Gériatrie de Montréal and the Institut Universitaire de Gériatrie de Sherbrooke. All participants signed an informed consent approved by the ethics committee at each institution.

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