HHS Public Access

Author manuscript

Int J Obes (Lond). Author manuscript; available in PMC 2019 January 24.

Published in final edited form as:

Int J Obes (Lond). 2015 August ; 39(8): 1249–1253. doi:10.1038/ijo.2015.51.

High sodium intake is associated with short leukocyte telomere length in overweight and obese adolescents

Haidong Zhu[1,*], **Jigar Bhagatwala**[1,2], **Norman K. Pollock**[1], **Samip Parikh**[1,2], **Bernard Gutin**[1], **Inger Stallmann-Jorgensen**[3], **Jeffrey Thomas**[1], **Gregory A. Harshfield**[1], and **Yanbin Dong**[1]

[1]Georgia Prevention Center, Department of Pediatrics, Medical College of Georgia, Georgia Regents University, Augusta, Georgia 30912

[2]Internal Medicine, Department of Medicine, Medical College of Georgia, Georgia Regents University, Augusta, Georgia 30912

[3]Department of Physiology, Medical College of Georgia, Georgia Regents University, Augusta, Georgia 30912

Abstract

Background/Objectives—Telomere shortening plays an important role in cellular aging. However, the impact of high sodium intake, an important risk factor of age-related diseases, on telomere shortening remains unknown. Therefore, we examined the relationship between high dietary sodium intake and leukocyte telomere length, particularly in the context of obesity since obesity increases salt sensitivity.

Subjects/Methods—Leukocyte telomere length (LTL) was determined by a quantitative polymerase chain reaction method in 766 adolescents aged 14–18 years (50% female, 49% African Americans). Dietary sodium intake was assessed by seven independent 24-h dietary recalls. We divided the sample into low sodium (mean 2388 ± 522 mg/day) or high sodium groups (mean 4142 ± 882 mg/day) based on the median value (3280.9 mg/day).

Results—In the entire cohort, there was no significant association between sodium intake and LTL ($r = -0.05$, $p = 0.24$). However, there was a significant interaction between sodium intake and obesity status ($p = 0.049$). Further multiple linear regression analyses revealed that higher dietary sodium intake was associated with shorter LTL in the overweight/obese group (BMI ≥ 85th percentile, $\beta = -0.37$, $p = 0.04$), but not in the normal weight group ($\beta = 0.01$, $p = 0.93$) after adjusting for multiple confounding factors. In the overweight/obese group, LTL was significantly shorter in the high sodium intake subjects vs. low sodium intake subjects (1.24 ± 0.22 vs. 1.32 ± 0.20, $p = 0.02$), but not the normal weight group (1.29 ± 0.24 vs. 1.30 ± 0.24, $p = 0.69$).

Conclusions—Higher dietary sodium intake is associated with shorter telomere length in overweight and obese adolescents.

[*]**Address for correspondence:** Haidong Zhu MD PhD, Georgia Prevention Center, Department of Pediatrics, Medical College of Georgia, Georgia Regents University, 1120 15th Street, HS-1640, Augusta, GA 30912-3715, Phone: (706) 721 5470, hzhu@gru.edu.

Conflict of interests: None

Keywords

Sodium intake; obesity; telomere length; 24-h dietary recall; adolescents

INTRODUCTION

Telomeres, specialized chromatin structures located at the chromosomal ends, protect chromosome integrity and stability. Telomeres naturally shorten with every cell cycle, and cells with critically short telomeres undergo replicative senescence and apoptosis. Telomere shortening, a widely accepted marker of biological aging, plays a key role in the cellular aging process.[1]

The aging process at the cellular level is a life-long event, which begins at birth.[2] Telomeres are rapidly shortened in infants very soon after birth, and for the first year of life, corresponding to the rapid growth rates and high production and turnover of cells.[3, 4] Telomere shortening then continues at a steadier and more moderate rate into childhood, adulthood, and old age.[4, 5] Children who experienced cumulative early life stress showed faster telomere shortening in buccal cells between age 5 years (baseline) and 10 years (follow up).[2, 6] In addition, healthy lifestyle and stress-coping strategies can decelerate the telomere erosion process.[7–11] Therefore, understanding the lifestyle and environmental factors affecting telomere erosion in children and adolescents is fundamental for preventing the acceleration of aging process early in life.

It is well-recognized that both obesity[12–15] and high sodium intake[16–20] are important risk factors for age-related diseases such as cardiovascular disease, stroke and cancer. Obesity, a chronic state of inflammation, has been shown to be inversely associated with telomere length in adults in a recent meta-analysis.[21] *In vitro* and *in vivo* studies reported that high salt diets through oxidative damage have promoted cell senescence, retarded growth and markedly decreased the life span of *C. elegans*.[22] In addition, high salt diets have promoted tissue inflammation and accelerated development of autoimmunity.[23, 24] A high salt condition also increased reactive oxygen species, resulting in oxidation of proteins both in cell culture and in cells of renal inner medulla *in vivo*.[25] We have recently shown that adolescents consume excessive sodium and that higher sodium intake is associated with higher level of inflammation.[26] Both inflammation and oxidative stress reduce telomere length. Therefore, we tested the hypotheses that high dietary sodium intake would be associated with short leukocyte telomere length, especially in obese adolescents.

METHODS

Study participants

Seven hundred and sixty six healthy adolescents aged 14–18 years including 389 Caucasians and 377 African Americans were recruited from local public high schools in Augusta, Georgia. Demographic information obtained from the school systems was used to select schools that enrolled both African American and Caucasian students. After receiving approval from the county superintendents and school principals, flyers were distributed to all

students in the selected schools. Inclusion criteria for the study were white/Caucasian or black/African American race and age 14–18 years. Adolescents were excluded if they were diagnosed with any disease or were taking medications or had any medical conditions that could affect growth, maturation, physical activity, nutritional status, or metabolism. Written informed consent was obtained from the 18 year olds. For the 14–17 year olds, parental consent and subject assent were obtained. Race was determined by self-report, or by a parent if subject was under 18 years of age. The Institutional Review Board at the Georgia Regents University approved the study. All measurements were performed between 2001 and 2005.[27]

Anthropometric measurements

Height and weight were obtained according to standard procedures, using a wall-mounted stadiometer (Tanita Corporation of American, Arlington Heights, IL) and calibrated electronic scale (model CN2OL; Cardinal Detecto, Webb City, MO). Prior to testing each week, the electronic scale was checked for accuracy using known weights. Body mass index (BMI) was calculated as weight (kg) divided by height (m^2). For subjects <18 years, the exact percentile of BMI was computed. According to the CDC Growth Charts (http://www.cdc.gov/nchs/about/major/nhanes/growthcharts/datafiles.htm), BMI≥5^{th} and <85^{th} percentile was defined as normal weight, BMI≥85^{th} and <95^{th} percentile was defined as overweight, and BMI≥95^{th} percentile was defined as obese.[28]

Dietary intake

Diet was assessed with individual, non-consecutive, 24-h recalls that covered the period from midnight to midnight for the previous day using the Nutrition Data System for Research (NDS-R) (Nutrition Coordinating Center, University of Minnesota, Minneapolis, MN) by trained dietitians assisted by dietetic interns. The first two recalls were performed in person at our institute within 1 week of testing with the use of food models, portion booklets, serving containers, and food measuring cups and spoons to assist in estimating serving size, and the remaining interviews were conducted by telephone weekly, with all 7 recalls completed within a period of 12 weeks. Participants were given a booklet describing food and beverage portions and had to have the booklet in hand for portion size estimation during telephone interviews. We sought to obtain 7 recalls from each participant, one for each day of the week. To minimize the potential for under-eating during the time frame for 24-h recalls, subjects were blinded to the telephone recall schedule. A total of 3, 4, 5, 6 and 7 day dietary recalls were collected in 3.3%, 8.7%, 17.2%, 18.4% and 50.2% of the adolescents, respectively. A total of 98% (n=750) and 95% (n=725) of the adolescents in our study completed at least 3 and 4 day dietary recalls, respectively. Dietary sodium intake was an average from all the recalls collected from each participant.

Physical activity

Free-living physical activities were assessed using CSA/MTI Actigraph monitors (model 7164; MTI Health Services, Fort Walton Beach, FL) as described previously.[27] Subjects were instructed to wear the monitor for 7 days, remove it for sleep and any activity that may cause harm to either the monitor or another person (e.g. during contact sports), and return the monitor 1 week later. Data from day 1 and day 7 were discarded because a full day of information was not available for those days. Daily movement counts were converted to

average minutes per day spent in moderate physical activity (MPA) [3–6 metabolic equivalents] and vigorous physical activity (VPA) (>6 metabolic equivalents) by the software accompanying the device.

Pubertal maturation

Pubertal maturation stage (or Tanner stage) was assessed using a five-stage scale ranging from I (prepubertal) to V (fully mature) as described by Tanner.[29] Using this gender-specific questionnaire, participants reported their pubertal stage by comparing their own physical development to the five stages in standard sets of diagrams. When an individual reported discordant stages of pubic hair and breast or genital development, the higher of the two stages was used.

Socioeconomic status

Parents completed questionnaires regarding their education and occupation. Family socioeconomic status (SES) was calculated using the Hollingshead Four-Factor Index of Social Status, a weighted average of parental education (scale 1–7) and occupations (scale 1–9). The validity and reliability of this instrument were established by Cirino *et al.*[30]

Measurement of telomere length

Mean leukocyte telomere length (LTL) was determined from leukocyte DNA by a modified quantitative polymerase chain reaction (PCR)-based assay as previously described.[31, 32] The relative ratio of telomere repeat copy number (T) to single copy gene copy number (36B4 gene, encoding ribosomal phosphoprotein, located on chromosome 12, S) was determined using an 7500 Fast Real-time PCR System (Applied Biosystems, Foster City, CA). Samples were done in triplicate. Threshold values (Ct) were obtained by averaging the triplicates. Each 96-well plate contained a 5-point standard curve using the same control genomic DNA from 3 to 48 ng to control the day-to-day variations. Standard curve with linearity $R2 > 0.98$ was accepted. Telomere PCRs and 36B4 PCRs were performed on separate plates, with the same sample well position. T/S ratio was calculated as: the amount of telomeric DNA (T) divided by the amount of single-copy control gene DNA (S). The intra-plate and inter-plate coefficients of variation for the T/S ratio were 5.6% and 6.8% respectively.[32]

Statistical analyses

Normal distribution and homogeneity of variances were confirmed by Shapiro-Wilks *W* and Levene's tests, respectively. Group differences were conducted by using analysis of covariance controlling for age, sex, race and energy intake. Group differences in categorical variables were tested by using chi-square tests. Descriptive statistics for raw variables are presented as mean ± SE. Overweight/obese was defined as BMI ≥ 85th percentile. We divided the sample into low sodium (mean 2388 ± 522 mg/day) or high sodium groups (mean 4142 ± 882 mg/day) based on the median value (3280.9 mg/day).

The interactions of dietary sodium intake with race, sex and obesity status were tested in separated models. Multivariate linear regression analyses were conducted to examine associations of dietary sodium intake with LTL. Potential confounding factors including age, sex, race, BMI, energy intake, Tanner stage, and vigorous physical activity were included in

the model, as we previously showed that there were significant race and sex differences in LTL and that vigorous physical activity was positively associated with telomere length in this cohort.[32] Data were analyzed using IBM SPSS statistics for windows, Version 20.0 (Armonk, NY) and statistical significance was set at $P < 0.05$.

RESULTS

Participant characteristics are presented in Table 1. The sample was composed of 766 Caucasian and African American adolescents aged 14–18 years (50% female, 49% African American, 25% overweight/obese). The gender distribution, age, SES, moderate physical activity, sodium intake, and LTL were not different between normal weight and overweight/obese groups. Overweight/obese adolescents were found to have higher Tanner stage, and lower levels of vigorous physical activity, and reported total energy intake than normal weight adolescents (all $Ps < 0.05$).

In the entire cohort, there was no significant association between sodium intake and leukocyte telomere length (r = −0.05, $p = 0.24$). We further tested whether there were any interactions between dietary sodium intake and race, sex or obesity status. No significant interactions with race or sex were identified (Ps = 0.29 and 0.09 respectively). However, there was a significant interaction between dietary sodium intake and obesity status (p=0.049). Stratification of the sample by obesity status showed that higher dietary sodium intake was associated with shorter LTL in the overweight/obese group (BMI ≥ 85th percentile, β = −0.37, p = 0.04), but not in the normal weight group (β = 0.01, p= 0.93) after adjusting for age, sex, race, BMI, energy intake, tanner stage and vigorous physical activity. In the overweight/obese group, LTL was significantly shorter in the high sodium intake subjects than those in the low sodium intake subjects (mean ± SD, 1.24 ± 0.22 vs. 1.32 ± 0.20, p = 0.02). But no difference was seen in the normal weight group (1.29 ± 0.24 vs. 1.30 ± 0.24, p = 0.69, Figure 1).

DISCUSSION

Our major finding is that higher dietary sodium intake is associated with shorter LTL in overweight/obese adolescents.

Obesity is recognized as a state of increased oxidative stress and inflammation. A recent meta-analyses of 16 studies, including 2 longitudinal studies, suggested a biologically plausible inverse association between BMI and LTL in adults.[21] However, the impact of high sodium intake on LTL remains unclear. An *in vivo* study has shown that high salt promotes cell senescence and aging, retards growth and markedly decreases the life span of *C. elegans,* an ideal model system to study aging.[22] Nettleton *et al.* examined associations between dietary pattern and leukocyte telomere length in the Multi-Ethnic Study of Atherosclerosis and reported that only processed meat, not other diet features including red meat, showed an expected inverse association with telomere length.[33] Processed meat is generally high in sodium; thus, it is possible that sodium may play a role in this process.

The present study shows that higher dietary sodium intake is associated with shorter LTL in overweight/obese adolescents, suggesting high sodium intake may promote leukocyte

turnover, leading to their accelerated aging in overweight/obese individuals. Increased inflammation and oxidative stress are the two most common pathways shared by both obesity and high salt intake. A high salt diet has been shown to trigger T-cell differentiation, promote tissue inflammation and exacerbate autoimmune disease in mice.[23, 24] A high salt condition also increased reactive oxygen species, resulting in oxidation of proteins both in cell culture and in cells of renal inner medulla *in vivo*.[25] Increasing evidence in humans, including our own, suggests a link between high salt intake and inflammation.[26, 34, 35] Several *in vitro* studies have demonstrated that inflammation and oxidative stress are important factors that cause reduced telomerase activity and shortened telomere length.[36–38] Further research is warranted to elucidate the underlying mechanisms.

Obesity itself was not associated with LTL in our adolescent population as we previously reported.[32] Four studies including our own have examined the relationship between obesity and LTL in children, with age ranging from 2 to 18 years.[32, 39–41] The results are not as consistent as in adults.[21] The inconsistency may result from the high heterogeneity of the study populations from Arab children, Caucasian and African American adolescents. It may take more years of exposure for the deleterious effects of obesity to be manifested in children and adolescents. Other factors, such as diet and physical activity, may also explain the heterogeneity in this relationship.

The significant interaction between sodium intake and obesity, as observed in the present study, suggests that high sodium intake and obesity may act synergistically to speed up the cellular aging process in adolescents. This is consistent with the description of impaired renal tubular sodium handling in obese individuals, making them particularly sensitive to the effects of high salt intake.[42] It is well recognized that obese individuals have increased sensitivity to salt,[43] which may help explain why higher sodium intake had a greater effect on cell aging in this group. The lack of association between sodium intake and LTL in the normal weight group may reflect the fact that our subjects were young and relatively healthy; thus they have had a relatively short duration of high sodium exposure. Salt sensitivity has been shown to increase with increasing age and to be more frequent in hypertensive than in normotensive subjects.[44, 45] Therefore, it is possible that the effect of high sodium on cell aging may become stronger with longer duration of exposure in the normal weight adults, elderly or hypertensive individuals.

The present study has several notable strengths. First, the collection of three to seven independent 24-h dietary recalls over a 12 week period provided more accurate dietary assessments of usual sodium intake compared to fewer recalls used in other epidemiological studies;[16, 46–48] this greatly reduced bias due to measurement error and random error due to within-person variability over time. Second, we had a relatively large, apparently healthy adolescent population with nearly equal distribution of males and females, and Caucasian and African Americans. Third, we recruited a narrow age range of adolescents, which minimizes the confounding effect of disease processes and chronological age on LTL.

Limitations should also be recognized. First, because of our cross-sectional study design, the associations between sodium consumption and LTL do not prove causality. Larger studies that involve other age groups are needed to confirm our findings. Second, adipose tissue

samples were not collected; unfortunately, only buffy coats samples were available for the present study. Nonetheless, TL from leukocytes is commonly used in epidemiological studies, and has been shown to be highly correlated with aorta, buccal cells, skin cells[49] , cerebellar tissue[50], suggesting that it represents systemic information. Third, our estimates of dietary sodium intake were based on self-reported 24-h dietary recalls rather than on 24-h urine collection, which is considered to be the most reliable and accurate method. Although 24-h dietary recalls may underestimate the usual sodium intake, sodium intake from repeated dietary recalls correlates significantly with 24-h urinary excretion and provided a valid method in previous association studies.[16, 46–48, 51, 52]

ACKNOWLEDGMENTS

We thank all of the schools, adolescents and parents who participated in the study funded by National Institute of Health (HL64157).

Sources of support: The participants in this study were previously recruited by NIH funded study (HL64157).

REFERENCES

1. Zhu H, Belcher M, van der Harst P. Healthy aging and disease: role for telomere biology? Clinical science. 2011; 120(10):427–440. [PubMed: 21271986]
2. Shalev I. Early life stress and telomere length: investigating the connection and possible mechanisms: a critical survey of the evidence base, research methodology and basic biology. Bioessays. 2012; 34(11):943–952. [PubMed: 22991129]
3. Rufer N, Brummendorf TH, Kolvraa S, Bischoff C, Christensen K, Wadsworth L, et al. Telomere fluorescence measurements in granulocytes and T lymphocyte subsets point to a high turnover of hematopoietic stem cells and memory T cells in early childhood. The Journal of experimental medicine. 1999; 190(2):157–167. [PubMed: 10432279]
4. Zeichner SL, Palumbo P, Feng Y, Xiao X, Gee D, Sleasman J, et al. Rapid telomere shortening in children. Blood. 1999; 93(9):2824–2830. [PubMed: 10216076]
5. Eisenberg DT. An evolutionary review of human telomere biology: the thrifty telomere hypothesis and notes on potential adaptive paternal effects. Am J Hum Biol. 2011; 23(2):149–167. [PubMed: 21319244]
6. Shalev I, Moffitt TE, Sugden K, Williams B, Houts R, Danese A, et al. Exposure to violence during childhood is associated with telomere erosion from 5 to 10 years of age: a longitudinal study. Mol Psychiatry. 2013; 18(5):576–581. [PubMed: 22525489]
7. Puterman E, Lin J, Blackburn E, O'Donovan A, Adler N, Epel E. The power of exercise: buffering the effect of chronic stress on telomere length. PLoS One. 2010; 5(5):e10837. [PubMed: 20520771]
8. Diaz VA, Mainous AG 3rd, Everett CJ, Schoepf UJ, Codd V, Samani NJ. Effect of healthy lifestyle behaviors on the association between leukocyte telomere length and coronary artery calcium. Am J Cardiol. 2010; 106(5):659–663. [PubMed: 20723641]
9. Boccardi V, Esposito A, Rizzo MR, Marfella R, Barbieri M, Paolisso G. Mediterranean diet, telomere maintenance and health status among elderly. PLoS One. 2013; 8(4):e62781. [PubMed: 23646142]
10. Garcia-Calzon S, Gea A, Razquin C, Corella D, Lamuela-Raventos RM, Martinez JA, et al. Longitudinal association of telomere length and obesity indices in an intervention study with a Mediterranean diet: the PREDIMED-NAVARRA trial. Int J Obes (Lond). 2014; 38(2):177–182. [PubMed: 23711776]
11. Daubenmier J, Lin J, Blackburn E, Hecht FM, Kristeller J, Maninger N, et al. Changes in stress, eating, and metabolic factors are related to changes in telomerase activity in a randomized mindfulness intervention pilot study. Psychoneuroendocrinology. 2012; 37(7):917–928. [PubMed: 22169588]

12. Iskander K, Farhour R, Ficek M, Ray A. Obesity-related complications: few biochemical phenomena with reference to tumorigenesis. The Malaysian journal of pathology. 2013; 35(1):1–15. [PubMed: 23817391]
13. Gukovsky I, Li N, Todoric J, Gukovskaya A, Karin M. Inflammation, autophagy, and obesity: common features in the pathogenesis of pancreatitis and pancreatic cancer. Gastroenterology. 2013; 144(6):1199–1209. e4. [PubMed: 23622129]
14. Ginter E, Simko V. Type 2 diabetes mellitus, pandemic in 21st century. Advances in experimental medicine and biology. 2012; 771:42–50. [PubMed: 23393670]
15. Pi-Sunyer X. The medical risks of obesity. Postgraduate medicine. 2009; 121(6):21–33. [PubMed: 19940414]
16. Yang Q, Zhang Z, Kuklina EV, Fang J, Ayala C, Hong Y, et al. Sodium intake and blood pressure among US children and adolescents. Pediatrics. 2012; 130(4):611–619. [PubMed: 22987869]
17. Hanevold CD. Sodium intake and blood pressure in children. Curr Hypertens Rep. 2013; 15(5): 417–425. [PubMed: 23949320]
18. D'Elia L, Rossi G, Ippolito R, Cappuccio FP, Strazzullo P. Habitual salt intake and risk of gastric cancer: a meta-analysis of prospective studies. Clin Nutr. 2012; 31(4):489–498. [PubMed: 22296873]
19. Strazzullo P, D'Elia L, Kandala NB, Cappuccio FP. Salt intake, stroke, and cardiovascular disease: meta-analysis of prospective studies. BMJ. 2009; 339:b4567. [PubMed: 19934192]
20. He FJ, Burnier M, Macgregor GA. Nutrition in cardiovascular disease: salt in hypertension and heart failure. Eur Heart J. 2011; 32(24):3073–3080. [PubMed: 21705359]
21. Muezzinler A, Zaineddin AK, Brenner H. Body mass index and leukocyte telomere length in adults: a systematic review and meta-analysis. Obesity reviews : an official journal of the International Association for the Study of Obesity. 2014; 15(3):192–201. [PubMed: 24165286]
22. Dmitrieva NI, Burg MB. High NaCl promotes cellular senescence. Cell Cycle. 2007; 6(24):3108–3113. [PubMed: 18073528]
23. Kleinewietfeld M, Manzel A, Titze J, Kvakan H, Yosef N, Linker RA, et al. Sodium chloride drives autoimmune disease by the induction of pathogenic TH17 cells. Nature. 2013; 496(7446):518–522. [PubMed: 23467095]
24. Wu C, Yosef N, Thalhamer T, Zhu C, Xiao S, Kishi Y, et al. Induction of pathogenic TH17 cells by inducible salt-sensing kinase SGK1. Nature. 2013; 496(7446):513–517. [PubMed: 23467085]
25. Zhang Z, Dmitrieva NI, Park JH, Levine RL, Burg MB. High urea and NaCl carbonylate proteins in renal cells in culture and in vivo, and high urea causes 8-oxoguanine lesions in their DNA. Proc Natl Acad Sci U S A. 2004; 101(25):9491–9496. [PubMed: 15190183]
26. Zhu H, Pollock NK, Kotak I, Gutin B, Wang X, Bhagatwala J, et al. Dietary sodium, adiposity, and inflammation in healthy adolescents. Pediatrics. 2014; 133(3):e635–e642. [PubMed: 24488738]
27. Gutin B, Yin Z, Humphries MC, Barbeau P. Relations of moderate and vigorous physical activity to fitness and fatness in adolescents. Am J Clin Nutr. 2005; 81(4):746–750. [PubMed: 15817847]
28. Kuczmarski RJ, Ogden CL, Guo SS, Grummer-Strawn LM, Flegal KM, Mei Z, et al. 2000 CDC Growth Charts for the United States: methods and development. Vital Health Stat. 2002; 11(246): 1–190.
29. Tanner, J. Growth and adolescence. 2nd ed. Oxford: Blackwell Scientific Publications; 1962.
30. Cirino PT, Chin CE, Sevcik RA, Wolf M, Lovett M, Morris RD. Measuring socioeconomic status: reliability and preliminary validity for different approaches. Assessment. 2002; 9(2):145–155. [PubMed: 12066829]
31. Cawthon RM. Telomere measurement by quantitative PCR. Nucleic Acids Res. 2002; 30(10):e47. [PubMed: 12000852]
32. Zhu H, Wang X, Gutin B, Davis CL, Keeton D, Thomas J, et al. Leukocyte telomere length in healthy Caucasian and African-American adolescents: relationships with race, sex, adiposity, adipokines, and physical activity. J Pediatr. 2011; 158(2):215–220. [PubMed: 20855079]
33. Nettleton JA, Diez-Roux A, Jenny NS, Fitzpatrick AL, Jacobs DR Jr. Dietary patterns, food groups, and telomere length in the Multi-Ethnic Study of Atherosclerosis (MESA). Am J Clin Nutr. 2008; 88(5):1405–1412. [PubMed: 18996878]

34. Rodrigues Telini LS, de Carvalho Beduschi G, Caramori JC, Castro JH, Martin LC, Barretti P. Effect of dietary sodium restriction on body water, blood pressure, and inflammation in hemodialysis patients: a prospective randomized controlled study. Int Urol Nephrol. 2014; 46(1): 91–97. [PubMed: 23340794]
35. Liu F, Mu J, Yuan Z, Wu G, Liu E, Zheng S, et al. High salt intake fails to enhance plasma adiponectin in normotensive salt-sensitive subjects. Nutrition. 2012; 28(4):422–425. [PubMed: 22189196]
36. Makpol S, Abidin AZ, Sairin K, Mazlan M, Top GM, Ngah WZ. gamma-Tocotrienol prevents oxidative stress-induced telomere shortening in human fibroblasts derived from different aged individuals. Oxid Med Cell Longev. 2010; 3(1):35–43. [PubMed: 20716926]
37. Scalera F, Closs EI, Flick E, et al. Paradoxical effect of L-arginine: acceleration of endothelial cell senescence. Biochem Biophys Res Commun. 2009; 386(4):650–655. [PubMed: 19545540]
38. Dixit D, Sharma V, Ghosh S, Koul N, Mishra PK, Sen E. Manumycin inhibits STAT3, telomerase activity, and growth of glioma cells by elevating intracellular reactive oxygen species generation. Free Radic Biol Med. 2009; 47(4):364–374. [PubMed: 19409983]
39. Zannolli R, Mohn A, Buoni S, et al. Telomere length and obesity. Acta Paediatr. 2008; 97(7):952–954. [PubMed: 18430074]
40. Al-Attas OS, Al-Daghri N, Bamakhramah A, Shaun Sabico S, McTernan P, Huang TT. Telomere length in relation to insulin resistance, inflammation and obesity among Arab youth. Acta Paediatr. 2010; 99(6):896–899. [PubMed: 20178511]
41. Buxton JL, Walters RG, Visvikis-Siest S, Meyre D, Froguel P, Blakemore AI. Childhood obesity is associated with shorter leukocyte telomere length. J Clin Endocrinol Metab. 2011; 96(5):1500–1505. [PubMed: 21349907]
42. Strazzullo P, Barba G, Cappuccio FP, Siani A, Trevisan M, Farinaro E, et al. Altered renal sodium handling in men with abdominal adiposity: a link to hypertension. J Hypertens. 2001; 19(12): 2157–2164. [PubMed: 11725158]
43. Rocchini AP, Key J, Bondie D, Chico R, Moorehead C, Katch V, et al. The effect of weight loss on the sensitivity of blood pressure to sodium in obese adolescents. N Engl J Med. 1989; 321(9):580–585. [PubMed: 2668763]
44. Weinberger MH, Miller JZ, Luft FC, Grim CE, Fineberg NS. Definitions and characteristics of sodium sensitivity and blood pressure resistance. Hypertension. 1986; 8(6 Pt 2):II127–II134. [PubMed: 3522418]
45. Luft FC, Weinberger MH. Heterogeneous responses to changes in dietary salt intake: the salt-sensitivity paradigm. Am J Clin Nutr. 1997; 65(2 Suppl):612S–617S. [PubMed: 9022556]
46. Cogswell ME, Zhang Z, Carriquiry AL, Gunn JP, Kuklina EV, Saydah SH, et al. Sodium and potassium intakes among US adults: NHANES 2003–2008. Am J Clin Nutr. 2012; 96(3):647–657. [PubMed: 22854410]
47. Song HJ, Cho YG, Lee HJ. Dietary sodium intake and prevalence of overweight in adults. Metabolism. 2013; 62(5):703–708. [PubMed: 23357528]
48. Yoon YS, Oh SW. Sodium density and obesity; the Korea National Health and Nutrition Examination Survey 2007–2010. Eur J Clin Nutr. 2013; 67(2):141–146. [PubMed: 23249877]
49. Butler MG, Tilburt J, DeVries A, Muralidhar B, Aue G, Hedges L, et al. Comparison of chromosome telomere integrity in multiple tissues from subjects at different ages. Cancer Genet Cytogenet. 1998; 105(2):138–144. [PubMed: 9723031]
50. Lukens JN, Van Deerlin V, Clark CM, Xie SX, Johnson FB. Comparisons of telomere lengths in peripheral blood and cerebellum in Alzheimer's disease. Alzheimers Dement. 2009; 5(6):463–469. [PubMed: 19896585]
51. Espeland MA, Kumanyika S, Wilson AC, Reboussin DM, Easter L, Self M, et al. Statistical issues in analyzing 24-hour dietary recall and 24-hour urine collection data for sodium and potassium intakes. Am J Epidemiol. 2001; 153(10):996–1006. [PubMed: 11384956]
52. Reinivuo H, Valsta LM, Laatikainen T, Tuomilehto J, Pietinen P. Sodium in the Finnish diet: II trends in dietary sodium intake and comparison between intake and 24-h excretion of sodium. Eur J Clin Nutr. 2006; 60(10):1160–1167. [PubMed: 16639417]

PERSPECTIVES

In this healthy adolescent cohort, we observed that higher dietary sodium intake was associated with shorter LTL in overweight/obese adolescents suggesting that high sodium intake and obesity may act synergistically to accelerate cellular aging. Longitudinal studies or randomized controlled trials are needed to establish the role of high sodium intake in cellular aging. Deep understanding of dietary sodium intake, obesity and cellular aging may open up new avenues for prevention and intervention of age-related disorders.

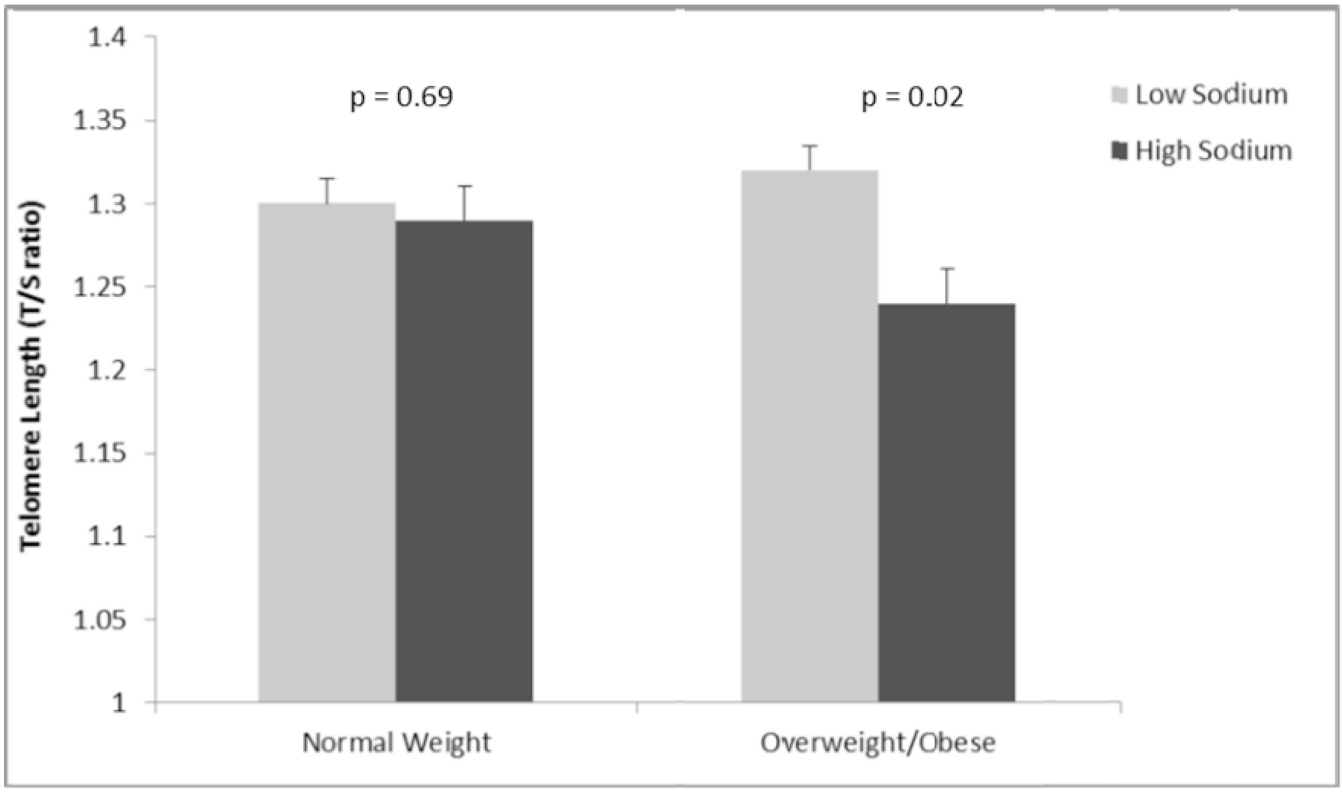

Figure 1.
Differences in leukocyte telomere length based on obesity and sodium intake. Telomere length is plotted as T/S ratio. The values are mean ± SE.

Table 1

General characteristics of study participants

	Total sample	Normal weight	Overweight/obese	*P*-value[b]
n	766	575	191	
Age (y)	16.1 ± 0.0	16.1 ± 0.1	16.2 ± 0.1	0.44
Female (%)[a]	50.3	49.2	53.4	0.32
African Americans (%)[a]	49.2	43.8	65.4	<0.01
Tanner stage	4.3 ± 0.0	4.3 ± 0.0	4.4 ± 0.1	0.04
SES	41.2 ± 0.6	41.2 ± 0.6	41.0 ± 1.2	0.88
Moderate/vigorous physical activity (min/d)	43.9 ± 1.1	43.4 ± 1.1	45.5 ± 2.0	0.37
Moderate physical activity (min/d)	39.1 ± 0.9	38.3 ± 0.9	41.6 ± 1.6	0.08
Vigorous physical activity (min/d)	4.8 ± 0.3	5.1 ± 0.3	3.9 ± 0.5	0.05
Dietary intake				
Energy (kcal/d)	1956.5 ± 21.5	1978.6 ± 22.6	1885.9 ± 39.5	0.04
Sodium (mg/d)[b]	3280.5 ± 41.5	3221.2 ± 23.1	3270.9 ± 40.4	0.29
Telomere length (T/S)	1.29 ± 0.01	1.29 ± 0.01	1.28 ± 0.02	0.50

SES, socioeconomic status; Values are age, sex and race adjusted means ± SE.
Tests of significance between groups were conducted by analysis of covariance (controlling for age, race and sex).

[a]Tests of significance between groups were based on the χ^2 test.

[b]Tests of significance between groups were conducted by using analysis of covariance (controlling for age, race, sex and energy intake).