



## Featured Article

## Sugary beverage intake and preclinical Alzheimer's disease in the community

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### Abstract

**Introduction:** Excess sugar consumption has been linked with Alzheimer's disease (AD) pathology in animal models.

**Methods:** We examined the cross-sectional association of sugary beverage consumption with neuropsychological ( $N = 4276$ ) and magnetic resonance imaging ( $N = 3846$ ) markers of preclinical Alzheimer's disease and vascular brain injury (VBI) in the community-based Framingham Heart Study. Intake of sugary beverages was estimated using a food frequency questionnaire.

**Results:** Relative to consuming less than one sugary beverage per day, higher intake of sugary beverages was associated with lower total brain volume (1–2/day,  $\beta \pm$  standard error [SE] =  $-0.55 \pm 0.14$  mean percent difference,  $P = .0002$ ; >2/day,  $\beta \pm$  SE =  $-0.68 \pm 0.18$ ,  $P < .0001$ ), and poorer performance on tests of episodic memory (all  $P < .01$ ). Daily fruit juice intake was associated with lower total brain volume, hippocampal volume, and poorer episodic memory (all  $P < .05$ ). Sugary beverage intake was not associated with VBI in a consistent manner across outcomes.

**Discussion:** Higher intake of sugary beverages was associated cross-sectionally with markers of preclinical AD.

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**Keywords:** Sugar; Diet; Dementia; Alzheimer's disease; Framingham Heart Study

### 1. Background

Sugar consumption is excessive in Western society [1], contributing to the burden of cardiometabolic disease [2,3]. Consumption of sugary beverages, including sugar-sweetened soft drinks, fruit drinks with added sugar, and 100% fruit juice, are major contributors to excess sugar

intake [1]. Studies in animal models suggest that excess sugar intake, including from sugary beverages, leads to the development of Alzheimer's disease (AD) pathology [4–7]. However, little is known about the long-term effect of sugary beverage intake on the human brain. Examining intake of sugary beverages provides a proxy for excess dietary intake of sugar. Using detailed neuropsychological assessments and brain magnetic resonance imaging (MRI), we examined the cross-sectional association between sugary beverage consumption and phenotypes of preclinical AD

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and vascular brain injury in the Framingham Heart Study (FHS)—a large, community-based, prospective cohort study from Massachusetts, USA. We hypothesized that higher consumption of sugary beverages would be associated with greater evidence of both subclinical vascular brain injury and preclinical AD.

## 2. Methods

The FHS commenced in 1948 with the aim to identify factors that contribute to cardiovascular disease [8]. At enrollment, the Original cohort comprised 5209 community-dwelling participants who did not yet have overt signs of cardiovascular disease. Surviving participants continue to be examined approximately every 2 years. In 1971, following a need to study younger adults, the children of the Original cohort and their spouses were invited to form the Offspring cohort [9]. The Offspring cohort enrolled 5124 participants who have been studied across nine quadrennial examination cycles. In 2002, a subset of the grandchildren of the Original cohort (the children of the Offspring cohort) was enrolled into the Third Generation cohort [10]. This cohort comprised 4095 participants at the initial examination and has now been studied twice, with a third examination cycle currently underway. All cohorts are observational with information collected on a wide variety of demographic, medical, and lifestyle indicators. Participants are also under constant surveillance for incident events such as myocardial infarction, stroke, and dementia. For the

present study, we examined food frequency questionnaire (FFQ) data collected during examination cycle 7 (1998–2001) for the Offspring cohort and during examination cycle 2 (2008–2011) for the Third Generation cohort. We excluded persons with prevalent dementia, stroke, or other significant neurological disease, those younger than 30 years of age, and participants who reported improbably high or low total energy intakes, suggesting that they had not filled out the FFQ accurately. A comparison of participants included in analysis versus excluded because of prevalent stroke, dementia, or other neurological disease can be seen in [Supplemental Table 1](#).

Participants underwent neuropsychological assessment and a brain MRI an average of 2 years (standard deviation [SD] = 1) from the examination cycle at which the FFQ was administered; most participants completed cognitive assessment and brain MRI on the same day (98%). The study flow diagram is presented in [Fig. 1](#). There were 4276 and 3846 participants available for analysis of the neuropsychological and MRI outcomes, respectively. All participants provided written informed consent, and the study was approved by the institutional review board and Boston University Medical Center.

### 2.1. Assessment of sugary beverage intake

Participants completed the Harvard semiquantitative FFQ at examination 7 for the Offspring cohort and examination 2 for the Third Generation cohort. This FFQ is designed to

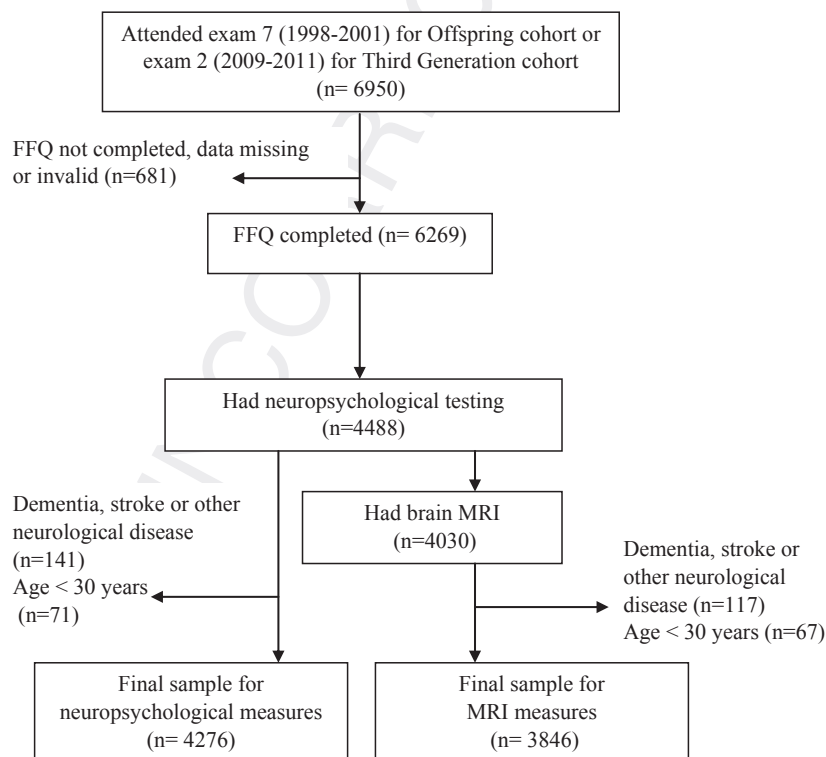


Fig. 1. Study flow diagram. Abbreviations: FFQ, food frequency questionnaire; MRI, magnetic resonance imaging.

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