

Nutrition and Cognitive Function in Amazonian Horticulturalists

by

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## ABSTRACT

Lifestyle factors including nutrition, may play a role in the development of cognitive impairment. Previous studies based in the United States have shown that nutrient deficiencies in vitamin B-12 and folate can increase the risk of developing mild cognitive impairment in adults, while high levels of potassium increase the risk of cognitive impairment. Among the Tsimane and Mosesten subsistence communities in Bolivia, there is a low prevalence of Alzheimer's dementia and related diseases, but any impacts of micronutrients on cognitive impairment have not been assessed. Using a mixed longitudinal design to estimate nutrient intake via 855 dietary recall questionnaires (24-hour) from 370 Tsimane and Mosesten aged 43-85 years (mean age 62 years, 47% male), a culturally specific dementia assessment (3MSE, KIKA, neurological exam) was conducted, and individuals were diagnosed as having normal cognition, mild cognitive impairment, or dementia. Logistic regressions with clustered standard errors (to account for multiple dietary questionnaires per individual) examined the association between dietary intake and cognitive impairment. Controlling for age, sex, body mass index, and education, those with higher daily caloric intake had a lower odds ratio of cognitive impairment, with every 100 additional calories associated with decreased risk (OR = 0.95,  $p=0.032$ ). Higher B-12 intake was associated with lower cognitive impairment, while higher potassium intake was associated with greater cognitive impairment. The presented data indicate a correlation between diet and nutrition and cognitive impairment within a subsistence population. This observation underscores the potential tradeoffs individuals face in allocating resources towards survival versus the upkeep of cognitive faculties, reflecting broader considerations in life history strategies.

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## INTRODUCTION

Noncommunicable diseases, like musculoskeletal, cardiac, and neurodegenerative diseases, are a leading cause of death in the developed world. Neurodegenerative disorders, which include Alzheimer's dementia and related diseases, are poised to create a "silver tsunami" in healthcare systems by the year 2050, as the number of cases in older adults has tripled since 2010 (Sarkar et al. 2016). Dementia and mild cognitive impairment, the stage between normal cognition and the stage that affects day-to-day life, are part of a class of major and minor neurocognitive disorders, respectively, that include Alzheimer's, Parkinson's, and Huntington's diseases among others (Hugo and Ganguli 2014). Though not as progressed as Alzheimer's dementia, mild cognitive impairment can also serve as a marker for the progression of cognitive decline. As of 2020, the prevalence of clinical Alzheimer's disease in adults aged over 65 in the US was 11.3%, with the prevalence of mild cognitive impairment at 22.7% (Rajan et al. 2021). The global burden of mild cognitive impairment in adults over the age of 50 was 15.56% (Bai et al. 2022).

Lifestyle factors, like highly nutritious diets, physical activity, and social support, are strongly supported to mitigate or exacerbate the progression of the illness (Hugo and Ganguli 2014). Previous studies based in the United States have shown that nutrient deficiencies in vitamin B-12 and folate can also increase the risk of developing mild cognitive impairment in adults (Lauer et al. 2022). Further research suggests that elevated serum homocysteine and methylmalonic acid levels are biomarkers for vitamin B-12 deficiency, which is linked with impaired memory, cognition, and poor myelination (Jatoi et al. 2020). Significantly low B-12 and high homocysteine levels are seen to contribute to oxidative stress on the brain and may be associated with cardiovascular and Alzheimer's disease. This poses a concern in aging populations,

where levels of this vitamin naturally decline with age. Additionally, in developing countries where poor nutrition may be indicative of lower socioeconomic status, a B-12 deficiency may also occur (Jatoi et al. 2020).

Among the Tsimane and Moseeten subsistence communities in Bolivia, there is a low prevalence of Alzheimer's dementia and related diseases, but its relation to micronutrients has not been assessed. Unlike industrialized communities, however, the Tsimane have minimal integration into Bolivian society and economy, leading them to primarily hunt, fish, and forage for their food (Gurven et al. 2017).

Consequently, their diets are heavily carbohydrate- and protein-based, with minimal additives such as fats or refined sugar, and have low overall diversity. The Tsimane also experience a high pathogenic burden, requiring a higher caloric intake to compensate for nutrients and energy lost to parasites (Gurven et al. 2016). This diet, in combination with an active lifestyle from their methods of food collection, results in a lowered risk of developing noncommunicable diseases, specifically cardiovascular and neurodegenerative diseases (Kraft et al. 2018). It is possible that at later ages, higher caloric intakes could contribute to the maintenance of cognitive function and development past the age of reproduction. Working with the Tsimane allows us to investigate risk factors for Alzheimer's disease without the influence of industrialization.

## METHODS

### **Study population**

The Tsimane Health and Life History Project (THLHP) has been working with the Tsimane population since 2002 to better understand aging in non-industrial contexts (Gurven et al. 2017). Since 2011, coverage expanded to over 100 Tsimane villages, where all individuals 60 years of age and greater were invited to enroll; individuals aged 40 to 59 were recruited by a random sample, stratified by community. In 2015, fifteen Mosenen villages were added to the project.

The Tsimane and Mosenen are neighboring indigenous forager-horticulturalist and agrarian populations residing in the Beni and La Paz Departments of lowland Bolivia, respectively (Lea et al 2023). The economy of both populations involves a combination of horticulture and intermittent wage labor, with the Tsimane also hunting, fishing, and gathering wild foods. The Mosenen, who are further integrated with broader Bolivian society than the relatively isolated Tsimane, speak fluent Spanish and have greater access to roads, vehicles, electricity, public health infrastructure, education, and market goods (Dinkel et al. 2020; Lea et al. 2023).

Ongoing assessment by THLHP physicians and Tsimane anthropologists includes medical evaluations with neurological exams, hearing and vision tests, lipid, thyroid, and immune panels, and cognitive testing, at approximately 2-year intervals. THLHP anthropologists update village censuses biennially to identify any intra-community migration, register any mortality, and establish the cause of death based on indirect reports and medical histories. The census has 95% coverage among participating villages (Gurven et al. 2017; Kraft et al. 2018).

## **Dementia assessment**

Dementia assessments were performed by a single, experienced Bolivian physician who had repeatedly examined each participant in the past as part of the ongoing THLHP. The physician was trained and overseen by faculty members of the University of Southern California Alzheimer's Center. Tsimane were interviewed in the Tsimane language; Mosen were interviewed in Spanish (Gatz et al. 2022). The clinical interview began with a self-reported evaluation of vision, hearing, memory, and thinking abilities. Next, the Modified Mini-Mental State Examination (3MS) was administered. This was further modified for illiteracy and lack of ability to count by substituting tasks from the same domain. Tsimane anthropologists on the team were iteratively consulted and piloted adjustments to the 3MS. Training and quality control included direct observation of Bolivian physicians in the field and by video. A subset of the 3MS items also provide a score for the Mini-Mental State Examination (MMSE). See Gatz et al 2023 for complete details.

## **Cognitive battery**

The cognitive battery is largely adapted from the Mexican Health and Aging Study (Gurven et al. 2016). The battery includes Visual Scan (searching for a target symbol amongst distractor symbols), Digit Span Forward, Immediate and Delayed Word Recall, and Semantic Fluency (naming animals and fish). Word recall and digit forward tasks were combined to create a composite variable for “fluid” cognition, or the ability to process information, while the semantic fluency scores were used to create a “crystallized” cognition, or accumulated knowledge, variable. These variables are used to create an overview of an individual's cognitive profile and assess the severity of cognitive decline.



## **Dietary recall**

Participants were recruited from 78 Tsimane and 4 Mosesten villages and were aged  $\geq 30$  years. In each village, there were attempts to sample all residents of appropriate age, and 88–95% participation was typically achieved among those present in the community. Some Tsimane, but not Mosesten, were sampled longitudinally over the study period (maximum = 9, median = 2; dietary recall interviews) (Kraft et al. 2018). 2496 dietary recall records (men, n = 1219; women, n = 1279) composed of 19,640 food-consumption events were obtained for the Tsimane, and 229 records (men, n = 120; women, n = 109) composed of 2265 events for the Mosesten. Each adult participant was interviewed about all food items or beverages consumed the previous day and, for each item, the time it was consumed, the mode of preparation (e.g., cooked in oil, salted, raw, etc.), and the estimated amount (Kraft et al. 2018).

## **Combined sample**

The final combined sample of cognitive and dementia assessments and nutritional data included 855 dietary recall questionnaires (24-hour) from 370 Tsimane and Mosesten aged 43-85 years (mean age 62 years, 47% male).

## **Statistical methods**

Logistic regressions with clustered standard errors were used to assess associations between cognitive impairment (normal vs cognitively impaired) and nutrition status (macronutrients and micronutrients), controlling for age, sex, BMI, and education. Standard errors were clustered by the individual to account for multiple nutritional status assessments. Linear mixed effects models examined the association between cognitive scores and nutritional status, controlling for age, sex, BMI, and education.

## **Ethics**

All phases of the study were approved by the ethics committee of the San Simon University School of Medicine (Cochabamba, Bolivia), the University of California, Santa Barbara, and Arizona State University. The Tsimane and Mosen governments, village leaders, and study participants approved all protocols. All participants provided informed consent in their native language.

## RESULTS

### Nutrition and dementia

Controlling for age, sex, body mass index, and education, those with higher daily caloric intake had a lower odds ratio of cognitive impairment, with every 100 additional calories associated with decreased risk (OR = 0.95,  $p=0.032$ ).

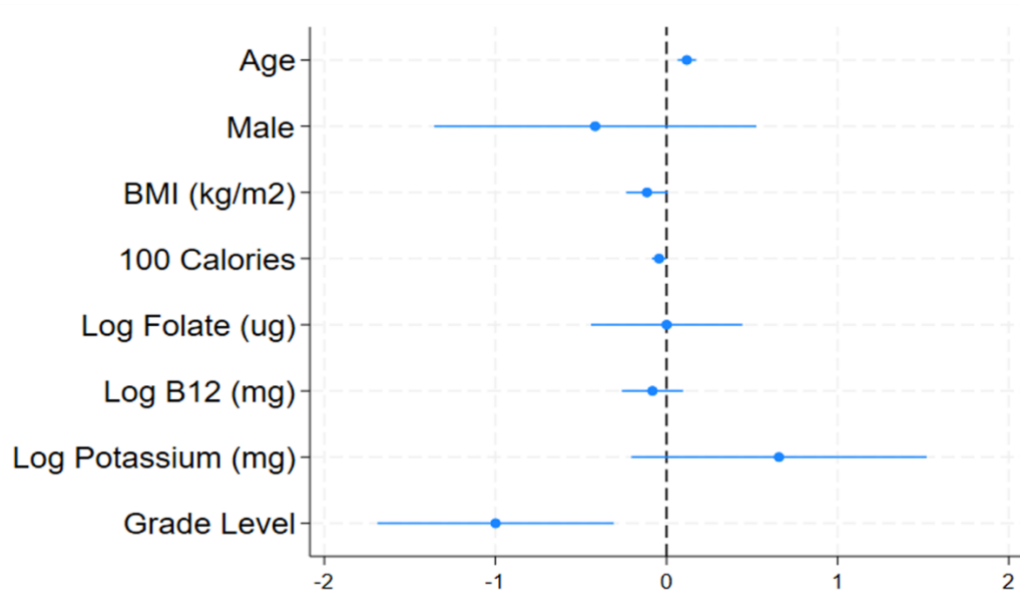


Figure 1. Logistic regression model controlling for age, sex, body mass index, and education for dementia

## Nutrition and cognitive function

Controlling for age, sex, body mass index, and education, those with higher folate intake had better fluid cognitive scores ( $b=0.31$ ,  $p=0.028$ ), while those with higher potassium intake had poorer fluid cognition ( $b=-.50$ ,  $p=0.038$ ). There was no observed impact of any nutritional marker on crystallized cognition. Higher folate intake was positively associated with fluid cognition while higher potassium was negatively associated with cognition.

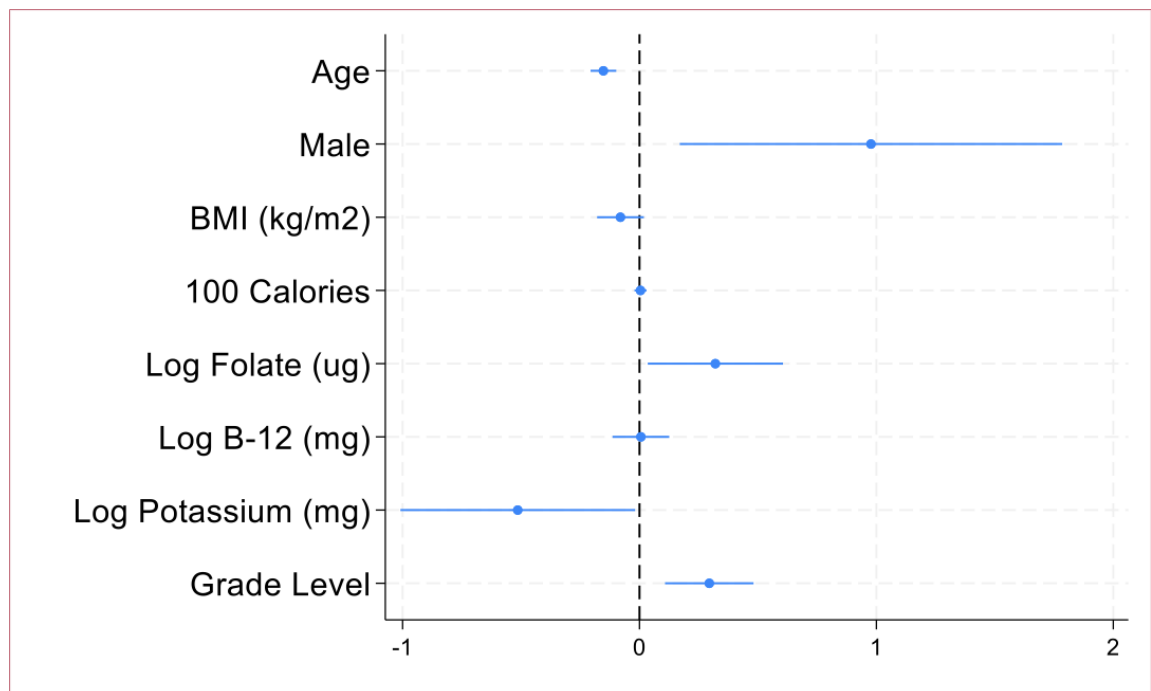


Figure 2. Mixed effects linear regression for cognition scores, controlling for age, sex, body mass index and education.

## DISCUSSION

After controlling for demographic factors, including age, sex, body mass index, and education, it was found that higher folate intake was associated with improved fluid cognitive scores, while those with higher potassium intake had poorer fluid cognition. There was no observed impact of any nutritional marker on crystallized cognition. Additionally, these data suggest that higher caloric intake is associated with lower odds of cognitive impairment in a subsistence population, highlighting potential life history tradeoffs in investing in the maintenance of cognitive function.

Previous US-based literature has identified that vitamin B-12 and folate deficiencies can increase the risk of developing mild cognitive impairment in older adults (Jatoi et al. 2020; Lauer et al. 2022; Wang et al. 2022). The significant positive association observed between folate intake and fluid cognition scores indicates that there is a protective effect on cognitive function. This study also identified a negative association between potassium intake and fluid cognition, which is consistent with findings from Vintimilla et al. 2018 that identified a link between elevated serum potassium levels and an increased risk of developing mild cognitive impairment in older Mexican American adults. Nutritional transition is currently occurring in the Tsimane due to rapid acculturation, thus, future research will explore how a higher diversity of nutrients and foods can affect cognitive health and function, longitudinally (Kraft et al. 2018). The findings of this study, based in a traditional environment with limited diets, are consistent with studies that are based in industrialized environments and contribute to a wider understanding of how dietary patterns affect cognitive ability.

## CONCLUSION

This study set out to identify a link between nutrition and cognitive ability, with a focus on the micronutrients folate, B-12, and potassium. Higher folate intake was associated with improved fluid cognitive scores, while those with higher potassium intake had poor fluid cognition. Further, higher caloric intake is associated with lower odds of cognitive impairment in a subsistence population, highlighting potential life history tradeoffs in investing in the maintenance of cognitive function.

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