

Prediagnostic plasma branched-chain amino acids and the risk of amyotrophic lateral sclerosis

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Study objective

To determine whether prediagnostic levels of plasma branched-chain amino acids (BCAAs) are associated with the risk of amyotrophic lateral sclerosis (ALS).

Summary results

BCAA levels are not associated with the risk of ALS.

What is known and what this paper adds

Because several clinical trials have found evidence that BCAAs worsen the conditions of patients with ALS, researchers have hypothesized that BCAAs are risk factors for ALS. This study reports evidence against that hypothesis.

Participants and setting

This study reviewed data for participants in 5 large prospective cohort studies: the Nurses' Health Study (1976–2010), the Health Professionals Follow-up Study (1986–2010), the Cancer Prevention Study II Nutrition (1992–2010), the Multiethnic Cohort (1993–2012), and the Women's Health Initiative (1993–2012). This study identified 275 individuals (27.3% male) from these cohorts who developed ALS during follow-up. For each case, this study selected 2 controls who were matched to the case by cohort, age, sex, fasting status, and time of blood draw.

Design, size, and duration

This study used hydrophilic interaction liquid chromatography coupled to positive ion mode mass spectrometry to assay plasma samples for metabolites. The technicians performing the assays were blinded as to case/control status for each plasma sample. Data for clinical covariates were obtained from the cohort study databases. This study used conditional logistic regression to estimate rate ratios (RRs) and 95% confidence intervals (CIs) for the associations between variables and ALS.

Table Associations between BCAA levels and the risk of ALS

BCAA	RR (95% CI) for ALS in top quartile vs bottom quartile	<i>P</i> _{trend}
Leucine	0.87 (0.57–1.33)	0.40
Isoleucine	0.81 (0.52–1.24)	0.29
Valine	0.80 (0.52–1.23)	0.14

The regression model included adjustments for the matching variables, body mass index, smoking, education, and physical activity.

Primary outcome measures

The primary outcomes were the associations between prediagnostic BCAA levels and ALS.

Main results and the role of chance

None of the BCAAs was a risk factor for ALS.

Bias, confounding, and other reasons for caution

The identification of only 275 cases of ALS might have limited this study's statistical power. This study only had a single plasma sample for each participant. This study cannot exclude the possibility of residual confounding.

Generalizability to other populations

Men were underrepresented in this study's sample of cases of ALS. This may limit the generalizability of this study's results.

Study funding/potential competing interests

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A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The authors of the full-length article and the journal editors edited and approved the final version.

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