Letter to the Editor in response to: Potential confounding in a study of dietary inflammatory index and cognitive function

We appreciate the opportunity to respond to the letter recently published by Dr Ma regarding our paper in the British Journal of Nutrition. We believe that Dr Ma makes some points that deserve a clarifying response. First, concern was expressed that we failed to control for potential confounding of the relationship between dietary inflammatory index (DII) scores and memory function by education and other aspects of socioeconomic status (SES). While factors related to SES, including education, often prove to be important predictors of health outcomes, recent findings from a cross-national study demonstrate that education fails to slow cognitive decline within ageing populations when controlling for income status. In addition, it appears that differences in baseline cognition are not modified by income or level of education. Furthermore, SES could modify cognitive decline via differences in health behaviours, including dietary habits. As dietary intake may be a mediator through which poverty influences cognitive decline, controlling for poverty may have the potential to over-adjust the model and underestimate the impact of diet on memory function. For example, if most of the ‘cause’ of decline in memory is due to diet-associated inflammation, and if SES is correlated with diet, then fitting the typical regression model will incorrectly ascribe the variance to SES (because each effect in the default orthogonal model is fit as though it entered last). Despite this, we agree that it is important to examine this issue further. Thus, we conducted additional analyses to address the aforementioned concerns. When controlling for income-to-poverty ratio alone and the combined effects income-to-poverty ratio and education level, among those with an elevated DII on memory functioning, these results obtained remained similar, though in some instances attenuated, across all DII quartiles when compared with the original results. As an example, for semantic memory, and when comparing those in quartile 4 v. 1, results were statistically significant in both the originally published results ($\beta = -1.18$, 95% CI $-2.17$, $-0.20$) and as well as in the new models including poverty ($\beta = -1.04$, 95% CI $-2.02$, $-0.06$) and both poverty and education ($\beta = -0.98$, 95% CI $-1.97$, $-0.01$).

In addition, Dr Ma cautions that generalisability of our findings may be limited by our decision to exclude individuals with various chronic disease diagnoses. We agree that excluding individuals who self-reported suffering from congestive heart failure, coronary artery disease, heart attack/myocardial infarction (MI), stroke, and/or physician-diagnosed diabetes reduces generalisability to these populations. However, our nationally representative sample retains the ability to adequately represent the remainder of the broader population reporting no evidence of these conditions. Further, our primary aim was to isolate the specific relationship between DII and cognitive function. To satisfy this objective, we felt it was critical to exclude participants with diseases that also have been found to influence cognitive functioning and are related to dietary behaviour, and thus, could markedly influence the magnitude of association observed between the noted variables of interest, DII and cognitive function. Further, including matching and statistical adjustment, ‘restriction’ (i.e. excluding subpopulations from an analysis) is a commonly employed epidemiological strategy to help control for confounding. Nevertheless, we conducted additional analyses (not excluding the noted comorbidities) to evaluate whether these comorbidities differentially influenced the relationship between DII and cognitive function. These additional statistical analyses: (1) included data from individuals with co-morbid conditions and (2) adjusted for these morbidities in the model. The results from both alternative models were similar to the original findings that excluded data from these participants. For example, for semantic memory, our original results showed that those in the upper DII quartile (v. lower quartile) had worse memory function ($\beta = -1.18$, 95% CI $-2.17$, $-0.20$). Results were attenuated, but the conclusion was unaltered when we included data from patients with the above-noted comorbidities ($\beta = -0.96$, 95% CI $-1.79$, $-0.12$) and when data were added as covariates ($\beta = -0.99$, 95% CI $-1.83$, $-0.15$).

We appreciate Dr Ma’s interest in our work and the opportunity to conduct alternative analyses to address the stated concerns. The main finding of our study was that higher DII was associated with worse memory performance. We feel confident in these findings, especially after utilising Dr Ma’s letter as constructive impetus to conduct additional analyses controlling for poverty, education and comorbidities. Future work in this arena should be conducted with an appreciation for the potential importance of social determinants of health outcomes and the relationship that these factors may have with dietary factors.

Emily Frith¹, Nitin Shivappa²,³, Joshua R. Mann⁴, James R. Hébert²,⁵, Michael D. Wirth⁵ and Paul D. Loprinzi¹

¹Physical Activity Epidemiology Laboratory, Exercise Psychology Laboratory, Department of Health, Exercise Science and Recreation Management, University of Mississippi, Oxford, MS 38677, USA
References


