Reply to Itzhaki

To the Editor—We thank Drs Itzhaki and Klapper for their interest in and comments regarding our study [1], which examined the relationship between cytomegalovirus (CMV) infection and risk of Alzheimer’s disease (AD). We found that CMV seropositivity was associated with a 2-fold increase in risk of AD and a faster rate of cognitive decline. The results were robust to a number of covariates, including herpes simplex virus type 1 (HSV-1). In addition, our findings support earlier cohort studies that have examined the association between CMV and cognitive function [2, 3]. Together, these studies suggest a potential role for CMV as a factor that may influence cognition and risk of AD in older ages.

As Itzhaki and Klapper state, one must use assays of equivalent sensitivity when comparing serological evidence of past exposure to HSV-1 with that of CMV. We agree. Although the assays used for immunoglobulin G antibodies to CMV and HSV-1 were different in antigenic composition, both have been widely used in epidemiologic studies in different populations. We reported that rates of positivity for HSV-1 in our sample were much lower than for CMV, and that this discrepancy might be a reason for the lack of associations with HSV-1. Few large epidemiologic studies with older adults have specifically addressed HSV-1 [4]. Nonetheless, the lack of an association between HSV-1 antibodies and AD in our study does not preclude a role for HSV-1 in some cases of AD, using more sensitive immunological or virologic methods.

The authors state that our findings contrast with others who have found a relationship between HSV-1 and cognitive decline. However, the studies cited are cross-sectional rather than longitudinal, which is needed to document cognitive decline, and most were small case-control studies of HSV-1 in the brain. Thus, the association of HSV-1 and incident AD remains unknown at this time. Overall, the evidence points to a role for herpesvirus infections in some cases of AD. Indeed, identifying an association between CMV and AD supports the hypothesis that herpesviruses may play an important role in disease risk, and does not negate a potential role for other pathogens in AD. A better understanding of the role of individual infectious agents or their combination will require large-scale studies involving different populations and, ultimately, intervention studies using specific prevention and treatment modalities.

Notes

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References


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