WriteClick: Editor's Choice

Editors' Note: Kezuka et al. report their experience with patients with neuromyelitis optica who were positive to both AQP4 antibodies and MOG antibodies, which seems to differ from the clinical profile reported by Sato et al. The latter wonder whether those findings are due to false-positive results on ELISA testing. Kabai suggests that the self-reported alcohol consumption in the study on alcohol consumption and cognitive decline in early old age may be underestimated and hence the study findings may be biased. Sabia and Singh-Manoux respond.

—Chafic Karam, MD, and Robert C. Griggs, MD

DISTINCTION BETWEEN MOG ANTIBODY–POSITIVE AND AQP4 ANTIBODY–POSITIVE NMO SPECTRUM DISORDERS

Takeshi Kezuka, Tokyo; Keiko Tanaka, Ishikawa, Japan; Yoshimichi Matsunaga, Hiroshi Goto, Tokyo: Sato et al.[1] reported results from Japanese and Brazilian patients with neuromyelitis optica (NMO) evaluated for the presence of serum antibodies targeting aquaporin-4 (AQP4) and myelin oligodendrocyte glycoprotein (MOG). In their study, none of the patients was positive for both anti-AQP4 and anti-MOG antibodies. However, in our previous study, 6 of 23 (26%) patients were seropositive for both anti-NMO and anti-MOG antibodies.[2] Editorialists Weinshenker and Wingerchuk[3] suggested that the difference in methodology of detection (ELISA in our study vs cell-based assay in Sato et al.) may have contributed to the discrepancy. However, in a recent cell-based assay using full-length human MOG cDNA-expressing HEK cells, we found 2 patients who were anti-AQP4+ and anti-MOG+. Both patients were middle-aged women with NMO and both had repeated ocular attacks; 4 times in one and 8 times in the other. Both had bilateral optic neuritis with longitudinally extensive myelitis. The clinical characteristics of these 2 patients are recurrent optic neuritis and poor visual outcome despite treatment, which differs from the clinical profile reported by Sato et al.[1] Our results indicate that anti-AQP4+ and anti-MOG+ NMO does exist, irrespective of the methodology of anti-MOG antibodies detection, and this form of NMO often has severe ocular disease.

Author Response: Douglas K. Sato, Toshiyuki Takahashi, Sendai, Japan; Patrick J. Waters, Oxford, UK; Kazuo Fujihara, Sendai, Japan: The authors thank Kezuka et al. for sharing their experience with 2 patients with NMO who were likely to be positive to both AQP4 antibodies and MOG antibodies. The clinical features of these 2 patients were compatible with AQP4 antibody–seropositive NMO as both were middle-aged women with severe attacks of optic neuritis and longitudinally extensive myelitis.[4,5] The patients with AQP4 antibodies were not expected to have a less severe disease course, as we found in our cases with MOG antibodies alone.[1] Similar to our results, Kitley et al.[6] reported patients with NMO spectrum disorder with AQP4 antibodies (n = 20) or MOG antibodies (n = 9) tested at Oxford University with no double-positive cases. However, this does not exclude the possibility of double-positive cases. Their and our patients with MOG antibodies have similarities. Currently, it is not clear if differences on the cell-based assays developed by each center could yield different results. The positivity for both antibodies, instead of nonspecific binding, might be clarified by testing MOG antibodies in preadsorbed sera for AQP4 and vice versa. Kezuka et al. also reported that 4 of 6 patients (66.7%) may have had false-positive results by ELISA for MOG antibodies, suggesting that ELISA failed to discriminate conformational-specific MOG antibodies.[7]

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ALCOHOL CONSUMPTION AND COGNITIVE DECLINE IN EARLY OLD AGE

Peter Kabai, Kaposvar, Hungary: Sabia et al.[1] correctly stated that "some participants may have underestimated their consumption." In 1999, total alcohol consumption for the United Kingdom per capita for those aged 15 years and older was estimated at 10.3 L reported plus about 1.7 L unreported absolute alcohol.[2] Drinking 12 L a year equals about 26 g of alcohol per day per person. Using data in table 1,[1] the median self-reported consumption is 10.6 g per day per person, which is less than half of the estimated consumption for the United Kingdom in 1999. However, the true average consumption of the study population may be different when taking the maximal consumed value for each category, as the calculated maximal consumption is still lower (22.5 g/day/person) than the average consumption in the United Kingdom. It is likely that the data are biased because heavy drinking was substantially underestimated.[3] The association between drinking habits and cognitive abilities at older age is a novel study and it is important to rigorously estimate the possible bias of the data.

Author Response: Severine Sabia, London; Archana Singh-Manoux, Paris: The authors thank Dr. Kabai for his comments on our article.[1] The Whitehall II study is not representative of the general population. Dr. Kabai estimated alcohol consumption in the United Kingdom at "26 g of alcohol/day per person"; in our study it was 16 g/day in men and 7 g/day in women. The difference is that our study comprised older adults with stable civil service jobs who were healthier than the general population.[4] We made no claims about calculating mean average consumption in the UK population. In addition, the lower prevalence of heavy drinkers in our study is unlikely to have biased associations with cognitive decline. To assess these associations, we modeled the continuum of alcohol consumption using refined categories in the supplementary analyses to show harm to cognitive health in those who drank 36 grams or more of alcohol every day. We could not examine the effects on cognitive decline among those drinking even higher quantities as few participants in our cohort drank more. However, this does not imply that the results for participants in the 36 g/day category are biased.

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