# *Helicobacter Pylori*-Related Vitamin B12 Deficiency: A Potential Contributor in Neuropsychiatric Disorders

Sir,

Issac *et al.* concluded that Vitamin B12 deficiency, common in India, increases the load of cognitive decline and accentuates vascular risk factors in neuropsychiatric illnesses; it also increases homocysteine (Hcy) levels contributing to the vascular comorbidity in cerebro- and cardio-vascular disorders, thereby correcting this reversible Vitamin B12 deficiency state is of profound importance.[1]

In this regard, *Helicobacter pylori* infection (*Hp*-I), also very common in India, is a potential environmental risk factor contributing to the pathophysiology of several neuropsychiatric diseases. Based on the histologic analysis of gastric mucosa biopsy for the documentation of *Hp*-I, a higher prevalence of *Hp*-I in Alzheimer's disease (AD) and mild cognitive impairment (MCI) patients in a Greek cohort has been found accompanied with increased Hcy concentration, an independent risk factor for dementia and AD,[2-4] also mentioned by the authors;[1] increased cerebrospinal fluid anti-*Hp* IgG antibody levels in AD patients may reflect the disease severity, and *Hp* eradication may positively influence AD manifestations at 2- and 5-year clinical endpoints.[2-4] Consistent associations with the Greek data were shown in subsequent studies from France, USA, and China, supporting *Hp*-I role in AD pathobiology.[5]

In our studies, multifocal chronic gastritis (body and antrum atrophy) was observed in the majority of our patients with AD and MCI compared with controls.[2,3] These patterns of *Hp*-related chronic gastritis have also been reported by others.[2,3] Moreover, the increased serum Hcy concentration observed in our AD and MCI patients, has been reported by others in MCI and AD,[2,3] including the authors as well.[1] Chronic gastritis

owing to *Hp*-I can lead to malabsorption of Vitamins B12 and folate, which results in failure of methylation by 5-methyl-tetrahydrofolic acid and hence accumulation of Hcy.[2,3] The increased Hcy, in turn, could trigger endothelial damage and result in atherothrombotic disorders and AD. In this respect, investigators reported that *Hp*-induced chronic atrophic gastritis or atrophic gastritis *per se* decreases serum Vitamin B12 and folate concentrations, thereby increasing the Hcy, a potent contributor to vascular disorders; serum Hcy concentrations correlated inversely with serum Vitamin B12 and folate levels and positively with atrophic scores. Hcy is thought to be implicated in endothelial damage and neurodegeneration via oxidative injury in these diseases; oxidative damage has been described in the brain of subjects with MCI, suggesting that oxidative damage may be one of the earliest events in the onset and progression of AD.[3] Importantly, serum Hcy concentrations are independently associated with the progression of MCI to AD and also correlate with the severity of dementia.[3] Considering the above mentioned data, we can speculate that *Hp*-I might contribute, at least in part, to the pathogenesis of AD through the sequence: Induction of chronic atrophic gastritis-malabsorption of Vitamins B12 and folate-increased Hcy — development of dementia and other neuropsychiatric disorders. Moreover, *Hp*-positive MCI patients accompanied by increased Hcy may be more likely to progress to AD. However, large-scale future studies are warranted to elucidate the proposed pathophysiological mechanisms involved in *Hp*-associated neuropsychiatric illnesses.

**Jannis Kountouras, Stergios A. Polyzos, Nikolaos Grigoriadis, Georgia Deretzi**

Department of Medicine, Second Medical Clinic, Aristotle University of Thessaloniki, Ippokration Hospital, Thessaloniki, Greece

**Address for correspondence:** Dr. Jannis Kountouras
Department of Medicine, 8 Fanariou St., Byzantio - 551 33, Thessaloniki, Macedonia, Greece.
E-mail: jannis@auth.gr

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