ABO blood group and neurodegenerative disorders: more than a casual association

Massimo Franchini¹, Giancarlo M. Liumbruno²

¹Department of Haematology and Transfusion Medicine, "Carlo Poma" Hospital, Mantua; ²Italian National Blood Centre, National Institute of Health, Rome, Italy

Along with their expression on red blood cells, ABO blood group antigens (namely, A, B, AB and O) are also highly expressed by a large number of human cells and tissues including epithelia, platelets, vascular endothelia and neurons. Over the last 50 years, various investigators have assessed whether this biological characteristic of the ABO blood system has a clinical significance beyond that played in transfusion and transplantation medicine. Indeed, there is now a large body of evidence on the role of ABO antigens in the pathogenesis of various systemic diseases, including cancer, infectious disorders and cardiovascular diseases. Considering the role played by the ABO system in neurogenesis, some investigators have studied the system’s relationship with ageing-related neurodegenerative disorders, but with conflicting results. While no significant differences was found in ABO blood group distribution in Parkinson’s disease patients compared with controls in two studies conducted by Strang and by Chia and Liu, in another study published by Kak and Gordon there was an excess of blood group B among patients with Parkinson’s disease. No significant association between ABO blood groups and Alzheimer’s disease was found by Renvoize or, more recently, by Vasan and colleagues. The interest in the link between ABO antigens and neurological disorders has been recently renewed thanks to two further published studies. The first case-control study (495 cases with cognitive impairment and 587 controls) was conducted by Alexander and colleagues and tested the possibility that non-O blood type adults might show poorer cognitive trajectories. The authors found that AB blood type and increased coagulation factor VIII levels were associated with a higher incidence (odd’s ratio for AB blood type vs O blood type: 1.82, 95% confidence interval: 1.15-2.90; odd’s ratio for each 40 IU/dL higher factor VIII: 1.24, 95% confidence interval: 1.10-1.38) of cognitive decline. In the second, more recent study, De Marco and Venneri investigated volumetric differences in grey matter between O (76 cases) and non-O (113 cases) healthy individuals. Surprisingly, the authors observed that O blood type, compared with non-O blood type, was associated with larger volumes of grey matter in the cerebellum and temporal-mediotemporal/limbic regions, suggesting that O blood group might play a protective role against those ageing-related neurodegenerative conditions, particularly Alzheimer’s disease, associated with volumetric loss in these cerebral areas. The most reasonable explanation for the protection exerted by O blood type against the cognitive decline typical of ageing-related neurodegenerative disorders lies in the lower levels of circulating von Willebrand factor and factor VIII levels observed in O blood type individuals than in non-O blood type individuals, which could reduce the risk of thrombotic adverse events, including those in the brain, in the former group. This hypothesis is compatible with the results of a recently published systematic review and meta-analysis documenting a positive association between increased levels of some haemostatic markers, including von Willebrand factor, in vascular dementia and cognitive impairment. The increased prevalence of O blood type found in centenarians in two recent studies by our group is also in agreement with these findings, suggesting that individuals with group O might be less vulnerable to age-related illnesses with a resulting longer life-expectancy. However, another possible intriguing mechanism could involve the anti-angiogenic properties of von Willebrand factor, resulting in a positive modulation of brain vascular endothelium in O blood type individuals, who have lower von Willebrand factor and factor VIII plasma levels than non-O subjects. Further experimental and clinical studies on large cohorts of patients are needed to elucidate the association between ABO blood type and degenerative neurological disorders and the underlying pathogenic mechanisms.

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References
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Correspondence: Massimo Franchini
Department of Haematology and Transfusion Medicine
Carlo Poma Hospital
Strada Lago Paiolo 10
46100 Mantova, Italy
e-mail: massimo.franchini@aopoma.it