Dear Sir,

What do platelets and their proteins have to do with Alzheimer's disease (AD)? To answer that question, we enrolled patients in the following pilot study. AD is the most common form of dementia in the elderly. Recent findings have suggested an involvement of brain-derived neurotrophic factor (BDNF) and altered platelet functions in the pathogenesis of AD (1, 2). BDNF is an endogenous protein involved in the maintenance of neuronal function, synaptic plasticity and structural integrity in the adult brain. Since platelets are supposed to be an important source of BDNF in the circulation (3), we examined blood levels of BDNF and β-thromboglobulin (β-TG), an established platelet activation marker (4), in AD patients and healthy controls.

Twenty-eight AD outpatients from our Memory clinic [11 males and 17 females, mean age 70.4 years, mean Mini-Mental State Examination (MMSE) score of 23.7] and 10 healthy elderly controls (six males and four females, mean age 69.1 years, mean MMSE score of 28.4) were included in the study. All AD patients met the diagnostic criteria of probable AD according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-4), the ICD-10 Classification of Mental and Behavioural Disorders (ICD-10) and the criteria of the National Institute of Neurologic and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) (5). The severity of dementia was assessed by MMSE (6). The control subjects were healthy elderly volunteers with normal clinical and cognitive status according to clinical examination and MMSE score. Patients or control subjects with current or a history of depression or psychosis, with neurologic disorders, major physical illness, alcohol or substance abuse or use of psychoactive medications were excluded from the study. The regional ethical committee approved the study and written informed consent was obtained from each individual. Peripheral venous blood was sampled between 8:00 and 9:00 a.m. taking in account a possible circadian rhythm. Serum and plasma were centrifuged within 30 minutes.

Figure 1: Box plot of BDNF serum (A) and β-TG plasma (B) concentration (ELISA). The box refers to the middle 50% (interquartile range) of the value distribution in each group. The bold line refers to the median. The whiskers represent minimum and maximum scores up to 1.5 times the interquartile range.

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after gaining and stored at –20°C until further analysis. Serum and plasma levels of BDNF were measured using an enzyme-linked immunosorbent assay (ELISA) kit (R&D Systems GmbH Wiesbaden-Nordenstadt, Germany) according to the manufacturer’s instructions. Plasma levels of β-TG were also measured using an ELISA kit (Roche Diagnostics, Mannheim, Germany). All samples and standards were measured in duplicates, and the means of the duplicates were used for statistical analyses. The detection limit for BDNF was 62.5 pg/ml. The detection range for β-TG was 5–220 IU/ml. The intra- and interassay coefficients of variation of both BDNF and β-TG were <10%. The statistical analysis of differences between two groups was performed using the two-tailed t-test. The correlation between two variables was determined by using Kendall-Tau-b-test. Significance for the results was set at p<0.05. All statistical analyses were carried out using the statistical analysis software package SPSS 12.0® (Munich, Germany).

AD patients and healthy controls were comparable regarding age and gender. In AD patients, BDNF plasma levels showed a trend of correlation with platelet count (r=0.257, p=0.055). We found no significant correlation between MMSE scores and BDNF levels in AD patients and controls (data not shown). We found significantly decreased BDNF serum concentrations in AD patients (18.3 ng/ml) as compared to healthy controls (21.6 ng/ml; p=0.048) (Fig. 1A) and no significant difference of BDNF plasma levels between AD (1.460.3 pg/ml) and control subjects (1.372.2 pg/ml; p=0.822). β-TG plasma levels were highly significantly decreased in AD patients (177.1 IU/ml) in comparison to healthy controls (192.0 IU/ml; p<0.0001) (Fig. 1B). Using a cut-off value for β-TG plasma concentration of 185.5 IU/ml efficiently distinguished AD patients from healthy controls with a sensitivity of 92.9 % and a specificity of 90.0 %. In AD patients, BDNF serum concentration correlated significantly with β-TG (r=0.307, p=0.022; Fig. 2) and BDNF plasma values (r=0.370, p=0.006). In contrast, BDNF and β-TG plasma values showed no significant correlation (r=0.111, p=0.407). In healthy controls, we found a tendency of a positive correlation between BDNF and β-TG plasma levels (r=0.467, p=0.060) and no correlation between BDNF serum and BDNF/β-TG plasma values (r=0.067, p=0.788/r=0.067, p=0.788).

In conclusion, levels of BDNF and β-TG in the blood of patients with Alzheimer’s disease are decreased compared with controls. In addition, our results confirm an association between BDNF serum concentration and the degree of platelet activation as measured by β-TG plasma levels. Regarding the neuroprotective role of BDNF in the brain and the implications of BDNF in the molecular biology of memory, these findings seem to be valuable for a putative diagnostic evaluation of BDNF levels in the serum of patients. Platelets could be part of the pathogenesis of AD, alternatively AD pathogenesis could be responsible for BDNF results. As a possible therapeutic hypothesis of this study, the influence of different strategies to increase the BDNF allocation in the brain and blood seems to be relevant for the prevention and possibly for the treatment of Alzheimer’s disease. Further research on the field of AD should focus more intensely on platelets and their proteins. Determination of BDNF may be of diagnostic or prognostic value for AD.

References