Inflammatory markers and their association with post stroke cognitive decline

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Introduction

Inflammation has been hypothesized to play a role in cognitive impairment, particularly in Alzheimer’s disease (AD) and vascular dementia (VAD). Studies have shown that AD patients have elevated levels of cytokines and acute phase reactants (1,2). Similarly, increasing levels of inflammatory markers have been linked with increased incidence of VAD (3). More recent studies in general populations have shown that blood markers of inflammation such as interleukin (IL)-6 (4) and C-reactive protein (CRP) (5) are predictive of both current cognitive function and subsequent cognitive decline. Several inflammatory markers could possibly be involved in mediating the inflammatory processes in acute stroke. CRP, IL-1β, IL-6, IL-8, IL-12, IL-10, and tumor necrosis factor-α (TNF-α) have all been hypothesized to have a role in prognosis after stroke (6).

Most studies examining the association between cognitive functioning and inflammation to date have been population based (7,8). Few studies have looked at the effect of inflammation on cognitive function in a poststroke setting (6). In addition, most studies to date have focused on IL-6 and CRP (4,5,7). Therefore, in this study we aimed to determine the association between a wider panel of inflammatory markers and poststroke cognitive function. In addition, we aimed to determine the association between inflammatory markers and poststroke cognitive decline.

Methods

Subjects

All patients with recent transient ischemic attacks (TIA) or non-disabling ischemic stroke who were seen in the Singapore General Hospital between 1999 and 2005 were screened for eligibility for the European Australasian Stroke Prevention in Reversible Ischemia Trial (ESPRIT). Detailed methodology for the main study have been previously reported (9). Briefly, patients were eligible if they were within six-months of a transient ischemic attack (including transient monocular blindness) or nondisabling ischemic stroke of presumed arterial origin. The exclusion criteria were a possible cardiac source of embolism, high-grade carotid stenosis for which carotid endarterectomy or endovascular treatment was planned, any blood coagulation disorder, any contraindication for aspirin or dipyridamole, and a limited life expectancy from comorbidities such as cancer or autoimmune and inflammatory conditions. Patients who were unstable at the baseline cognitive assessment due to acute infection were also excluded. In addition, as the mechanisms behind the association of cognition and inflammatory markers may be different in patients with TIAS versus ischemic strokes, we have excluded patients with TIAS from the current analyses.

Standard protocol approvals, registrations, and patient consents

The study protocol was approved by Singapore General Hospital’s Institutional Review Board and Ethics Committee. Written informed consent was obtained from all patients or legal guardians. The ESPRIT Trial was registered under clinicaltrials.gov with the identifier NCT00161070.