Association of silent lacunar infarct with brain atrophy and cognitive impairment

Jamie Yu Jin Thong,1 Saima Hilal,2 Yanbo Wang,1 Hock Wei Soon,1 Yanhong Dong,2 Simon Lowes Collinson,3 Tuan Ta Anh,1 Mohammad Kamran Ikram,4,5 Tien Yin Wong,4,5 Narayanaswamy Venketasubramanian,6 Christopher Chen,2 Anqi Qiu1,7,8

ABSTRACT
Objective Silent lacunar infarct (SLI) is associated with cognitive decline and linked to an increased risk of stroke and dementia. We examined the association of SLI with MRI measures of cortical thickness, subcortical and lateral ventricular shapes and cognition in 285 ethnic Chinese elderly.

Methods SLI, cortical thickness, shapes of subcortical and ventricular structures were quantified using MRI. The cognitive performance was assessed using comprehensive neuropsychological tests. Linear regression was used to examine associations among SLI, brain measures and cognition.

Results SLI was associated with atrophy in multiple subcortical structures, ventricular enlargement and widespread cortical thinning. Both SLI and atrophy were independently related to poorer performance in attention, memory and language domains. Only SLI was associated with visuomotor speed and executive function, while atrophy mediated the association between SLI and visuoconstruction.

Conclusions Our findings support a vascular contribution to neurodegeneration and cognitive impairment.

INTRODUCTION
Silent lacunar infarcts (SLI) are often detected with MRI or CT, but are not accompanied by any overt symptoms. SLI is now known to be linked to an increased risk of stroke and dementia.1 Additionally, SLI is associated with reductions in global cognitive ability and specific cognitive domains such as memory and psychomotor speed.2, 3 Blum et al4 recently reported that the hippocampus is smaller in elderly people with SLI than in controls and that SLI contributes to memory deficits independent of hippocampal atrophy. Blum et al4 focused only on hippocampal atrophy; however, infarcts in subcortical regions can also lead to hyperfusion and hypometabolism in both subcortical and cortical regions5–7 and may lead to global neuronal loss.8 Nonetheless, it remains largely unknown to what extent SLI is associated with cortical and subcortical atrophy in the elderly. It is also unclear if SLI as well as cortical and subcortical atrophy independently contribute to impairment in multiple cognitive domains (eg, executive function, attention, language, memory, visuomotor speed and visuoconstruction) or to which extent atrophy mediates the relationship between SLI and impairment in specific cognitive domains.

Here, we employed an advanced brain mapping technique, large deformation diffeomorphic metric mapping (LDDMM),9 to examine cortical thickness as well as subcortical and lateral ventricular shapes in association with SLI and cognition in Chinese elderly. We hypothesised that SLI would be associated with widespread cortical atrophy and that subcortical shape abnormalities in SLI would be observed not only in the hippocampus but also in the basal ganglia and thalamus. Moreover, in the view of the work in Blum et al4, we anticipated independent contributions of SLI to memory loss as well as to cognitive deficits in other domains, including executive function, attention, language, visuomotor speed and visuoconstruction, beyond the contributions of cortical and subcortical atrophy.

METHODS
Subjects
The present study involved 330 ethnic Chinese subjects drawn from the Epidemiology of Dementia in Singapore (EDIS) study, which is a population-based study among Chinese, Malays and Indians. In the present study, we restricted analysis to the Chinese component of EDIS, as the recruitment of the other ethnicities is still ongoing. In the first phase of the EDIS recruitment, Chinese participants aged >60 years underwent cognitive screening using the Abbreviated Mental Test (AMT) and a self-report of progressive forgetfulness. The AMT is a 10-item self-report scale that was initially designed to rapidly assess the elderly for the possibility of dementia. It is now used widely as a screening tool for cognitive impairment.10 This screening tool has been previously validated in Singapore.11, 12 Screen positives were defined as AMT score ≤6 among those with ≤6 years of formal education or ≤8 among those with >6 years of formal education, or if the subject or caregiver reported progressive forgetfulness. Screen-positive subjects were invited to take part in the second phase of this study. During the second phase of this study, participants underwent extensive clinical and neuropsychological examination along with laboratory tests and MRI. The recruitment procedure, the details of the EDIS study methodology and an accompanying flowchart depicting the recruitment flow have been described elsewhere.13