A population-based study of cognitive decline and peripheral inflammatory gene expression

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Abstract

Neuroinflammation has a key role in the pathology of cognitive decline. This study sought to determine whether peripherally expressed inflammatory transcripts had significant associations with cognitive performance or cognitive decline, using genome-wide and focussed candidate gene analyses.

The study used data from 691 participants from the InCHIANTI study of ageing. Participants had undertaken Mini-Mental State Examinations at enrolment and at year 9 of follow-up, and provided peripheral whole blood samples for RNA extraction at year 9. Global gene expression data was generated using the Illumina Human HT12 BeadChip microarray. The study analysed global and inflammatory-focussed gene expression associations with cognitive performance and decline, and gene pathway associations with cognitive performance/decline. A candidate-driven RT-PCR expression quantitative trait locus (eQTL) analysis was also performed to determine whether genetic variants associated with cognitive decline affected gene expression abundance in association with phenotypic variation.

Raised expression of a single transcript, C-C chemokine receptor 2 (*CCR2*), had a significant association with poor cognitive performance at global expression analysis and with both cognitive performance and cognitive decline in focussed inflammatory subset analysis. Expression of *CCR2* in transgenic animals has previously been associated with both cortical Alzheimer disease pathology and peripheral vascular disease. eQTL analysis identified five significant eQTLs for local genes but no significant associations between peripheral expression of these genes and cognitive decline.

This study's analyses present little evidence that peripheral inflammatory gene expression is playing a significant role in cognitive impairment or preceding 9-year cognitive decline in this cohort. Only one inflammatory transcript (*CCR2*) was significantly associated with cognitive impairment at genome-wide analysis. The *CCR2* knockout mouse has been shown

to have Alzheimer's-like pathology; results of this study indicate that the mouse model may have relevance for the human population.

List of contents