

The Role of the Kynurenine pathway in Vascular Cognitive Impairment: A Prospective Clinical Study

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Background:

The kynurenine pathway (KP) is the main metabolic pathway of tryptophan degradation and has been associated with neurological diseases such as stroke and cognitive functioning. However, as studies investigating associations between the KP and post-stroke cognitive impairment are scarce, contain a relatively small sample size or focused on a limited number of metabolites, the role of the KP in this condition remains unclear. Therefore, the present study aimed to investigate KP metabolites as potential early markers for changes in post-stroke cognitive functioning over time.

Methods/ analysis:

Data was used from 200 patients aged 65.4 ± 10.8 years, 69.5% men, who were followed up over a period of 3 years after stroke. At baseline, plasma concentrations of tryptophan and eight kynurenines were quantified. Neuropsychiatric assessment consisted of a standardized test battery. Baseline and longitudinal associations of kynurenines with vascular cognitive impairment (VCI) and cognitive domain scores were investigated using linear mixed models, while adjusting for important covariates. Non-linear associations were investigated by including a quadratic term of the metabolites.

Results:

Baseline levels of kynurenic acid and xanthurenic acid were associated with a decrease in working memory performance at 12 months compared to baseline and with lower scores 12 months after stroke. Kynurenic acid was also associated with an improvement in working memory performance 36 months after stroke compared to baseline and with better working memory scores at 36 months. Non-linear associations were found as well. Here, kynurenine was associated with a decrease in working memory and episodic memory performance between baseline and 12 months, whereas 3-hydroxykynurenine, quinolinic acid and neopterin were all associated with an improvement in processing speed between baseline at 36 months, and with better scores at 36 months. No evidence of associations were found with VCI.

Discussion:

These results are surprising given the current understanding of the role of kynurenines in neurological diseases, but should be verified in other prospective studies.

Keywords: kynurenines, stroke patients, vascular cognitive impairment