

**Breaking News on Supplements, Nutrition & Healthy Foods**

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## Further evidence for homocysteine, stroke link

**17/01/2005 - People genetically prone to high concentrations of homocysteine have a higher risk of stroke than other individuals, according to a new study that supports the theory of a causal relationship between the amino acid and stroke.**

Establishing homocysteine, an amino acid in the blood, as a cause of stroke is important for the vitamin and supplements industry as there is evidence that folic acid and B vitamins can lower its concentration, therefore protecting heart health.

Stroke is the third most common cause of death in developed countries. There are 125,000 cases of stroke in the UK each year and 60,000 deaths.

Observational studies measuring homocysteine concentrations in healthy individuals have found that, on average, those with high levels of homocysteine in their blood are more likely to have a stroke. But other factors that increase homocysteine concentration and stroke risk— such as smoking and socioeconomic class—may be responsible for the relationship observed in these studies, confounding the result.

Writing in the 15 January issue of *The Lancet* (365: 217-23), Aroon Hingorani from the University College London and colleagues describe an approach known as Mendelian randomisation used to overcome some of the problems of confounding factors seen in observational studies.

The investigators analysed published data on the association between stroke and common variation in a gene called MTHFR, which is known to influence homocysteine concentration. People randomly inherit variant (TT) of the gene, which gives them a higher concentration of blood homocysteine, or variant (CC), which results in lower levels of the amino acid in their blood.

The authors compared risk estimates from observational studies of homocysteine and stroke with those obtained from genetic studies of MTHFR and stroke. They found individuals who carried the TT genotype of MTHFR had, on average, both a higher concentration of homocysteine, and a small increase in the risk of stroke. The effect of the variant on stroke risk was close to that expected from its effect on homocysteine concentration.

*"Because of the random allocation of the gene variant in advance of disease development this concordance of risk estimates implies that the relation between homocysteine and stroke seen in observational studies is not substantially confounded by other factors,"* said Dr Hingorani.

*"Our study therefore provides evidence for a role of homocysteine in the development of stroke, though it must be emphasized that a systematic review of published studies such as this might be affected to some degree by reporting bias,"* he added.

Professor Peter Weissberg of the British Heart Foundation which funded the study told BBC News: *"We've known there is a link between blood homocysteine levels and stroke for many years, but research in this area has been complicated as homocysteine can be difficult to manipulate."*

*"Promisingly, this has revealed a much clearer relationship between homocysteine and stroke, suggesting that high levels may themselves cause stroke."*

But in an accompanying commentary in the journal (p194), Graeme Hankey and John Eikelboom from Royal Perth Hospital, Australia write that the results do not provide conclusive evidence of a causal association between homocysteine concentration and stroke because the MTHFR gene

variations might affect behavioural or socioeconomic factors. Unhealthy behaviour or low socioeconomic status may therefore be alternative explanations for the finding.

If the findings are confirmed, there is still some work to be done before the vitamin supplements are recommended to those with high homocysteine levels.

Although it is already known that folic acid can lower people's homocysteine, large randomised clinical trials of supplementation with folic acid, with or without vitamin B, will be necessary to test the therapeutic approach of lowering homocysteine concentrations to prevent stroke, said Dr Hingorani.

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