



International Congress on Economics, Management and Business Studies

Hosted Online from New York, USA

Date: 23rd June , 2026

Website: <https://econferencia.com>

PATHWAY-SPECIFIC GENETIC DETERMINANTS OF TWO COMPLICATION PHENOTYPES AFTER OPEN TRAUMATIC BRAIN INJURY

Sharifbaev S. A.

Aleynik V. A.

Vasilevskiy E. A.

Dadabaev O. T.

Andijan State Medical Institute, Andijan, Republic of Uzbekistan

Institute of Immunology and Human Genomics, Tashkent,

Republic of Uzbekistan

Background

Secondary injury after traumatic brain injury proceeds through several partly independent mechanisms, of which neuroinflammation [1], oxidative stress [2] and disruption of the blood-brain barrier with endothelial dysfunction [3] are the best characterised. Genetic association studies in this field are usually organised one gene against one outcome, most often mortality or a dichotomised functional score. Whether the biochemical pathway to which a gene belongs predicts the type of complication that develops, and not merely its likelihood, has rarely been tested directly.

Objective

To test whether six polymorphisms drawn from four biochemical pathways segregate into pathway-specific associations with two clinically distinct complication phenotypes of open traumatic brain injury.



International Congress on Economics, Management and Business Studies

Hosted Online from New York, USA

Date: 23rd June , 2026

Website: <https://econferencia.com>

Methods

The study included 101 patients with open traumatic brain injury and 80 healthy controls. Six polymorphisms were genotyped by real-time polymerase chain reaction with allelic discrimination: IL-6 rs1800795 and TNF-alpha rs1800629 (inflammatory response), APOE rs769452 (lipid transport and membrane repair), SOD2 rs4880 (antioxidant defence), eNOS rs1799983 (endothelial function) and MTHFR rs1801133 (folate metabolism). Two complication phenotypes were defined before analysis. The infectious and inflammatory phenotype comprised meningitis, ventriculitis, wound suppuration, brain abscess and cerebrospinal fluid leak. The vascular and metabolic phenotype comprised cerebral oedema, ischaemia and hypoxia. Three pathway biomarkers were measured: C-reactive protein, malondialdehyde and homocysteine. Associations were assessed by logistic regression adjusted for injury severity, age and sex.

Results

The six loci separated into two association patterns that matched their biochemical pathways, and no locus was associated with both phenotypes.

Genes of the inflammatory response were associated exclusively with the infectious and inflammatory phenotype. Carriage of the IL-6 CC genotype gave an odds ratio of 6.5 (95% CI 1.7-24.8; $p=0.003$) and carriage of the TNF-alpha A allele an odds ratio of 2.2 (95% CI 1.0-4.9; $p=0.04$). Both were accompanied by a rise in the corresponding pathway biomarker, C-reactive protein reaching 35.2 ± 11.8 mg/L in IL-6 CC carriers and 37.9 ± 12.4 mg/L in TNF-alpha AA carriers [4].

Genes of antioxidant defence, endothelial function and folate metabolism were associated exclusively with the vascular and metabolic phenotype. The SOD2 Val/Val genotype gave an odds ratio of 12.1 (95% CI 3.2-45.8; $p<0.001$) with



International Congress on Economics, Management and Business Studies

Hosted Online from New York, USA

Date: 23rd June , 2026

Website: <https://econferencia.com>

malondialdehyde of 5.9 ± 1.5 micromol/L [5], carriage of the eNOS T allele an odds ratio of 3.5 (95% CI 1.5-8.2; $p=0.003$) with homocysteine of 24.7 ± 6.9 micromol/L, and the MTHFR TT genotype an odds ratio of 8.8 (95% CI 1.7-44.5; $p=0.004$) with homocysteine of 26.8 ± 7.2 micromol/L [6].

Each association was therefore accompanied by a change in the biomarker of the same pathway, which gives a consistent chain running from genotype through biomarker to complication phenotype. APOE rs769452 did not fit either pattern and reached trend level only (odds ratio 2.5; 95% CI 0.9-6.8; $p=0.06$); it is treated as exploratory and excluded from the model. The absence of cross-pathway associations should be interpreted with caution, since the sample size limits power for the rarer genotypes and a weak cross-pathway effect could have been missed.

Conclusions

1. Five of the six polymorphisms segregate into two non-overlapping association patterns that correspond to their biochemical pathways: inflammatory response genes with infectious and inflammatory complications, and antioxidant, endothelial and folate metabolism genes with vascular and metabolic complications.
2. Every association is accompanied by a change in the biomarker of the same pathway, which supports a consistent genotype to biomarker to complication chain rather than an isolated statistical association.
3. Pathway membership predicts the type of complication and not only its probability, which argues for assembling marker panels according to coverage of pathogenetic pathways rather than according to the effect size of individual loci.
4. APOE rs769452 does not fit either pattern and reaches trend level only, so it should be reported separately as an exploratory marker.



International Congress on Economics, Management and Business Studies

Hosted Online from New York, USA

Date: 23rd June , 2026

Website: <https://econferencia.com>

REFERENCES

- [1] Simon D.W., McGeachy M.J., Bayir H., Clark R.S.B., Loane D.J., Kochanek P.M. The far-reaching scope of neuroinflammation after traumatic brain injury. *Nature Reviews Neurology*. 2017;13(3):171-191.
- [2] Fesharaki-Zadeh A. Oxidative stress in traumatic brain injury. *International Journal of Molecular Sciences*. 2022;23(21):13000.
- [3] Cash A., Theus M.H. Mechanisms of blood-brain barrier dysfunction in traumatic brain injury. *International Journal of Molecular Sciences*. 2020;21(9):3344.
- [4] Fishman D., Faulds G., Jeffery R., Mohamed-Ali V., Yudkin J.S., Humphries S., Woo P. The effect of novel polymorphisms in the interleukin-6 (IL-6) gene on IL-6 transcription and plasma IL-6 levels. *Journal of Clinical Investigation*. 1998;102(7):1369-1376.
- [5] Broz M., Furlan V., Lesnik S., Jukic M., Bren U. The effect of the Ala16Val mutation on the secondary structure of the manganese superoxide dismutase mitochondrial targeting sequence. *Antioxidants*. 2022;11(12):2348.
- [6] Kumar A., Kumar P., Prasad M., Sagar R., Yadav A.K., Pandit A.K., Jali V.P., Pathak A. Association of C677T polymorphism in the methylenetetrahydrofolate reductase gene (MTHFR) with ischemic stroke: a meta-analysis. *Neurological Research*. 2015;37(7):568-577.