GUT MICROBIOTA COMPOSITION IN HYPERTENSIVE INTRACEREBRAL HAEMORRHAGE (ICH) AND ITS ASSOCIATION WITH OUTCOMES: A SYSTEMATIC REVIEW



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Abstract

Intracerebral haemorrhage (ICH), a devastating stroke subtype with high mortality, necessitates novel therapeutic approaches. The gut-brain axis, with its influence on stroke outcomes via gut microbiota and immune responses, presents a promising avenue. We conducted a systematic review to explore associations between cytokine responses and disease progression in ICH patients

Background Cerebral Vascular Diseases: Intrinsic factors: Extrinsic factors: Atherosclerosis Metabolite Multiple sclerosis Immunity Neonatal exposure Ischemic and hemorrhagic stroke Hormone Arteriovenous malformation Neuropsychiatric dysfunction: Pain and migraine Anxiety and depression Autism spectrum disorder Neuronal-glial-epithelial axis Visceral nerve **HPA** axis Neurodegenerative diseases: Alzheimer disease Parkinson's disease **Brain-gut Axis** Amyotrophic lateral sclerosis

Figure 1 The gut-brain axis refers to the bidirectional communication between the gastrointestinal tract and the central nervous system. This complex network involves various pathways, including neural, hormonal, and immune mechanisms. Its significance in cerebrovascular diseases, particularly in conditions like intracerebral hemorrhage (ICH), is becoming increasingly evident.

Gut microbiota-targeted therapies for cerebrovascular diseases

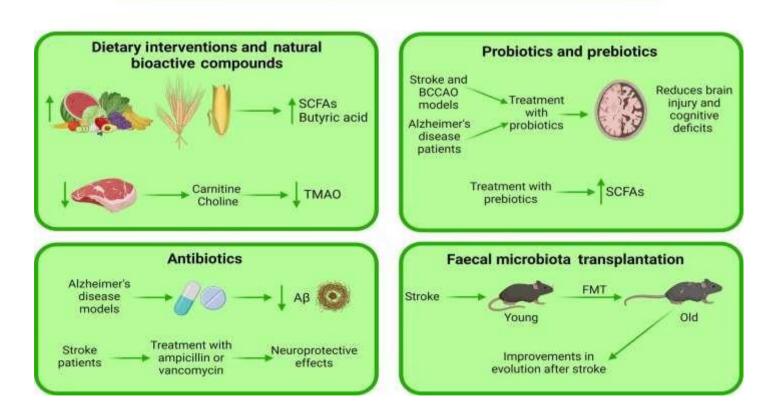


Figure 2- Gut microbiota-targeted therapies focus on modulating the composition and activity of the gut microbiome to improve health outcomes, particularly in various diseases, including neurological conditions, metabolic disorders, and gastrointestinal diseases. Here are key approaches and their implications:

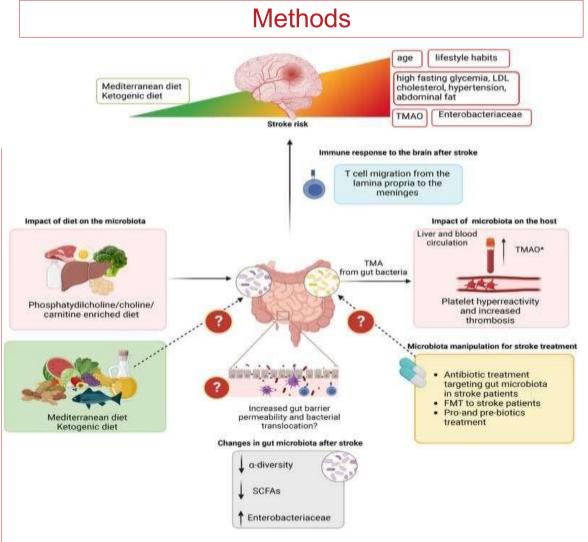


Figure 3- Overall work flow. Known human disease variants are first run through a functional enrichment to find molecular features (GO and KEGG associations) that link gene and phenotype.

Combining these features with patient symptom data will allow us to better classify patients and personalize/optimize diagnosis.

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Conclusion

This review highlights the association between Enterococcus enrichment and Prevotella depletion in gut microbiota with poor ICH outcomes. Additionally, altered cytokine levels suggest microbiota-mediated effects on host immune responses, critical for understanding ICH pathogenesis. These findings propose gut microbiota and serum cytokine profiles as potential biomarkers for ICH triggers and highlight the potential for gut microbiota modulation as a therapeutic strategy targeting dysbiosis in ICH patients

Results

Our research explored post-ICH cytokine dynamics and their influence on outcomes, revealing significant changes in Eotaxin, GM-CSF, IL-8, IL-9, IL-10, IL-12p70, IL-15, IL-23, IL-1RA, IP-10, RANTES, and TNF- α associated with poor 90-day outcomes. Notably, GM-CSF showed potential benefits in experimental stroke models. We identified 1,505 host SNPs linked to 119 gut microbiota traits and 1,873 SNPs associated with 81 gut metabolite traits. Specific gut bacteria correlated with increased or decreased risks of ICH, subarachnoid hemorrhage, and various stroke subtypes, with some bacteria negatively linked to large artery and small vessel strokes.

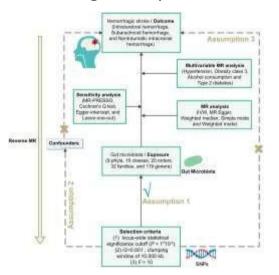


Figure 4. Overall work flow

Future Work

- Obtain complete coverage of variants and different LPS levels.
- Complete functional enrichment for additional unique phenotypes, specifically with microbiota.
- Incorporate EHR and use machine learning techniques to reclassify patients using genomic data in addition to phenotype

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