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# The effect of fecal microbiota transplantation on stroke outcomes: A systematic review

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## Abstract

### Background and Purpose

Fecal microbiota transplantation (FMT) is a novel microbiota-based therapeutic method that transfers stool from donor into a recipient and its application is under investigating for neurological disorders such as stroke. In this systematic review, we assessed the effect of FMT in the treatment of stroke and recovery of post-stroke complications.

## Methods

Preliminary studies were searched in MEDLINE via PubMed, Scopus, COCHRANE library and Google Scholar, databases up to February 2022. The search strategy was restricted to articles about FMT in stroke. The initial search yielded 4570 articles, of which 19 publications were included in our systematic review.

## Results

Based on outcomes transferring microbiome from healthy or ischemic donor to other ischemic recipient can affect brain infarct volume and survival rate, neurological and behavioral outcomes, and inflammatory pathways.

## Conclusions

Our systematic review on preclinical studies showed that manipulating gut microbiota via FMT can be a possible therapeutic approach for treatment of stroke and recovery of post-stroke complications.

## Keyword

[Fecal microbiota transplantation](#) • [Stroke](#) • [Ischemia](#) • [Gut–brain axis](#)

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## References

1. Feigin VL • Norrving B • Mensah GA  
**Global burden of stroke.**  
*Circulation research*. 2017; **120**: 439-448  
  
[View in Article](#) ^  
[Scopus \(1096\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)
2. Johnson CO • Nguyen M • Roth GA • et al.  
**Regional, and national burden of stroke, 1990–2016: A systematic analysis for the global burden of disease study 2016.**  
*The Lancet Neurology*. 2019; **18**: 439-458  
  
[View in Article](#) ^  
[Scopus \(1461\)](#) • [PubMed](#) • [Abstract](#) • [Full Text](#) • [Full Text PDF](#) • [Google Scholar](#)
3. Katan M • Luft A  
**Global Burden of Stroke. Seminars in Neurology.**  
Thieme Medical Publishers, 2018: 208-211  
  
[View in Article](#) ^  
[Google Scholar](#)
4. Saini V • Guada L • Yavagal DR



**Global epidemiology of stroke and access to acute ischemic stroke interventions.***Neurology*. 2021; **97**: S6-S16[View in Article](#) ^[Scopus \(66\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

5. Grotta JC.

**Fifty years of acute ischemic stroke treatment: A personal history.***Cerebrovascular Diseases*. 2021; **50**: 666-680[View in Article](#) ^[Scopus \(5\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

6. Katsanos AH.

**Updates in stroke treatment, diagnostic methods and predictors of outcome.***Journal of Clinical Medicine*. 2020; **9**: 2789[View in Article](#) ^[Scopus \(3\)](#) • [Crossref](#) • [Google Scholar](#)

7. Patel VP • Heit JJ

**Ischemic stroke treatment trials: Neuroimaging advancements and implications.***Topics in Magnetic Resonance Imaging*. 2017; **26**: 133-139[View in Article](#) ^[Scopus \(8\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

8. Durgan DJ • Lee J • McCullough LD • Bryan Jr RM

**Examining the role of the microbiota-gut-brain axis in stroke.***Stroke*. 2019; **50**: 2270-2277[View in Article](#) ^[Scopus \(63\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

9. Arneeth BM.



**Gut–brain axis biochemical signalling from the gastrointestinal tract to the central nervous system: Gut dysbiosis and altered brain function.**

*Postgraduate medical journal.* 2018; **94**: 446-452

[View in Article](#) ^

[Scopus \(31\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

10. Carabotti M • Scirocco A • Maselli MA • Severi C

**The gut-brain axis: Interactions between enteric microbiota, central and enteric nervous systems.**

*Annals of gastroenterology.* 2015; **28**: 203

[View in Article](#) ^

[PubMed](#) • [Google Scholar](#)

11. Rhee SH • Pothoulakis C • Mayer EA

**Principles and clinical implications of the brain–gut–enteric microbiota axis.**

*Nature reviews Gastroenterology hepatology.* 2009; **6**: 306-314

[View in Article](#) ^

[Scopus \(840\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

12. Bäckhed F • Fraser CM • Ringel Y • et al.

**Defining a healthy human gut microbiome: Current concepts, future directions, and clinical applications.**

*Cell host.* 2012; **12**: 611-622

[View in Article](#) ^

[Scopus \(488\)](#) • [PubMed](#) • [Abstract](#) • [Full Text](#) • [Full Text PDF](#) • [Google Scholar](#)

13. Qin J • Li R • Raes J • et al.

**A human gut microbial gene catalogue established by metagenomic sequencing.**

*Nature.* 2010; **464**: 59-65

[View in Article](#) ^

[Scopus \(7391\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)



14. Huang L • Wang T • Wu Q • et al.

**Analysis of microbiota in elderly patients with acute cerebral infarction.**

*PeerJ.* 2019; **7**: e6928

[View in Article](#) ^

[Scopus \(13\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

15. Tan C • Wu Q • Wang H • et al.

**Dysbiosis of gut microbiota and short-chain fatty acids in acute ischemic stroke and the subsequent risk for poor functional outcomes.**

*Journal of Parenteral Enteral Nutrition.* 2021; **45**: 518-529

[View in Article](#) ^

[Scopus \(54\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

16. Yin J • Liao SX • He Y • et al.

**Dysbiosis of gut microbiota with reduced trimethylamine-n-oxide level in patients with large-artery atherosclerotic stroke or transient ischemic attack.**

*Journal of the American Heart Association.* 2015; **4**e002699

[View in Article](#) ^

[Scopus \(362\)](#) • [Crossref](#) • [Google Scholar](#)

17. Ling Y • Gong T • Zhang J • et al.

**Gut microbiome signatures are biomarkers for cognitive impairment in patients with ischemic stroke.**

*Frontiers in Aging Neuroscience.* 2020; : 297

[View in Article](#) ^

[Google Scholar](#)

18. Chen R • Wu P • Cai Z • et al.

**Puerariae lobatae radix with chuanxiong rhizoma for treatment of cerebral ischemic stroke by remodeling gut microbiota to regulate the brain–gut barriers.**

*The Journal of Nutritional Biochemistry.* 2019; **65**: 101-114



[View in Article](#) [Scopus \(78\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

19. Ling Y • Gu Q • Zhang J • et al.

**Structural change of gut microbiota in patients with post-stroke comorbid cognitive impairment and depression and its correlation with clinical features.**

*Journal of Alzheimer's Disease.* 2020; **77**: 1595-1608

[View in Article](#) [Scopus \(17\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

20. Roth WH • Cai A • Zhang C • Chen ML • Merkler AE • Kamel H

**Gastrointestinal disorders and risk of first-ever ischemic stroke.**

*Stroke.* 2020; **51**: 3577-3583

[View in Article](#) [Scopus \(9\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

21. Vemuri R • Gundamaraju R • Shinde T • Eri R

**Therapeutic interventions for gut dysbiosis and related disorders in the elderly: Antibiotics, probiotics or faecal microbiota transplantation?.**

*Beneficial microbes.* 2017; **8**: 179-192

[View in Article](#) [Scopus \(40\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

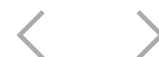
22. Meyyappan AC • Forth E • Wallace CJ • Milev R

**Effect of fecal microbiota transplant on symptoms of psychiatric disorders: A systematic review.**

*BMC psychiatry.* 2020; **20**: 1-19

[View in Article](#) [PubMed](#) • [Google Scholar](#)

23. Vindigni SM • Surawicz CM



**Fecal microbiota transplantation.**

*Gastroenterology Clinics*. 2017; **46**: 171-185

[View in Article](#) ^

[Scopus \(128\)](#) • [PubMed](#) • [Abstract](#) • [Full Text](#) • [Full Text PDF](#) • [Google Scholar](#)

24. Mikolašević I • Hauser G • Abram M • Filipec T

**Fecal microbiota transplantation—where are we?.**

*Croatian Medical Journal*. 2021; **62**: 52

[View in Article](#) ^

[PubMed](#) • [Crossref](#) • [Google Scholar](#)

25. Bafeta A • Yavchitz A • Riveros C • Batista R • Ravaud P

**Methods and reporting studies assessing fecal microbiota transplantation: A systematic review.**

*Annals of Internal Medicine*. 2017; **167**: 34-39

[View in Article](#) ^

[Scopus \(76\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

26. Stalder T • Kapel N • Diaz S • et al.

**A systematic review of economic evaluation in fecal microbiota transplantation.**

*Infection Control Hospital Epidemiology*. 2020; **41**: 458-466

[View in Article](#) ^

[Scopus \(3\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

27. Wang S • Xu M • Wang W • et al.

**Systematic review: Adverse events of fecal microbiota transplantation.**

*PloS one*. 2016; **11**e0161174

[View in Article](#) ^

[Google Scholar](#)

28. Moher D • Liberati A • Tetzlaff J • Altman DG





## Preferred reporting items for systematic reviews and meta-analyses: The prisma statement.

*International Journal of Surgery.* 2010; **8**: 336-341

[View in Article](#) 

[Scopus \(7303\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

29. Beller EM • Glasziou PP • Altman DG • et al.

### Prisma for abstracts: Reporting systematic reviews in journal and conference abstracts.

*PLoS Medicine.* 2013; **10**e1001419

[View in Article](#) 

[Scopus \(398\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

30. Macleod MR • O'Collins T • Howells DW • Donnan GA

### Pooling of animal experimental data reveals influence of study design and publication bias.

*Stroke.* 2004; **35**: 1203-1208

[View in Article](#) 

[Scopus \(421\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

31. Winek K • Engel O • Koduah P • et al.

### Depletion of cultivatable gut microbiota by broad-spectrum antibiotic pretreatment worsens outcome after murine stroke.

*Stroke.* 2016; **47**: 1354-1363

[View in Article](#) 

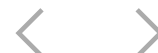
[Scopus \(128\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

32. Benakis C • Brea D • Caballero S • et al.

### Commensal microbiota affects ischemic stroke outcome by regulating intestinal γδ T cells.

*Nature medicine.* 2016; **22**: 516-523

[View in Article](#) 



[Scopus \(581\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

33. Jandzinski M.

Manipulation of the microbiome and its impact on functional recovery following ischemic stroke.  
University of Connecticut, 2015

[View in Article](#) ^

[Google Scholar](#)

34. Spychala MS • Venna VR • Jandzinski M • et al.

**Age-related changes in the gut microbiota influence systemic inflammation and stroke outcome.**

*Annals of Neurology*. 2018; **84**: 23-36

[View in Article](#) ^

[Scopus \(196\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

35. Park MJ • Pilla R • Panta A • et al.

**Reproductive senescence and ischemic stroke remodel the gut microbiome and modulate the effects of estrogen treatment in female rats.**

*Translational Stroke Research*. 2020; **11**: 812-830

[View in Article](#) ^

[Scopus \(25\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

36. Feng Y • Zhang D • Zhao Y • et al.

**Effect of intestinal microbiota transplantation on cerebral ischemia reperfusion injury in aged mice via inhibition of il-17.**

*Neurogastroenterology Motility*. 2022; e14313

[View in Article](#) ^

[Scopus \(3\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

37. Lee J • d'Aigle J • Atadja L • et al.



**Gut microbiota–derived short-chain fatty acids promote poststroke recovery in aged mice.**

*Circulation Research*. 2020; **127**: 453-465

[View in Article](#) ^

[Scopus \(156\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

38. Singh V • Roth S • Llovera G • et al.

**Microbiota dysbiosis controls the neuroinflammatory response after stroke.**

*Journal of Neuroscience*. 2016; **36**: 7428-7440

[View in Article](#) ^

[Scopus \(363\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

39. Huang Q • Di L • Yu F • et al.

**Alterations in the gut microbiome with hemorrhagic transformation in experimental stroke.**

*CNS Neuroscience Therapeutics*. 2022; **28**: 77-91

[View in Article](#) ^

[Scopus \(10\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

40. Hafez S • Hoda MN • Guo X • Johnson MH • Fagan SC • Ergul A

**Comparative analysis of different methods of ischemia/reperfusion in hyperglycemic stroke outcomes: Interaction with tpa.**

*Translational Stroke Research*. 2015; **6**: 171-180

[View in Article](#) ^

[Scopus \(45\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

41. Lee K-E • Kim J-K • Kim D-H

**Orally administered antibiotics vancomycin and ampicillin cause cognitive impairment with gut dysbiosis in mice with transient global forebrain ischemia.**

*Frontiers in Microbiology*. 2020; : 2347

[View in Article](#) ^



[Google Scholar](#)

42. Wang H • Ren S • Lv H • Cao L

**Gut microbiota from mice with cerebral ischemia-reperfusion injury affects the brain in healthy mice.**

*Aging*. 2021; **13**: 10058

[View in Article](#) ^

[Scopus \(4\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

43. Dou Z • Rong X • Zhao E • Zhang L • Lv Y

**Neuroprotection of resveratrol against focal cerebral ischemia/reperfusion injury in mice through a mechanism targeting gut-brain axis.**

*Molecular Neurobiology*. 2019; **39**: 883-898

[View in Article](#) ^

[Scopus \(59\)](#) • [Crossref](#) • [Google Scholar](#)

44. Im Jeong S • Shin JA • Cho S • et al.

**Resveratrol attenuates peripheral and brain inflammation and reduces ischemic brain injury in aged female mice.**

*Neurobiology of Aging*. 2016; **44**: 74-84

[View in Article](#) ^

[Scopus \(38\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

45. Chen R • Xu Y • Wu P • et al.

**Transplantation of fecal microbiota rich in short chain fatty acids and butyric acid treat cerebral ischemic stroke by regulating gut microbiota.**

*Pharmacological Research*. 2019; **148**: 104403

[View in Article](#) ^

[Scopus \(142\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

46. Wang H • Song W • Wu Q • et al.



**Fecal transplantation from db/db mice treated with sodium butyrate attenuates ischemic stroke injury.***Microbiology Spectrum*. 2021; **9**: e00042-00021[View in Article](#) [Scopus \(18\)](#) • [Crossref](#) • [Google Scholar](#)

47. Zhou Z • Xu N • Matei N • et al.

**Sodium butyrate attenuated neuronal apoptosis via gpr41/gβγ/pi3k/akt pathway after mcao in rats.***Journal of Cerebral Blood Flow Metabolism*. 2021; **41**: 267-281[View in Article](#) [Scopus \(43\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

48. Zhang F • Zhai M • Wu Q • et al.

**Protective effect of tong-qiao-huo-xue decoction on inflammatory injury caused by intestinal microbial disorders in stroke rats.***Biological Pharmaceutical Bulletin*. 2020; **43**: 788-800[View in Article](#) [PubMed](#) • [Crossref](#) • [Google Scholar](#)

49. Li L • Wang N • Jin Q • et al.

**Protection of tong-qiao-huo-xue decoction against cerebral ischemic injury through reduction blood–brain barrier permeability.***Chemical Pharmaceutical Bulletin*. 2017; **65**: 1004-1010[View in Article](#) [Scopus \(27\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

50. Zhang P • Zhang X • Huang Y • et al.

**Atorvastatin alleviates microglia-mediated neuroinflammation via modulating the microbial composition and the intestinal barrier function in ischemic stroke mice.***Free Radical Biology Medicine*. 2021; **162**: 104-117

[View in Article](#) [Scopus \(29\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

51. Wang L • Zhang X • Liu L • Yang R • Cui L • Li M

**Atorvastatin protects rat brains against permanent focal ischemia and downregulates hmgb1, hmgb1 receptors (rage and tlr4), nf-kb expression.**

*Neuroscience letters*. 2010; **471**: 152-156

[View in Article](#) [Scopus \(98\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

52. Huang J-T • Mao Y-Q • Han B • et al.

**Calorie restriction conferred improvement effect on long-term rehabilitation of ischemic stroke via gut microbiota.**

*Pharmacological Research*. 2021; **170**: 105726

[View in Article](#) [Scopus \(14\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

53. de Carvalho TS.

**Calorie restriction or dietary restriction: How far they can protect the brain against neurodegenerative diseases?.**

*Neural Regeneration Research*. 2022; **17**: 1640

[View in Article](#) [Scopus \(8\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

54. Zhu W • Romano KA • Li L • et al.

**Gut microbes impact stroke severity via the trimethylamine n-oxide pathway.**

*Cell Host*. 2021; **29**: 1199-1208

[View in Article](#) [Scopus \(31\)](#) • [PubMed](#) • [Abstract](#) • [Full Text](#) • [Full Text PDF](#) • [Google Scholar](#)

55. Haghikia A • Li X • Liman T • et al.



**Gut microbiota-dependent tmao predicts risk of cardiovascular events in patients with stroke and is related to proinflammatory monocytes. Arteriosclerosis, Thrombosis, and Vascular.**

*Biology.* 2018; **38**: 2225-2235

[View in Article](#) ^

[Google Scholar](#)

56. Zhai Q • Wang X • Chen C • et al.

**Prognostic value of plasma trimethylamine n-oxide levels in patients with acute ischemic stroke.**

*Molecular Neurobiology.* 2019; **39**: 1201-1206

[View in Article](#) ^

[Scopus \(23\)](#) • [Crossref](#) • [Google Scholar](#)

57. Rexidamu M • Li H • Jin H • Huang J

**Serum levels of trimethylamine-n-oxide in patients with ischemic stroke.**

*Bioscience Reports.* 2019; **39**

[View in Article](#) ^

[Scopus \(38\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

58. Schneider C • Okun J • Schwarz K • et al.

**Trimethylamine-n-oxide is elevated in the acute phase after ischaemic stroke and decreases within the first days.**

*European Journal of Neurology.* 2020; **27**: 1596-1603

[View in Article](#) ^

[Scopus \(21\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

59. Xia G-H • You C • Gao X-X • et al.

**Stroke dysbiosis index (sdi) in gut microbiome are associated with brain injury and prognosis of stroke.**

*Frontiers in Neurology.* 2019; **10**: 397



[View in Article](#) [Scopus \(88\)](#) • [PubMed](#) • [Crossref](#) • [Google Scholar](#)

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