

DAFTAR PUSTAKA

- Aronowski J, Zhao X. Molecular pathophysiology of cerebral hemorrhage: secondary brain injury. *Stroke*. 2011 Jun;42(6):1781-6. doi: 10.1161/STROKEAHA.110.596718. Epub 2011 Apr 28. PMID: 21527759; PMCID: PMC3123894.
- Ashburner BP, Westerheide SD, Baldwin AS Jr. The p65 (RelA) subunit of NF-kappaB interacts with the histone deacetylase (HDAC) corepressors HDAC1 and HDAC2 to negatively regulate gene expression. *Mol Cell Biol*. 2001 Oct;21(20):7065-77. doi: 10.1128/MCB.21.20.7065-7077.2001. PMID: 11564889; PMCID: PMC99882.
- Bachmann C, Colombo JP, Berüter J. Short chain fatty acids in plasma and brain: quantitative determination by gas chromatography. *Clin Chim Acta*. 1979 Mar 1;92(2):153-9. doi: 10.1016/0009-8981(79)90109-8. PMID: 487569.
- Bansal V, Ryu SY, Lopez N, Alexan S, Krzyzaniak M, Eliceiri B, Baird A, Coimbra R. Vagal stimulation modulates inflammation through a ghrelin mediated mechanism in traumatic brain injury. *Inflammation*. 2012 Feb;35(1):214-20. doi: 10.1007/s10753-011-9307-7. PMID: 21360048; PMCID: PMC3282000.
- Baldwin AS Jr. The NF-kappa B and I kappa B proteins: new discoveries and insights. *Annu Rev Immunol*. 1996;14:649-83. doi: 10.1146/annurev.immunol.14.1.649. PMID: 8717528.
- Bansal V, Costantini T, Kroll L, Peterson C, Loomis W, Eliceiri B, Baird A, Wolf P, Coimbra R. Traumatic brain injury and intestinal dysfunction: uncovering the neuro-enteric axis. *J Neurotrauma*. 2009 Aug;26(8):1353-9. doi: 10.1089/neu.2008.0858. PMID: 19344293; PMCID: PMC2989839.
- Barrett K, Brooks H, Boitano S, Barman S. Cellular and molecular basis of medical physiology. In: *Ganong's Review of Medical Physiology*. 23rd ed. USA: McGraw-Hill Publishers; 2010. pp. 51-61
- Barnes PJ, Karin M. Nuclear factor-kappaB: a pivotal transcription factor in chronic inflammatory diseases. *N Engl J Med*. 1997 Apr 10;336(15):1066-71. doi: 10.1056/NEJM199704103361506. PMID: 9091804.
- Bassi TG, Rohrs EC, Fernandez KC, Ornowska M, Nicholas M, Gani M, Evans D, Reynolds SC. Brain injury after 50 h of lung-protective mechanical ventilation in a preclinical model. *Sci Rep*. 2021 Mar 3;11(1):5105. doi: 10.1038/s41598-021-84440-1. PMID: 33658581; PMCID: PMC7930247.
- Bassi TG, Rohrs EC, Reynolds SC. Systematic review of cognitive impairment and brain insult after mechanical ventilation. *Crit Care*. 2021 Mar 10;25(1):99. doi: 10.1186/s13054-021-03521-9. PMID: 33691752; PMCID: PMC7945325.

- Berson A, Nativio R, Berger SL, Bonini NM. Epigenetic Regulation in Neurodegenerative Diseases. *Trends Neurosci.* 2018 Sep;41(9):587-598. doi: 10.1016/j.tins.2018.05.005. Epub 2018 Jun 7. PMID: 29885742; PMCID: PMC6174532.
- Blanke EN, Holmes GM, Besecker EM. Altered physiology of gastrointestinal vagal afferents following neurotrauma. *Neural Regen Res.* 2021 Feb;16(2):254-263. doi: 10.4103/1673-5374.290883. PMID: 32859772; PMCID: PMC7896240.
- Brenner LA, Stamper CE, Hoisington AJ, Stearns-Yoder KA, Stanislawski MA, Brostow DP, Hoffmire CA, Forster JE, Schneider AL, Postolache TT, Lowry CA. Microbial Diversity and Community Structures Among Those With Moderate to Severe TBI: A United States-Veteran Microbiome Project Study. *J Head Trauma Rehabil.* 2020 Sep/Oct;35(5):332-341. doi: 10.1097/HTR.0000000000000615. PMID: 32881767.
- Browning KN, Travagli RA. Plasticity of vagal brainstem circuits in the control of gastrointestinal function. *Auton Neurosci.* 2011 Apr 26;161(1-2):6-13. doi: 10.1016/j.autneu.2010.11.001. Epub 2010 Dec 13. PMID: 21147043; PMCID: PMC3061976.
- Caetano-Silva ME, Rund L, Hutchinson NT, Woods JA, Steelman AJ, Johnson RW. Inhibition of inflammatory microglia by dietary fiber and short-chain fatty acids. *Sci Rep.* 2023 Feb 16;13(1):2819. doi: 10.1038/s41598-022-27086-x. PMID: 36797287; PMCID: PMC9935636.
- Celorrío M, Abellanas MA, Rhodes J, Goodwin V, Moritz J, Vadivelu S, Wang L, Rodgers R, Xiao S, Anabayan I, Payne C, Perry AM, Baldrige MT, Aymerich MS, Steed A, Friess SH. Gut microbial dysbiosis after traumatic brain injury modulates the immune response and impairs neurogenesis. *Acta Neuropathol Commun.* 2021 Mar 10;9(1):40. doi: 10.1186/s40478-021-01137-2. PMID: 33691793; PMCID: PMC7944629.
- Chen Lf, Fischle W, Verdin E, Greene WC. Duration of nuclear NF-kappaB action regulated by reversible acetylation. *Science.* 2001 Aug 31;293(5535):1653-7. doi: 10.1126/science.1062374. PMID: 11533489.
- Chen C, Zhang Z, Chen T, Peng M, Xu X, Wang Y. Prolonged mechanical ventilation-induced neuroinflammation affects postoperative memory dysfunction in surgical mice. *Crit Care.* 2015 Apr 10;19(1):159. doi: 10.1186/s13054-015-0882-0. PMID: 25887955; PMCID: PMC4423516.
- Cummings JH, Pomare EW, Branch WJ, Naylor CP, Macfarlane GT. Short chain fatty acids in human large intestine, portal, hepatic and venous blood. *Gut.* 1987 Oct;28(10):1221-7. doi: 10.1136/gut.28.10.1221. PMID: 3678950; PMCID: PMC1433442.
- Dahlan, M. Sopiudin. Besar sampel dan cara pengambilan sampel dalam penelitian kedokteran dan kesehatan. Jakarta: Salemba Medika 29. 2010.

- Dalile B, Van Oudenhove L, Vervliet B, Verbeke K. The role of short-chain fatty acids in microbiota-gut-brain communication. *Nat Rev Gastroenterol Hepatol*. 2019 Aug;16(8):461-478. doi: 10.1038/s41575-019-0157-3. PMID: 31123355.
- Deczkowska A, Keren-Shaul H, Weiner A, Colonna M, Schwartz M, Amit I. Disease-Associated Microglia: A Universal Immune Sensor of Neurodegeneration. *Cell*. 2018 May 17;173(5):1073-1081. doi: 10.1016/j.cell.2018.05.003. PMID: 29775591.
- Denes A, Thornton P, Rothwell NJ, Allan SM. Inflammation and brain injury: acute cerebral ischaemia, peripheral and central inflammation. *Brain Behav Immun*. 2010 Jul;24(5):708-23. doi: 10.1016/j.bbi.2009.09.010. Epub 2009 Sep 19. PMID: 19770034.
- Dewan MC, Rattani A, Gupta S, Baticulon RE, Hung YC, Punchak M, Agrawal A, Adeleye AO, Shrimel MG, Rubiano AM, Rosenfeld JV, Park KB. Estimating the global incidence of traumatic brain injury. *J Neurosurg*. 2018 Apr 1:1-18. doi: 10.3171/2017.10.JNS17352. Epub ahead of print. PMID: 29701556.
- Diebel LN, Dulchavsky SA, Wilson RF. Effect of increased intra-abdominal pressure on mesenteric arterial and intestinal mucosal blood flow. *J Trauma*. 1992 Jul;33(1):45-8; discussion 48-9. doi: 10.1097/00005373-199207000-00010. PMID: 1635105.
- Donia T, Khamis A. Management of oxidative stress and inflammation in cardiovascular diseases: mechanisms and challenges. *Environ Sci Pollut Res Int*. 2021 Jul;28(26):34121-34153. doi: 10.1007/s11356-021-14109-9. Epub 2021 May 8. PMID: 33963999.
- Dombrowsky H, Uhlig S. Steroids and histone deacetylase in ventilation-induced gene transcription. *Eur Respir J*. 2007 Nov;30(5):865-77. doi: 10.1183/09031936.00134006. Epub 2007 Jul 11. PMID: 17626110.
- Eikelenboom P, van Gool WA. Neuroinflammatory perspectives on the two faces of Alzheimer's disease. *J Neural Transm (Vienna)*. 2004 Mar;111(3):281-94. doi: 10.1007/s00702-003-0055-1. Epub 2003 Dec 3. PMID: 14991455.
- Esterov D, Greenwald BD. Autonomic Dysfunction after Mild Traumatic Brain Injury. *Brain Sci*. 2017 Aug 11;7(8):100. doi: 10.3390/brainsci7080100. PMID: 28800081; PMCID: PMC5575620.
- Fischer A. Targeting histone-modifications in Alzheimer's disease. What is the evidence that this is a promising therapeutic avenue? *Neuropharmacology*. 2014 May;80:95-102. doi: 10.1016/j.neuropharm.2014.01.038. Epub 2014 Jan 31. PMID: 24486385.

- Fragas MG, Oliveira DM, Hiyane MI, Braga TT, Camara NOS. The dual effect of acetate on microglial TNF- α production. *Clinics (Sao Paulo)*. 2022 Jun 29;77:100062. doi: 10.1016/j.clinsp.2022.100062. PMID: 35779458; PMCID: PMC9254000.
- Frisvold S, Coppola S, Ehrmann S, Chiumello D, Guérin C. Respiratory challenges and ventilatory management in different types of acute brain-injured patients. *Crit Care*. 2023 Jun 23;27(1):247. doi: 10.1186/s13054-023-04532-4. PMID: 37353832; PMCID: PMC10290317.
- Garcia ER, Vergara A, Aziz F, Narváez S, Cuesta G, Hernández M, Toapanta D, Marco F, Fernández J, Soriano A, Vila J, Casals-Pascual C. Changes in the gut microbiota and risk of colonization by multidrug-resistant bacteria, infection, and death in critical care patients. *Clin Microbiol Infect*. 2022 Jul;28(7):975-982. doi: 10.1016/j.cmi.2022.01.004. Epub 2022 Jan 20. PMID: 35066206.
- Giordano G, Pugliese F, Bilotta F. Neuroinflammation, neuronal damage or cognitive impairment associated with mechanical ventilation: A systematic review of evidence from animal studies. *J Crit Care*. 2021 Apr;62:246-255. doi: 10.1016/j.jcrc.2020.12.017. Epub 2020 Dec 25. PMID: 33454552.
- Goldsmith ZG, Dhanasekaran DN. G protein regulation of MAPK networks. *Oncogene*. 2007 May 14;26(22):3122-42. doi: 10.1038/sj.onc.1210407. PMID: 17496911.
- Goodman, J. Clay, Claudia S. Robertson, Robert G. Grossman, Raj K. Narayan, Elevation of tumor necrosis factor in head injury, *Journal of Neuroimmunology*, Volume 30, Issues 2–3,1990, Pages 213-217, ISSN 0165-5728, [https://doi.org/10.1016/0165-5728\(90\)90105-V](https://doi.org/10.1016/0165-5728(90)90105-V). Gu C, Hu Q, Wu J, Mu C, Ren H,
- Liu CF, Wang G. P7C3 Inhibits LPS-Induced Microglial Activation to Protect Dopaminergic Neurons Against Inflammatory Factor-Induced Cell Death in vitro and in vivo. *Front Cell Neurosci*. 2018 Nov 5;12:400. doi: 10.3389/fncel.2018.00400. PMID: 30455635; PMCID: PMC6230654.
- Gupta SC, Sundaram C, Reuter S, Aggarwal BB. Inhibiting NF- κ B activation by small molecules as a therapeutic strategy. *Biochim Biophys Acta*. 2010 Oct-Dec;1799(10-12):775-87. doi: 10.1016/j.bbagr.2010.05.004. Epub 2010 May 21. PMID: 20493977; PMCID: PMC2955987.
- Haberland M, Montgomery RL, Olson EN. The many roles of histone deacetylases in development and physiology: implications for disease and therapy. *Nat Rev Genet*. 2009 Jan;10(1):32-42. doi: 10.1038/nrg2485. PMID: 19065135; PMCID: PMC3215088.
- Hang CH, Shi JX, Li JS, Wu W, Li WQ, Yin HX. Levels of vasoactive intestinal peptide, cholecystinin and calcitonin gene-related peptide in plasma and

- jejunum of rats following traumatic brain injury and underlying significance in gastrointestinal dysfunction. *World J Gastroenterol.* 2004 Mar 15;10(6):875-80. doi: 10.3748/wjg.v10.i6.875. PMID: 15040036; PMCID: PMC4727008.
- Hanscom M, Loane DJ, Shea-Donohue T. Brain-gut axis dysfunction in the pathogenesis of traumatic brain injury. *J Clin Invest.* 2021 Jun 15;131(12):e143777. doi: 10.1172/JCI143777. PMID: 34128471; PMCID: PMC8203445.
- Harrison-Felix CL, Whiteneck GG, Jha A, DeVivo MJ, Hammond FM, Hart DM. Mortality over four decades after traumatic brain injury rehabilitation: a retrospective cohort study. *Arch Phys Med Rehabil.* 2009 Sep;90(9):1506-13. doi: 10.1016/j.apmr.2009.03.015. PMID: 19735778.
- Helmy A, Carpenter KL, Menon DK, Pickard JD, Hutchinson PJ. The cytokine response to human traumatic brain injury: temporal profiles and evidence for cerebral parenchymal production. *J Cereb Blood Flow Metab.* 2011; 31(2): 658-70
- Hirasawa A, Hara T, Katsuma S, Adachi T, Tsujimoto G. Free fatty acid receptors and drug discovery. *Biol Pharm Bull.* 2008 Oct;31(10):1847-51. doi: 10.1248/bpb.31.1847. PMID: 18827341.
- Holzer P. Role of visceral afferent neurons in mucosal inflammation and defense. *Curr Opin Pharmacol.* 2007 Dec;7(6):563-9. doi: 10.1016/j.coph.2007.09.004. Epub 2007 Oct 29. PMID: 18029228; PMCID: PMC4370836.
- Hong YH, Nishimura Y, Hishikawa D, Tsuzuki H, Miyahara H, Gotoh C, Choi KC, Feng DD, Chen C, Lee HG, Katoh K, Roh SG, Sasaki S. Acetate and propionate short chain fatty acids stimulate adipogenesis via GPCR43. *Endocrinology.* 2005 Dec;146(12):5092-9. doi: 10.1210/en.2005-0545. Epub 2005 Aug 25. PMID: 16123168.
- Hou Y, Xu L, Song S, Fan W, Wu Q, Tong X, Yan H. Oral Administration of Brain Protein Combined With Probiotics Induces Immune Tolerance Through the Tryptophan Pathway. *Front Mol Neurosci.* 2021 May 28;14:634631. doi: 10.3389/fnmol.2021.634631. Retraction in: *Front Mol Neurosci.* 2023 Aug 29;16:1279716. PMID: 34122006; PMCID: PMC8192843.
- Hoyles L, Snelling T, Umlai UK, Nicholson JK, Carding SR, Glen RC, McArthur S. Microbiome-host systems interactions: protective effects of propionate upon the blood-brain barrier. *Microbiome.* 2018 Mar 21;6(1):55. doi: 10.1186/s40168-018-0439-y. PMID: 29562936; PMCID: PMC5863458.
- Iftikhar PM, Anwar A, Saleem S, Nasir S, Inayat A. Traumatic brain injury causing intestinal dysfunction: A review. *J Clin Neurosci.* 2020 Sep;79:237-240. doi: 10.1016/j.jocn.2020.07.019. Epub 2020 Aug 11. PMID: 33070903.

- Kaltschmidt B, Kaltschmidt C. NF-kappaB in the nervous system. *Cold Spring Harb Perspect Biol.* 2009 Sep;1(3):a001271. doi: 10.1101/cshperspect.a001271. Erratum in: *Cold Spring Harb Perspect Biol.* 2010 Jan;2(1):a001271. PMID: 20066105; PMCID: PMC2773634.
- Kaltschmidt B, Widera D, Kaltschmidt C. Signaling via NF-kappaB in the nervous system. *Biochim Biophys Acta.* 2005 Sep 30;1745(3):287-99. doi: 10.1016/j.bbamcr.2005.05.009. PMID: 15993497.
- Kasubuchi M, Hasegawa S, Hiramatsu T, Ichimura A, Kimura I. Dietary gut microbial metabolites, short-chain fatty acids, and host metabolic regulation. *Nutrients.* 2015 Apr 14;7(4):2839-49. doi: 10.3390/nu7042839. PMID: 25875123; PMCID: PMC4425176.
- Kim HJ, Bae SC. Histone deacetylase inhibitors: molecular mechanisms of action and clinical trials as anti-cancer drugs. *Am J Transl Res.* 2011 Feb;3(2):166-79. Epub 2010 Dec 26. PMID: 21416059; PMCID: PMC3056563.
- Kimura I, Inoue D, Maeda T, Hara T, Ichimura A, Miyauchi S, Kobayashi M, Hirasawa A, Tsujimoto G. Short-chain fatty acids and ketones directly regulate sympathetic nervous system via G protein-coupled receptor 41 (GPR41). *Proc Natl Acad Sci U S A.* 2011 May 10;108(19):8030-5. doi: 10.1073/pnas.1016088108. Epub 2011 Apr 25. PMID: 21518883; PMCID: PMC3093469.
- Keren-Shaul H, Spinrad A, Weiner A, Matcovitch-Natan O, Dvir-Szternfeld R, Ulland TK, David E, Baruch K, Lara-Astaiso D, Toth B, Itzkovitz S, Colonna M, Schwartz M, Amit I. A Unique Microglia Type Associated with Restricting Development of Alzheimer's Disease. *Cell.* 2017 Jun 15;169(7):1276-1290.e17. doi: 10.1016/j.cell.2017.05.018. Epub 2017 Jun 8. PMID: 28602351.
- Knoblauch SM, Fan L, Faden AI. Early neuronal expression of tumor necrosis factor-alpha after experimental brain injury contributes to neurological impairment. *J Neuroimmunol.* 1999 Mar 1;95(1-2):115-25. doi: 10.1016/s0165-5728(98)00273-2. PMID: 10229121.
- Krakovski MA, Arora N, Jain S, Glover J, Dombrowski K, Hernandez B, Yadav H, Sarma AK. Diet-microbiome-gut-brain nexus in acute and chronic brain injury. *Front Neurosci.* 2022 Sep 16;16:1002266. doi: 10.3389/fnins.2022.1002266. PMID: 36188471; PMCID: PMC9523267.
- Lakhan SE, Kirchgessner A, Hofer M. Inflammatory mechanisms in ischemic stroke: therapeutic approaches. *J Transl Med.* 2009 Nov 17;7:97. doi: 10.1186/1479-5876-7-97. PMID: 19919699; PMCID: PMC2780998.
- Lal S, Kirkup AJ, Brunnsden AM, Thompson DG, Grundy D. Vagal afferent responses to fatty acids of different chain length in the rat. *Am J Physiol*

- Gastrointest Liver Physiol. 2001 Oct;281(4):G907-15. doi: 10.1152/ajpgi.2001.281.4.G907. PMID: 11557510.
- Layden BT, Angueira AR, Brodsky M, Durai V, Lowe WL Jr. Short chain fatty acids and their receptors: new metabolic targets. *Transl Res.* 2013 Mar;161(3):131-40. doi: 10.1016/j.trsl.2012.10.007. Epub 2012 Nov 9. Erratum in: *Transl Res.* 2013 Oct;162(4):269. PMID: 23146568.
- Lee SU, In HJ, Kwon MS, Park BO, Jo M, Kim MO, Cho S, Lee S, Lee HJ, Kwak YS, Kim S. β -Arrestin 2 mediates G protein-coupled receptor 43 signals to nuclear factor- κ B. *Biol Pharm Bull.* 2013;36(11):1754-9. doi: 10.1248/bpb.b13-00312. Epub 2013 Aug 29. PMID: 23985900.
- Lee Y, Morrison BM, Li Y, Lengacher S, Farah MH, Hoffman PN, Liu Y, Tsingalia A, Jin L, Zhang PW, Pellerin L, Magistretti PJ, Rothstein JD. Oligodendroglia metabolically support axons and contribute to neurodegeneration. *Nature.* 2012 Jul 26;487(7408):443-8. doi: 10.1038/nature11314. PMID: 22801498; PMCID: PMC3408792.
- Lemke DM. Riding out the storm: sympathetic storming after traumatic brain injury. *J Neurosci Nurs.* 2004 Feb;36(1):4-9. PMID: 14998101.
- Li Y. Sensory signal transduction in the vagal primary afferent neurons. *Curr Med Chem.* 2007;14(24):2554-63. doi: 10.2174/092986707782023334. PMID: 17979708.
- Li M, van Esch BCAM, Wagenaar GTM, Garssen J, Folkerts G, Henricks PAJ. Pro- and anti-inflammatory effects of short chain fatty acids on immune and endothelial cells. *Eur J Pharmacol.* 2018 Jul 15;831:52-59. doi: 10.1016/j.ejphar.2018.05.003. Epub 2018 May 9. PMID: 29750914.
- Li S, Hua D, Wang Q, Yang L, Wang X, Luo A, Yang C. The Role of Bacteria and Its Derived Metabolites in Chronic Pain and Depression: Recent Findings and Research Progress. *Int J Neuropsychopharmacol.* 2020 Mar 10;23(1):26-41. doi: 10.1093/ijnp/pyz061. PMID: 31760425; PMCID: PMC7064053.
- Liu J, Li H, Gong T, Chen W, Mao S, Kong Y, Yu J, Sun J. Anti-neuroinflammatory Effect of Short-Chain Fatty Acid Acetate against Alzheimer's Disease via Upregulating GPR41 and Inhibiting ERK/JNK/NF- κ B. *J Agric Food Chem.* 2020 Jul 8;68(27):7152-7161. doi: 10.1021/acs.jafc.0c02807. Epub 2020 Jun 25. PMID: 32583667.
- Liu C, Tang J. Expression levels of tumor necrosis factor- α and the corresponding receptors are correlated with trauma severity. *Oncol Lett.* 2014 Dec;8(6):2747-2751. doi: 10.3892/ol.2014.2575. Epub 2014 Sep 29. PMID: 25364459; PMCID: PMC4214438.
- Liu X, Jiao B, Shen L. The Epigenetics of Alzheimer's Disease: Factors and Therapeutic Implications. *Front Genet.* 2018 Nov 30;9:579. doi: 10.3389/fgene.2018.00579. PMID: 30555513; PMCID: PMC6283895.

- Love R, Choe E, Lipton H, Flint L, Steinberg S. Positive end-expiratory pressure decreases mesenteric blood flow despite normalization of cardiac output. *J Trauma*. 1995 Aug;39(2):195-9. doi: 10.1097/00005373-199508000-00003. PMID: 7674385.
- Ma Y, Liu S, Shu H, Crawford J, Xing Y, Tao F. Resveratrol alleviates temporomandibular joint inflammatory pain by recovering disturbed gut microbiota. *Brain Behav Immun*. 2020 Jul;87:455-464. doi: 10.1016/j.bbi.2020.01.016. Epub 2020 Jan 27. PMID: 32001342; PMCID: PMC9444375.
- Maas AIR, Menon DK, Adelson PD, Andelic N, Bell MJ, Belli A, Bragge P, Brazinova A, Büki A, Chesnut RM, Citerio G, Coburn M, Cooper DJ, Crowder AT, Czeiter E, Czosnyka M, Diaz-Arrastia R, Dreier JP, Duhaime AC, Ercole A, van Essen TA, Feigin VL, Gao G, Giacino J, Gonzalez-Lara LE, Gruen RL, Gupta D, Hartings JA, Hill S, Jiang JY, Ketharanathan N, Kompanje EJO, Lanyon L, Laureys S, Lecky F, Levin H, Lingsma HF, Maegele M, Majdan M, Manley G, Marsteller J, Mascia L, McFadyen C, Mondello S, Newcombe V, Palotie A, Parizel PM, Peul W, Piercy J, Polinder S, Puybasset L, Rasmussen TE, Rossaint R, Smielewski P, Söderberg J, Stanworth SJ, Stein MB, von Steinbüchel N, Stewart W, Steyerberg EW, Stocchetti N, Synnot A, Te Ao B, Tenovuo O, Theadom A, Tibboel D, Videtta W, Wang KKW, Williams WH, Wilson L, Yaffe K; InTBIR Participants and Investigators. Traumatic brain injury: integrated approaches to improve prevention, clinical care, and research. *Lancet Neurol*. 2017 Dec;16(12):987-1048. doi: 10.1016/S1474-4422(17)30371-X. Epub 2017 Nov 6. PMID: 29122524.
- Mahajan C, Khurana S, Kapoor I, Sokhal S, Kumar S, Prabhakar H, Mathur P, Mani K. Characteristics of Gut Microbiome After Traumatic Brain Injury. *J Neurosurg Anesthesiol*. 2023 Jan 1;35(1):86-90. doi: 10.1097/ANA.0000000000000789. Epub 2021 Jul 8. PMID: 34238913.
- Majetschak M, Flach R, Heukamp T, Jennissen V, Obertacke U, Neudeck F, Schmit-Neuerburg KP, Schade FU. Regulation of whole blood tumor necrosis factor production upon endotoxin stimulation after severe blunt trauma. *J Trauma*. 1997 Dec;43(6):880-7. doi: 10.1097/00005373-199712000-00002. PMID: 9420099.
- Marshall, W.A., Adams, L.M. & Weaver, J.L. The Brain–Gut Axis in Traumatic Brain Injury: Implications for Nutrition Support. *Curr Surg Rep* 10, 172–179 (2022). <https://doi.org/10.1007/s40137-022-00325-w>
- Martin-Loeches I, Dickson R, Torres A, Hanberger H, Lipman J, Antonelli M, de Pascale G, Bozza F, Vincent JL, Murthy S, Bauer M, Marshall J, Cilloniz C, Bos LD. The importance of airway and lung microbiome in the critically ill. *Crit Care*. 2020 Aug 31;24(1):537. doi: 10.1186/s13054-020-03219-4. PMID: 32867808; PMCID: PMC7457224.

- Meffert MK, Baltimore D. Physiological functions for brain NF-kappaB. *Trends Neurosci.* 2005 Jan;28(1):37-43. doi: 10.1016/j.tins.2004.11.002. PMID: 15626495.
- Mohajeri MH, Brummer RJM, Rastall RA, Weersma RK, Harmsen HJM, Faas M, Eggersdorfer M. The role of the microbiome for human health: from basic science to clinical applications. *Eur J Nutr.* 2018 May;57(Suppl 1):1-14. doi: 10.1007/s00394-018-1703-4. PMID: 29748817; PMCID: PMC5962619.
- Moreira TJ, Pierre K, Maekawa F, Repond C, Cebere A, Liljequist S, Pellerin L. Enhanced cerebral expression of MCT1 and MCT2 in a rat ischemia model occurs in activated microglial cells. *J Cereb Blood Flow Metab.* 2009 Jul;29(7):1273-83. doi: 10.1038/jcbfm.2009.50. Epub 2009 Apr 29. PMID: 19401710.
- Moskowitz MA, Lo EH, Iadecola C. The science of stroke: mechanisms in search of treatments. *Neuron.* 2010 Jul 29;67(2):181-98. doi: 10.1016/j.neuron.2010.07.002. Erratum in: *Neuron.* 2010 Oct 6;68(1):161. PMID: 20670828; PMCID: PMC2957363.
- Muhammad M. Tumor Necrosis Factor Alpha: A Major Cytokine of Brain Neuroinflammation [Internet]. *Cytokines.* IntechOpen; 2020. Available from: <http://dx.doi.org/10.5772/intechopen.85476>
- Ni YF, Wang J, Yan XL, Tian F, Zhao JB, Wang YJ, Jiang T. Histone deacetylase inhibitor, butyrate, attenuates lipopolysaccharide-induced acute lung injury in mice. *Respir Res.* 2010 Mar 20;11(1):33. doi: 10.1186/1465-9921-11-33. PMID: 20302656; PMCID: PMC2848144.
- Niccolai E, Baldi S, Ricci F, Russo E, Nannini G, Menicatti M, Poli G, Taddei A, Bartolucci G, Calabrò AS, Stingo FC, Amedei A. Evaluation and comparison of short chain fatty acids composition in gut diseases. *World J Gastroenterol.* 2019 Sep 28;25(36):5543-5558. doi: 10.3748/wjg.v25.i36.5543. PMID: 31576099; PMCID: PMC6767983.
- Nogal A, Asnicar F, Vijay A, Kouraki A, Visconti A, Louca P, Wong K, Baleanu AF, Giordano F, Wolf J, Hadjigeorgiou G, Davies R, Michelotti GA, Franks PW, Berry SE, Falchi M, Ikram A, Ollivere BJ, Zheng A, Nightingale J, Mangino M, Segata N, Bultman WJ, Spector TD, Valdes AM, Menni C. Genetic and gut microbiome determinants of SCFA circulating and fecal levels, postprandial responses and links to chronic and acute inflammation. *Gut Microbes.* 2023 Jan-Dec;15(1):2240050. doi: 10.1080/19490976.2023.2240050. PMID: 37526398; PMCID: PMC10395212.
- Norins LC. The Beehive Theory: Role of microorganisms in late sequelae of traumatic brain injury and chronic traumatic encephalopathy. *Med Hypotheses.* 2019 Jul;128:1-5. doi: 10.1016/j.mehy.2019.04.019. Epub 2019 Apr 26. PMID: 31203899.

- Oeckinghaus A, Ghosh S. The NF-kappaB family of transcription factors and its regulation. *Cold Spring Harb Perspect Biol.* 2009 Oct;1(4):a000034. doi: 10.1101/cshperspect.a000034. PMID: 20066092; PMCID: PMC2773619.
- Offermanns S, Schwaninger M. Nutritional or pharmacological activation of HCA(2) ameliorates neuroinflammation. *Trends Mol Med.* 2015 Apr;21(4):245-55. doi: 10.1016/j.molmed.2015.02.002. Epub 2015 Mar 9. PMID: 25766751.
- Oktavian, Puguh & Romdhoni, Achmad & Dewanti, Linda & al Fauzi, Asra. (2021). Clinical and Radiological Study of Patients With Skull Base Fracture After Head Injury. *Folia Medica Indonesiana.* 57. 192. 10.20473/fmi.v57i3.22824.
- Olsen AB, Hetz RA, Xue H, Aroom KR, Bhattarai D, Johnson E, Bedi S, Cox CS Jr, Uray K. Effects of traumatic brain injury on intestinal contractility. *Neurogastroenterol Motil.* 2013 Jul;25(7):593-e463. doi: 10.1111/nmo.12121. Epub 2013 Apr 2. PMID: 23551971; PMCID: PMC3982791.
- Opeyemi OM, Rogers MB, Firek BA, Janesko-Feldman K, Vagni V, Mullett SJ, Wendell SG, Nelson BP, New LA, Mariño E, Kochanek PM, Bayır H, Clark RSB, Morowitz MJ, Simon DW. Sustained Dysbiosis and Decreased Fecal Short-Chain Fatty Acids after Traumatic Brain Injury and Impact on Neurologic Outcome. *J Neurotrauma.* 2021 Sep 15;38(18):2610-2621. doi: 10.1089/neu.2020.7506. Epub 2021 Jun 7. PMID: 33957773; PMCID: PMC8403202.
- Oldendorf WH. Carrier-mediated blood-brain barrier transport of short-chain monocarboxylic organic acids. *Am J Physiol.* 1973 Jun;224(6):1450-3. doi: 10.1152/ajplegacy.1973.224.6.1450. PMID: 4712154.
- Olsson A, Gustavsen S, Nguyen TD, Nyman M, Langkilde AR, Hansen TH, Sellebjerg F, Oturai AB, Bach Søndergaard H. Serum Short-Chain Fatty Acids and Associations With Inflammation in Newly Diagnosed Patients With Multiple Sclerosis and Healthy Controls. *Front Immunol.* 2021 May 6;12:661493. doi: 10.3389/fimmu.2021.661493. PMID: 34025661; PMCID: PMC8134701.
- O'Riordan KJ, Collins MK, Moloney GM, Knox EG, Aburto MR, Fülling C, Morley SJ, Clarke G, Schellekens H, Cryan JF. Short chain fatty acids: Microbial metabolites for gut-brain axis signalling. *Mol Cell Endocrinol.* 2022 Apr 15;546:111572. doi: 10.1016/j.mce.2022.111572. Epub 2022 Jan 20. PMID: 35066114.
- O'leary RA, Nichol AD. Pathophysiology of severe traumatic brain injury. *J Neurosurg Sci.* 2018 Oct;62(5):542-548. doi: 10.23736/S0390-5616.18.04501-0. Epub 2018 May 22. PMID: 29790727.

- Parker A, Fonseca S, Carding SR. Gut microbes and metabolites as modulators of blood-brain barrier integrity and brain health. *Gut Microbes*. 2020;11(2):135-157. doi: 10.1080/19490976.2019.1638722. Epub 2019 Aug 1. PMID: 31368397; PMCID: PMC7053956.
- Pimentel TC, Rosset M, de Sousa JMB, de Oliveira LIG, Mafaldo IM, Pintado MME, de Souza EL, Magnani M. Stingless bee honey: An overview of health benefits and main market challenges. *J Food Biochem*. 2022 Mar;46(3):e13883. doi: 10.1111/jfbc.13883. Epub 2021 Aug 2. PMID: 34338341.
- Prinz M, Masuda T, Wheeler MA, Quintana FJ. Microglia and Central Nervous System-Associated Macrophages-From Origin to Disease Modulation. *Annu Rev Immunol*. 2021 Apr 26;39:251-277. doi: 10.1146/annurev-immunol-093019-110159. Epub 2021 Feb 8. PMID: 33556248; PMCID: PMC8085109.
- Racki LR, Narlikar GJ. ATP-dependent chromatin remodeling enzymes: two heads are not better, just different. *Curr Opin Genet Dev*. 2008 Apr;18(2):137-44. doi: 10.1016/j.gde.2008.01.007. Epub 2008 Mar 12. PMID: 18339542; PMCID: PMC2494867.
- Renz M, Müller L, Herbst M, Riedel J, Mohnke K, Ziebart A, Ruemmler R. Analysis of cerebral Interleukin-6 and tumor necrosis factor alpha patterns following different ventilation strategies during cardiac arrest in pigs. *PeerJ*. 2023 Sep 29;11:e16062. doi: 10.7717/peerj.16062. PMID: 37790622; PMCID: PMC10544304.
- Richards JL, Yap YA, McLeod KH, Mackay CR, Mariño E. Dietary metabolites and the gut microbiota: an alternative approach to control inflammatory and autoimmune diseases. *Clin Transl Immunology*. 2016 May 13;5(5):e82. doi: 10.1038/cti.2016.29. PMID: 27350881; PMCID: PMC4910123.
- Rinaldi, Sony Faisal, Mujianto, Bagya. (2017). *Metodologi Penelitian dan Statistik* (Ed. 1). Jakarta: Pusat Pendidikan Sumber Daya Manusia Kesehatan.
- Robinson DR, Gebhart GF. Inside information: the unique features of visceral sensation. *Mol Interv*. 2008 Oct;8(5):242-53. doi: 10.1124/mi.8.5.9. PMID: 19015388; PMCID: PMC2732716.
- Robba C, Poole D, McNett M, Asehnoune K, Bösel J, Bruder N, Chierigato A, Cinotti R, Duranteau J, Einav S, Ercole A, Ferguson N, Guerin C, Siempos II, Kurtz P, Juffermans NP, Mancebo J, Mascia L, McCredie V, Nin N, Oddo M, Pelosi P, Rabinstein AA, Neto AS, Seder DB, Skrifvars MB, Suarez JJ, Taccone FS, van der Jagt M, Citerio G, Stevens RD. Mechanical ventilation in patients with acute brain injury: recommendations of the European Society of Intensive Care Medicine consensus. *Intensive Care*

Med. 2020 Dec;46(12):2397-2410. doi: 10.1007/s00134-020-06283-0. Epub 2020 Nov 11. PMID: 33175276; PMCID: PMC7655906.

Ross, S. A., Halliday, M. I., Campbell, G. C., Byrnes, D. P., & Rowlands, B. J. The presence of tumour necrosis factor in CSF and plasma after severe head injury. *British Journal of Neurosurgery*, 8(4), 419–425.1994. <https://doi.org/10.3109/02688699408995109>

Samma, Linda & Widodo, Djoko. (2019). A case evaluation of traumatic brain injury in Wahidin Sudirohusodo Hospital, Makassar during January 2016 - December 2017. *Bali Medical Journal*. 8. 542. 10.15562/bmj.v8i3.1569.

Schell KR, Fernandes KE, Shanahan E, Wilson I, Blair SE, Carter DA, Cokcetin NN. The Potential of Honey as a Prebiotic Food to Re-engineer the Gut Microbiome Toward a Healthy State. *Front Nutr*. 2022 Jul 28;9:957932. doi: 10.3389/fnut.2022.957932. PMID: 35967810; PMCID: PMC9367972.

Sedger LM, McDermott MF. TNF and TNF-receptors: From mediators of cell death and inflammation to therapeutic giants - past, present and future. *Cytokine Growth Factor Rev*. 2014 Aug;25(4):453-72. doi: 10.1016/j.cytogfr.2014.07.016. Epub 2014 Aug 1. PMID: 25169849.

Sharma B, Lawrence DW. Top-cited articles in traumatic brain injury. *Front Hum Neurosci*. 2014 Nov 5;8:879. doi: 10.3389/fnhum.2014.00879. PMID: 25414657; PMCID: PMC4220681.

Silva YP, Bernardi A, Frozza RL. The Role of Short-Chain Fatty Acids From Gut Microbiota in Gut-Brain Communication. *Front Endocrinol (Lausanne)*. 2020 Jan 31;11:25. doi: 10.3389/fendo.2020.00025. PMID: 32082260; PMCID: PMC7005631.

Singh SS, Rai SN, Birla H, Zahra W, Rathore AS, Singh SP. NF- κ B-Mediated Neuroinflammation in Parkinson's Disease and Potential Therapeutic Effect of Polyphenols. *Neurotox Res*. 2020 Mar;37(3):491-507. doi: 10.1007/s12640-019-00147-2. Epub 2019 Dec 10. PMID: 31823227.

Soliman ML, Puig KL, Combs CK, Rosenberger TA. Acetate reduces microglia inflammatory signaling in vitro. *J Neurochem*. 2012 Nov;123(4):555-67. doi: 10.1111/j.1471-4159.2012.07955.x. Epub 2012 Sep 28. PMID: 22924711; PMCID: PMC3472042.

Song JH, Lee JW, Shim B, Lee CY, Choi S, Kang C, Sohn NW, Shin JW. Glycyrrhizin alleviates neuroinflammation and memory deficit induced by systemic lipopolysaccharide treatment in mice. *Molecules*. 2013 Dec 17;18(12):15788-803. doi: 10.3390/molecules181215788. PMID: 24352029; PMCID: PMC6269849.

Stein DM, Lindel AL, Murdock KR, Kufera JA, Menaker J, Scalea TM. Use of serum biomarkers to predict secondary insults following severe traumatic

brain injury. Shock. 2012 Jun;37(6):563-8. doi: 10.1097/SHK.0b013e3182534f93. PMID: 22552017.

Spielmann S, Kerner T, Ahlers O, Keh D, Gerlach M, Gerlach H. Early detection of increased tumour necrosis factor alpha (TNFalpha) and soluble TNF receptor protein plasma levels after trauma reveals associations with the clinical course. *Acta Anaesthesiol Scand*. 2001 Mar;45(3):364-70. doi: 10.1034/j.1399-6576.2001.045003364.x. PMID: 11207475.

Sun B, Hu C, Fang H, Zhu L, Gao N, Zhu J. The Effects of *Lactobacillus acidophilus* on the Intestinal Smooth Muscle Contraction through PKC/MLCK/MLC Signaling Pathway in TBI Mouse Model. *PLoS One*. 2015 Jun 1;10(6):e0128214. doi: 10.1371/journal.pone.0128214. PMID: 26030918; PMCID: PMC4451510.

Sun M, Wu W, Liu Z, Cong Y. Microbiota metabolite short chain fatty acids, GPCR, and inflammatory bowel diseases. *J Gastroenterol*. 2017 Jan;52(1):1-8. doi: 10.1007/s00535-016-1242-9. Epub 2016 Jul 23. PMID: 27448578; PMCID: PMC5215992.

Sundman MH, Chen NK, Subbian V, Chou YH. The bidirectional gut-brain-microbiota axis as a potential nexus between traumatic brain injury, inflammation, and disease. *Brain Behav Immun*. 2017 Nov;66:31-44. doi: 10.1016/j.bbi.2017.05.009. Epub 2017 May 17. PMID: 28526435.

Te Ao B, Brown P, Tobias M, Ameratunga S, Barker-Collo S, Theadom A, McPherson K, Starkey N, Dowell A, Jones K, Feigin VL; BIONIC Study Group. Cost of traumatic brain injury in New Zealand: evidence from a population-based study. *Neurology*. 2014 Oct 28;83(18):1645-52. doi: 10.1212/WNL.0000000000000933. Epub 2014 Sep 26. PMID: 25261503.

Tedelind S, Westberg F, Kjerrulf M, Vidal A. Anti-inflammatory properties of the short-chain fatty acids acetate and propionate: a study with relevance to inflammatory bowel disease. *World J Gastroenterol*. 2007 May 28;13(20):2826-32. doi: 10.3748/wjg.v13.i20.2826. PMID: 17569118; PMCID: PMC4395634.

Tracey KJ. The inflammatory reflex. *Nature*. 2002 Dec 19-26;420(6917):853-9. doi: 10.1038/nature01321. PMID: 12490958. Vallabhapurapu S, Karin M. Regulation and function of NF-kappaB transcription factors in the immune system. *Annu Rev Immunol*. 2009;27:693-733. doi: 10.1146/annurev.immunol.021908.132641. PMID: 19302050.

van Berlo D, Knaapen AM, van Schooten FJ, Schins RP, Albrecht C. NF-kappaB dependent and independent mechanisms of quartz-induced proinflammatory activation of lung epithelial cells. *Part Fibre Toxicol*. 2010 May 21;7:13. doi: 10.1186/1743-8977-7-13. PMID: 20492675; PMCID: PMC2885999.

- Vidinopoulos K, Azman Z, Somers A, Zahra VA, Thiel A, Lu H, Pham Y, Tran NT, Allison BJ, Herlenius E, Hooper S, Galinsky R, Polglase GR. Mechanical ventilation induces brainstem inflammation in preterm fetal sheep. *Front Pediatr.* 2023 Oct 23;11:1225294. doi: 10.3389/fped.2023.1225294. PMID: 37936886; PMCID: PMC10626530.
- Vieira LV, Pedrosa LAC, Souza VS, Paula CA, Rocha R. Incidence of diarrhea and associated risk factors in patients with traumatic brain injury and enteral nutrition. *Metab Brain Dis.* 2018 Oct;33(5):1755-1760. doi: 10.1007/s11011-018-0287-2. Epub 2018 Jul 16. PMID: 30014176.
- Vijay N, Morris ME. Role of monocarboxylate transporters in drug delivery to the brain. *Curr Pharm Des.* 2014;20(10):1487-98. doi: 10.2174/13816128113199990462. PMID: 23789956; PMCID: PMC4084603.
- Vinolo MA, Rodrigues HG, Hatanaka E, Sato FT, Sampaio SC, Curi R. Suppressive effect of short-chain fatty acids on production of proinflammatory mediators by neutrophils. *J Nutr Biochem.* 2011 Sep;22(9):849-55. doi: 10.1016/j.jnutbio.2010.07.009. Epub 2010 Dec 16. PMID: 21167700.
- von Bethmann AN, Brasch F, Nüsing R, Vogt K, Volk HD, Müller KM, Wendel A, Uhlig S. Hyperventilation induces release of cytokines from perfused mouse lung. *Am J Respir Crit Care Med.* 1998 Jan;157(1):263-72. doi: 10.1164/ajrccm.157.1.9608052. PMID: 9445308.
- Wang HX, Wang YP. Gut Microbiota-brain Axis. *Chin Med J (Engl).* 2016 Oct 5;129(19):2373-80. doi: 10.4103/0366-6999.190667. PMID: 27647198; PMCID: PMC5040025.
- Wang J, Yang Z, Liu C, Zhao Y, Chen Y. Activated microglia provide a neuroprotective role by balancing glial cell-line derived neurotrophic factor and tumor necrosis factor- α secretion after subacute cerebral ischemia. *Int J Mol Med.* 2013 Jan;31(1):172-8. doi: 10.3892/ijmm.2012.1179. Epub 2012 Nov 13. PMID: 23151666; PMCID: PMC3573737.
- Wenzel TJ, Gates EJ, Ranger AL, Klegeris A. Short-chain fatty acids (SCFAs) alone or in combination regulate select immune functions of microglia-like cells. *Mol Cell Neurosci.* 2020 Jun;105:103493. doi: 10.1016/j.mcn.2020.103493. Epub 2020 Apr 22. PMID: 32333962.
- Wishart DS, Feunang YD, Marcu A, Guo AC, Liang K, Vázquez-Fresno R, Sajed T, Johnson D, Li C, Karu N, Sayeeda Z, Lo E, Assempour N, Berjanskii M, Singhal S, Arndt D, Liang Y, Badran H, Grant J, Serra-Cayuela A, Liu Y, Mandal R, Neveu V, Pon A, Knox C, Wilson M, Manach C, Scalbert A. HMDB 4.0: the human metabolome database for 2018. *Nucleic Acids Res.* 2018 Jan 4;46(D1):D608-D617. doi: 10.1093/nar/gkx1089. PMID: 29140435; PMCID: PMC5753273.

- Wrba L, Halbgebauer R, Roos J, Huber-Lang M, Fischer-Posovszky P. Adipose tissue: a neglected organ in the response to severe trauma? *Cell Mol Life Sci.* 2022 Mar 26;79(4):207. doi: 10.1007/s00018-022-04234-0. PMID: 35338424; PMCID: PMC8956559.
- Yu S, Wang L, Jing X, Wang Y, An C. Features of gut microbiota and short-chain fatty acids in patients with first-episode depression and their relationship with the clinical symptoms. *Front Psychol.* 2023 Apr 24;14:1088268. doi: 10.3389/fpsyg.2023.1088268. PMID: 37168424; PMCID: PMC10165121.
- Zhou L, Lin J, Lin J, Kui G, Zhang J, Yu Y. Neuroprotective effects of vagus nerve stimulation on traumatic brain injury. *Neural Regen Res.* 2014 Sep 1;9(17):1585-91. doi: 10.4103/1673-5374.141783. PMID: 25368644; PMCID: PMC4211199.
- Zhou P, Zou Z, Wu W, Zhang H, Wang S, Tu X, Huang W, Chen C, Zhu S, Weng Q, Zheng S. The gut-lung axis in critical illness: microbiome composition as a predictor of mortality at day 28 in mechanically ventilated patients. *BMC Microbiol.* 2023 Dec 18;23(1):399. doi: 10.1186/s12866-023-03078-3. PMID: 38110878; PMCID: PMC10726596.
- Zhu CS, Grandhi R, Patterson TT, Nicholson SE. A Review of Traumatic Brain Injury and the Gut Microbiome: Insights into Novel Mechanisms of Secondary Brain Injury and Promising Targets for Neuroprotection. *Brain Sci.* 2018 Jun 19;8(6):113. doi: 10.3390/brainsci8060113. PMID: 29921825; PMCID: PMC6025245

LAMPIRAN

REKAPITULASI UJI STATISTIK

Severity	Control					Nilai p
	Mean	SD	Median	Minimum	Maximum	
SCFA_1	53.16	19.94	57.64	21.90	77.43	0.368**
SCFA_3	60.02	23.90	63.10	23.69	84.61	
SCFA_5	59.80	26.40	69.10	22.73	94.80	
TNF_1	10.29	6.54	7.72	4.92	22.25	0.417*
TNF_3	10.66	5.16	10.99	5.20	19.09	
TNF_5	6.47	3.87	7.59	0.35	10.16	
Severity	Mild					Nilai p
	Mean	SD	Median	Minimum	Maximum	
SCFA_1	45.67	30.71	38.11	10.36	109.42	0.000*
SCFA_3	74.15	41.05	71.21	13.36	204.73	
SCFA_5	70.42	54.08	60.24	12.96	283.73	
TNF_1	11.56	17.98	7.88	2.00	89.78	0.279*
TNF_3	8.77	8.08	7.11	1.93	40.28	
TNF_5	5.69	3.47	4.98	1.25	15.81	
Severity	Moderate					Nilai p
	Mean	SD	Median	Minimum	Maximum	
SCFA_1	44.16	24.07	42.56	2.41	97.69	0.004*
SCFA_3	66.38	38.34	57.69	14.70	203.49	
SCFA_5	78.91	74.20	65.80	14.34	386.86	
TNF_1	29.69	92.53	9.13	1.93	461.74	0.041*
TNF_3	22.61	77.78	4.70	1.66	387.06	
TNF_5	7.38	7.23	6.63	0.86	37.31	
Severity	Severe					Nilai p
	Mean	SD	Median	Minimum	Maximum	
SCFA_1	63.67	11.33	63.92	49.60	77.24	0.412**
SCFA_3	52.06	35.06	50.97	17.69	88.60	
SCFA_5	58.71	35.63	66.63	9.80	91.77	
TNF_1	10.03	6.38	8.33	4.29	19.16	0.733**
TNF_3	5.58	0.36	5.68	5.09	5.87	
TNF_5	5.80	4.63	5.83	1.30	10.22	

* Uji Friedman

** Uji Repeated Anova

Ventilation	Control					Nilai p
	Mean	SD	Median	Minimum	Maximum	
SCFA_1	53.16	19.94	57.64	21.90	77.43	0.368**
SCFA_3	60.02	23.90	63.10	23.69	84.61	
SCFA_5	59.80	26.40	69.10	22.73	94.80	

TNF_1	10.29	6.54	7.72	4.92	22.25	0.417*
TNF_3	10.66	5.16	10.99	5.20	19.09	
TNF_5	6.47	3.87	7.59	0.35	10.16	
Ventilation	Delayed extubation					Nilai p
	Mean	SD	Median	Minimum	Maximum	
SCFA_1	48.08	31.78	42.48	3.73	104.30	0.751*
SCFA_3	54.98	27.55	53.08	13.36	113.14	
SCFA_5	75.21	92.44	50.64	12.96	386.86	
TNF_1	7.12	2.60	7.22	1.93	11.25	0.526*
TNF_3	8.20	10.54	3.88	1.93	40.28	
TNF_5	7.64	8.96	6.19	2.15	37.31	
Ventilation	Extubation					Nilai p
	Mean	SD	Median	Minimum	Maximum	
SCFA_1	40.96	24.36	40.13	10.47	109.42	0.000*
SCFA_3	79.03	37.27	77.42	33.81	204.73	
SCFA_5	78.24	60.63	62.83	14.34	283.73	
TNF_1	36.47	101.84	8.87	2.00	461.74	0.002*
TNF_3	25.48	85.15	6.59	1.66	387.06	
TNF_5	4.33	2.76	3.64	0.86	11.19	
Ventilation	Ventilation					Nilai p
	Mean	SD	Median	Minimum	Maximum	
SCFA_1	63.42	19.55	63.42	49.60	77.24	0.223*
SCFA_3	22.24	6.43	22.24	17.69	26.79	
SCFA_5	33.22	33.12	33.22	9.80	56.65	
TNF_1	8.33	0.46	8.33	8.00	8.66	0.135*
TNF_3	5.45	0.51	5.45	5.09	5.82	
TNF_5	9.78	0.62	9.78	9.33	10.22	
Ventilation	Tanpa Ventilasi					Nilai p
	Mean	SD	Median	Minimum	Maximum	
SCFA_1	50.02	25.82	45.43	2.41	92.70	0.000*
SCFA_3	74.13	47.20	69.97	14.70	203.49	
SCFA_5	70.96	24.45	67.98	22.79	107.94	
TNF_1	11.51	12.04	8.52	2.97	51.02	0.607*
TNF_3	8.75	5.17	7.79	2.00	20.73	
TNF_5	8.03	3.92	8.78	1.87	15.81	

* Uji Friedman

** Uji Repeated Anova

		SCFA_1	SCFA_3	SCFA_5
Mild	SCFA_1		0.000*	0.000*
	SCFA_3			0.570*
	SCFA_5			
Moderate	SCFA_1		0.007*	0.001*

	SCFA_3			0.278*
	SCFA_5			
Severe	SCFA_1		0.560**	0.770**
	SCFA_3			0.472**
	SCFA_5			
Control	SCFA_1		0.018**	0.343**
	SCFA_3			0.973**
	SCFA_5			
		TNF_1	TNF_3	TNF_5
Mild	TNF_1		0.520*	0.042*
	TNF_3			0.067*
	TNF_5			
Moderate	TNF_1		0.022*	0.014*
	TNF_3			0.886*
	TNF_5			
Severe	TNF_1		0.247**	0.426**
	TNF_3			0.934**
	TNF_5			
Control	TNF_1		0.889*	0.093*
	TNF_3			0.161*
	TNF_5			

* Uji Wilcoxon

** Uji t Berpasangan

		SCFA_1	SCFA_3	SCFA_5
Control	SCFA_1		0.018**	0.343**
	SCFA_3			0.973**
	SCFA_5			
Delayed Extubation	SCFA_1		0.594*	0.397*
	SCFA_3			0.594*
	SCFA_5			
Extubation	SCFA_1		0.000*	0.000*
	SCFA_3			0.911*
	SCFA_5			
Ventilation	SCFA_1		0.180*	0.180*
	SCFA_3			0.655*
	SCFA_5			
Tanpa Ventilasi	SCFA_1		0.035*	0.000*
	SCFA_3			0.433*
	SCFA_5			
		TNF_1	TNF_3	TNF_5
Control	TNF_1		0.889*	0.093*
	TNF_3			0.161*

	TNF_5			
Delayed Extubation	TNF_1		0.572*	0.363*
	TNF_3			0.875*
	TNF_5			
Extubation	TNF_1		0.009*	0.002*
	TNF_3			0.025*
	TNF_5			
Ventilation	TNF_1		0.180*	0.180*
	TNF_3			0.180*
	TNF_5			
Tanpa Ventilasi	TNF_1		0.875*	0.158*
	TNF_3			0.638*
	TNF_5			

* Uji Wilcoxon

** Uji t Berpasangan

Severity			Delta_TNF_1_3	Delta_TNF_1_5	Delta_TNF_3_5
Control	Delta_SCFA_1_3	Nilai r	0.437	0.297	-0.177
		Nilai p	0.279*	0.474*	0.675*
	Delta_SCFA_1_5	Nilai r	-0.191	-0.043	0.149
		Nilai p	0.651*	0.919*	0.724*
	Delta_SCFA_3_5	Nilai r	-0.333	-0.429	-0.167
		Nilai p	0.420**	0.289**	0.693**
Mild	Delta_SCFA_1_3	Nilai r	0.030	-0.062	0.091
		Nilai p	0.895**	0.786**	0.687**
	Delta_SCFA_1_5	Nilai r	-0.401	-0.259	0.080
		Nilai p	0.064**	0.244**	0.725**
	Delta_SCFA_3_5	Nilai r	-0.333	-0.248	-0.042
		Nilai p	0.130**	0.266**	0.852**
Moderate	Delta_SCFA_1_3	Nilai r	-0.361	-0.030	0.133
		Nilai p	0.083**	0.888**	0.535**
	Delta_SCFA_1_5	Nilai r	-0.614	-0.248	0.159
		Nilai p	0.001**	0.243**	0.458**
	Delta_SCFA_3_5	Nilai r	-0.377	-0.202	0.023
		Nilai p	0.069**	0.343**	0.913**
Severe	Delta_SCFA_1_3	Nilai r	-0.456	-	-0.977
		Nilai p	0.544*	-	0.023*
	Delta_SCFA_1_5	Nilai r	-0.495	-0.800	-0.956
		Nilai p	0.505*	0.200**	0.044*
	Delta_SCFA_3_5	Nilai r	0.053	0.200	0.315
		Nilai p	0.947*	0.800**	0.685*

* Uji Korelasi Pearson

** Uji Korelasi Spearman

Ventilation			Delta_TNF_1_3	Delta_TNF_1_5	Delta_TNF_3_5
Control	Delta_SCFA_1_3	Nilai r	0.437	0.297	-0.177
		Nilai p	0.279*	0.474*	0.675*
	Delta_SCFA_1_5	Nilai r	-0.191	-0.043	0.149
		Nilai p	0.651*	0.919*	0.724*
	Delta_SCFA_3_5	Nilai r	-0.333	-0.429	-0.167
		Nilai p	0.420**	0.289**	0.693**
Delayed Extubation	Delta_SCFA_1_3	Nilai r	-0.705	0.103	0.420
		Nilai p	0.005**	0.725**	0.135**
	Delta_SCFA_1_5	Nilai r	-0.776	0.310	0.675
		Nilai p	0.001**	0.281**	0.008**
	Delta_SCFA_3_5	Nilai r	-0.490	0.499	0.732
		Nilai p	0.075**	0.069**	0.003**
Extubation	Delta_SCFA_1_3	Nilai r	0.445	0.310	0.095
		Nilai p	0.049**	0.184**	0.691**
	Delta_SCFA_1_5	Nilai r	-0.362	-0.460	-0.374
		Nilai p	0.116**	0.041**	0.104**
	Delta_SCFA_3_5	Nilai r	-0.605	-0.638	-0.329
		Nilai p	0.005**	0.002**	0.156**
Ventilation	Delta_SCFA_1_3	Nilai r	-	-	-
		Nilai p	-	-	-
	Delta_SCFA_1_5	Nilai r	-	-	-
		Nilai p	-	-	-
	Delta_SCFA_3_5	Nilai r	-	-	-
		Nilai p	-	-	-
Without Ventilation	Delta_SCFA_1_3	Nilai r	-0.185	0.059	0.358
		Nilai p	0.527**	0.840**	0.208**
	Delta_SCFA_1_5	Nilai r	-0.288	-0.407	0.239
		Nilai p	0.318**	0.149**	0.411*
	Delta_SCFA_3_5	Nilai r	0.055	-0.191	-0.218
		Nilai p	0.852**	0.513**	0.455**

* Uji Korelasi Pearson

** Uji Korelasi Spearman

REKAPITULASI SAMPEL PENELITIAN

									SCFA 1	SCFA 3	SCFA 5	TNF α 1	TNF α 3	TNF α 5
1	656741	64	P	11	moderate	Temporal	surgical	extubation	18.746	83.3855	47.5675	6.4165	1.656	6.4165
2	739234	9	L	15	control	Ekstrakranial	conservative	control	58.869	62.035	76.6015	6.5583	5.535	5.5913
3	1140623	63	L	14	mild	Parietal	conservative	without ventilation	26.727	33.0485	67.965	2.9669	7.482	4.522
4	1140857	21	L	11	moderate	Frontal	conservative	without ventilation	2.4085	14.6985	22.786	8.8271	4.4064	10.0361
5	1140973	62	L	8	severe	Bilateral	surgical	delayed extubation	65.132	75.147	76.6085	4.2902	5.5401	2.3291
6	1141067	42	L	13	mild	Bilateral	surgical	delayed extubation	26.8875	35.8635	12.9585	5.8716	6.0906	7.2712
7	1141094	80	L	15	control	Ekstrakranial	conservative	control	25.236	23.689	24.165	8.3145	9.4351	0.3528
8	1141299	13	L	10	moderate	Bilateral	surgical	delayed extubation	31.509	25.195	31.3665	1.9305	6.632	6.8463
9	1141340	17	L	4	severe	Bilateral	conservative	ventilator	49.6	17.694	9.803	8.0042	5.0923	9.3343
10	1141341	17	L	15	control	Ekstrakranial	conservative	control	21.898	25.245	22.7315	4.9793	5.2049	9.4351
11	1145116	10	P	15	mild	Parietal	surgical	extubation	14.1415	42.095	28.4085	5.2049	1.9305	3.3371
12	1145226	18	L	10	moderate	Posterior	surgical	delayed extubation	40.0355	28.4085	37.156	3.5797	2.0649	3.4588
13	1147785	29	L	15	mild	Frontal	surgical	extubation	38.7985	89.8545	34.675	2.0649	9.7364	6.8463
14	1147795	44	L	15	mild	Frontal	surgical	extubation	10.472	69.7175	67.201	8.1078	3.6998	3.8192
15	1147851	65	L	15	mild	Frontal	surgical	extubation	20.683	121.352	35.7325	8.2113	8.2113	3.8192
16	1147895	15	L	9	moderate	Parietal	surgical	delayed extubation	3.7285	71.6995	40.7685	7.1654	2.5877	2.7152
17	1147941	23	L	11	moderate	Frontal	surgical	extubation	12.866	35.7325	14.3395	8.3145	3.9379	8.3145
18	1148600	16	L	15	mild	Parietal	surgical	delayed extubation	10.356	13.356	29.018	7.2712	2.7152	8.6227
19	1151240	16	P	15	mild	Temporal	conservative	without ventilation	38.6735	72.6955	56.335	4.2902	8.6227	2.3291
20	1151565	71	L	10	moderate	Frontal	surgical	delayed extubation	44.924	44.8075	88.5125	8.3145	3.9379	37.3083
21	1154965	30	L	15	mild	Frontoparietal	conservative	extubation	10.9545	80.3665	54.0365	2.1978	9.595	5.4288
22	1156833	32	L	13	mild	Temporal	conservative	without ventilation	70.927	77.173	95.754	12.5326	8.1078	9.2332
23	1156882	42	L	13	mild	Frontal	surgical	extubation	109.4205	204.73	283.728	8.2722	6.7393	3.4588
24	1156904	15	L	13	mild	Parietal	surgical	delayed extubation	20.683	30.936	40.89	6.632	1.9305	2.7899

25	1157109	19	P	9	moderate	Frontal	surgical	extubation	59.9235	104.8545	171.7855	461.7441	387.0585	2.0649
26	1157345	17	P	10	moderate	Frontotemporal	surgical	delayed extubation	56.88	113.1365	386.858	9.4351	2.2754	9.3343
27	1159593	25	L	14	mild	Temporal	conservative	without ventilation	88.7555	138.1455	103.0555	8.2113	3.8192	9.5357
28	1159610	66	L	15	control	Ekstrakranial	conservative	control	51.275	64.159	63.3945	9.4351	5.3171	9.6362
29	1159623	9	P	12	moderate	Frontotemporal	surgical	extubation	61.4425	93.967	120.5305	9.595	4.819	1.4573
30	1159708	61	L	14	mild	Temporal	conservative	without ventilation	92.7	83.9715	107.9395	7.6593	20.7298	15.8115
31	1159709	12	P	14	mild	Temporoparietal	surgical	extubation	61.2885	66.9375	90.9195	19.4206	10.0367	2.9234
32	1159713	53	L	10	moderate	Falx	conservative	without ventilation	27.3175	203.486	53.046	4.056	4.2902	1.8749
33	1159714	53	L	13	mild	Parietal	surgical	delayed extubation	104.2975	64.6265	60.3845	9.7364	40.2796	5.535
34	1160086	15	L	12	moderate	Temporal	surgical	extubation	41.468	43.2775	67.467	9.4354	4.5885	5.6477
35	1160089	14	L	11	moderate	Frontotemporal	conservative	without ventilation	48.372	56.001	48.5935	5.5913	10.339	7.8935
36	1160112	21	L	12	moderate	Frontotemporal	surgical	delayed extubation	76.2535	56.8045	33.541	6.7308	3.8257	2.1535
37	1160155	9	L	15	mild	Frontoparietal	surgical	extubation	48.372	69.5805	50.492	11.4968	10.1575	1.2515
38	1160176	17	L	10	moderate	Parietal	conservative	without ventilation	28.912	49.7725	48.372	4.5335	6.7884	4.3142
39	1160240	63	L	7	severe	Frontoparietal	surgical	ventilator	77.2435	26.788	56.6455	8.6604	5.8172	10.2179
40	1160501	15	L	10	moderate	Frontal	conservative	without ventilation	72.8805	58.572	88.82	51.0171	12.2353	13.0413
41	1160631	13	L	15	mild	Frontal	surgical	extubation	31.838	33.805	65.5545	10.3995	9.3157	7.7763
42	1163695	19	L	12	moderate	Frontoparietal	conservative	without ventilation	42.483	34.0635	65.5545	10.8247	16.2578	6.101
43	1164128	20	L	11	moderate	Frontal	surgical	extubation	32.1375	55.591	43.2775	21.6521	8.1286	11.1907
44	1164524	36	L	12	moderate	Temporoparietal	surgical	delayed extubation	20.893	49.351	66.0405	9.9161	3.4508	7.2513
45	1166783	32	P	15	control	Ekstrakranial	conservative	control	56.4055	60.03	74.8045	22.2474	15.1131	9.3157
46	1166784	7	P	15	control	Ekstrakranial	conservative	control	77.4315	84.6135	45.39	4.9202	12.5446	1.4151
47	1166785	15	L	15	control	Ekstrakranial	conservative	control	65.6765	84.0685	94.8045	7.1353	19.0949	5.8738
48	1166801	11	L	15	mild	Parietal	surgical	extubation	46.7555	77.096	60.1015	7.1933	6.4436	3.1331
49	1166811	14	L	15	mild	Frontoparietal	surgical	extubation	34.1705	78.657	42.1805	2.003	4.8647	5.4788
50	1169669	15	P	14	mild	Frontal	conservative	without ventilation	37.552	69.636	73.3515	14.7969	5.6477	10.2179

51	1169758	13	P	12	moderate	Parietal	surgical	extubation	42.632	63.3535	106.668	18.7699	6.158	0.8551
52	1170165	60	L	15	mild	Parietal	surgical	extubation	60.314	77.734	88.4615	89.7843	6.7308	2.1032
53	1170375	8	L	8	severe	Temporal	surgical	extubation	62.7005	88.596	91.7655	19.16	5.8738	1.2989
54	1172387	51	P	10	moderate	Temporal	conservative	without ventilation	58.272	76.2035	93.8555	14.9866	2.003	8.4827
55	1172424	55	L	10	moderate	Frontal	surgical	delayed extubation	97.6865	83.5575	73.1425	11.2519	13.2905	2.3561
56	1172427	21	L	12	moderate	Ekstrakranial	conservative	without ventilation	64.249	70.301	67.99	10.8247	11.8039	9.0768
57	1172428	36	P	15	control	Ekstrakranial	conservative	control	68.45	76.298	76.5245	18.7049	13.0413	10.1575
58	1172435	31	L	12	moderate	Frontal	surgical	delayed extubation	73.87	76.849	75.7535	7.6008	20.1394	9.0171