

DAFTAR ISI

LEMBAR PERSETUJUAN	Error! Bookmark not defined.
DAFTAR ISI	Error! Bookmark not defined.
DAFTAR TABEL	iii
DAFTAR GAMBAR	iv
DAFTAR SINGKATAN	6
PERNYATAAN	Error! Bookmark not defined.
KATA PENGANTAR	Error! Bookmark not defined.
ABSTRAK	Error! Bookmark not defined.
BAB I	Error! Bookmark not defined.
PENDAHULUAN	Error! Bookmark not defined.
A. Latar Belakang Masalah	Error! Bookmark not defined.
B. Pertanyaan Penelitian	Error! Bookmark not defined.
C. Tujuan Penelitian	Error! Bookmark not defined.
D. Manfaat Penelitian	Error! Bookmark not defined.
E. Keaslian Penelitian	Error! Bookmark not defined.
BAB II	Error! Bookmark not defined.
TINJAUAN PUSTAKA	Error! Bookmark not defined.
A. Tinjauan Pustaka	Error! Bookmark not defined.
B. Landasan Teori	Error! Bookmark not defined.
C. Kerangka Teori	Error! Bookmark not defined.
D. Hipotesis Penelitian	Error! Bookmark not defined.
BAB III	Error! Bookmark not defined.
METODE PENELITIAN	Error! Bookmark not defined.
A. Rancangan Penelitian	Error! Bookmark not defined.
B. Waktu dan Tempat Penelitian	Error! Bookmark not defined.
C. Subyek Penelitian	Error! Bookmark not defined.
D. Variabel Penelitian	Error! Bookmark not defined.
BAB IV	Error! Bookmark not defined.
HASIL DAN PEMBAHASAN	Error! Bookmark not defined.
A. Hasil	Error! Bookmark not defined.
1. Penelitian Tahap 1	Error! Bookmark not defined.
2. Penelitian Tahap 2	Error! Bookmark not defined.
3. Penelitian Tahap 3	Error! Bookmark not defined.

B.	Pembahasan	Error! Bookmark not defined.
1.	Penelitian Tahap 1	Error! Bookmark not defined.
2.	Penelitian Tahap 2	Error! Bookmark not defined.
3.	Penelitian Tahap 3	Error! Bookmark not defined.
BAB V	Error! Bookmark not defined.
A.	Kesimpulan	Error! Bookmark not defined.
B.	Saran	Error! Bookmark not defined.
Ringkasan	Error! Bookmark not defined.
1.	Penelitian Tahap 1	Error! Bookmark not defined.
2.	Penelitian Tahap 2	Error! Bookmark not defined.
3.	Penelitian Tahap 3	Error! Bookmark not defined.
SUMMARY	Error! Bookmark not defined.
DAFTAR PUSTAKA	Error! Bookmark not defined.
LAMPIRAN	Error! Bookmark not defined.
DAFTAR RIWAYAT HIDUP	Error! Bookmark not defined.

DAFTAR TABEL

- Tabel 1. Strain Hewan Coba, Durasi BCCAO, Area iskemia, Pewarnaan TTC dan Penggunaan Stereologi Metode Cavalieri pada Model Hewan Coba Iskemia **Error! Bookmark not defined.**
- Tabel 2. Peningkatan ROS, kalsium, LDH, SOD, MDA, *superoxide*, GFAP pasca iskemia**Error! Bookmark not defined.**
- Tabel 3. Uji Fungsi Neurologis Pada Model tBCCAO Tikus**Error! Bookmark not defined.**
- Tabel 4. Definisi Operasional**Error! Bookmark not defined.**
- Tabel 5 Volume iskemia dihitung dengan hitung titik.**Error! Bookmark not defined.**
- Tabel 6. Nilai yang digunakan dalam penentuan V_{ref} dan $V_{disektor}$**Error! Bookmark not defined.**
- Tabel 7 Hubungan antara durasi iskemia, durasi reperfusi dan volume iskemia hippocampus menggunakan analisis korelasi Pearson.**Error! Bookmark not defined.**
- Tabel 8. Hubungan volume iskemia hippocampus dengan durasi hiperglikemia dan GDP**Error! Bookmark not defined.**
- Tabel 9. Rentang jumlah irisan, rentang jumlah Q^+ , pada hitung neuron CA1 dan CA2CA3 hippocampus**Error! Bookmark not defined.**

DAFTAR GAMBAR

- Gambar 1. Skema fase I dan II iskemia.. **Error! Bookmark not defined.**
- Gambar 2. Skema fase III iskemia..... **Error! Bookmark not defined.**
- Gambar 3. Bagan mekanisme yang terlibat dalam stres oksidatif.... **Error! Bookmark not defined.**
- Gambar 4. Mekanisme cedera iskemia/reperfusi..... **Error! Bookmark not defined.**
- Gambar 5. Perubahan kadar kalsium pada cedera iskemia reperfusi global.)..... **Error! Bookmark not defined.**
- Gambar 6. Periode cedera iskemia reperfusi. **Error! Bookmark not defined.**
- Gambar 7. Pengaruh iskemia *reperfusi* pada kondisi hiperglikemia. **Error! Bookmark not defined.**
- Gambar 8. Keterlibatan hiperglikemia, iskemia reperfusi dan inflamasi. **Error! Bookmark not defined.**
- Gambar 9. Keterlibatan iskemia otak dan hiperglikemia pada proses infark otak.
..... **Error! Bookmark not defined.**
- Gambar 10. Peningkatan COX-2 pada hiperglikemia dan iskemia otak. **Error! Bookmark not defined.**
- Gambar 11. Infark otak pada iskemia reperfusi dengan hiperglikemia.. **Error! Bookmark not defined.**
- Gambar 12. Neuronal preconditioning pada iskemia reperfusi.. **Error! Bookmark not defined.**
- Gambar 13. Tahap pembentukan AGEs. **Error! Bookmark not defined.**
- Gambar 14. Metabolisme glukosa dan pembentukan AGEs.....**Error! Bookmark not defined.**
- Gambar 15. Hubungan hiperglikemia dengan disfungsi pembuluh darah. **Error! Bookmark not defined.**
- Gambar 16. Hubungan hiperglikemia, AGEs, RAGE dan gangguan pembuluh darah..
..... **Error! Bookmark not defined.**
- Gambar 17. Distribusi RAGE pada tikus..... **Error! Bookmark not defined.**
- Gambar 18. *AGEs-RAGE signaling pathway* pada komplikasi diabetes **Error! Bookmark not defined.**
- Gambar 19. Mekanisme aksi AGEs-RAGE..... **Error! Bookmark not defined.**
- Gambar 20. Mekanisme aksi BDNF dan reseptor TrkB.....**Error! Bookmark not defined.**

- Gambar 21. Mekanisme BDNF mempertahankan neuron pasca hipoksia dan iskemia. **Error! Bookmark not defined.**
- Gambar 22. Gangguan sinyal BDNF/TrkB pada stroke **Error! Bookmark not defined.**
- Gambar 23. Mekanisme kerja proBDNF dan p75 NTR **Error! Bookmark not defined.**
- Gambar 24. *Lactate dehydrogenase* (LDH) **Error! Bookmark not defined.**
- Gambar 25. Pewarnaan TTC pada otak tikus. **Error! Bookmark not defined.**
- Gambar 26. Struktur hippocampus. **Error! Bookmark not defined.**
- Gambar 27. Kerangka teori penelitian **Error! Bookmark not defined.**
- Gambar 28. Alur Penelitian Tahap I **Error! Bookmark not defined.**
- Gambar 29. Alur penelitian tahap II **Error! Bookmark not defined.**
- Gambar 30. Alur Penelitian Tahap III **Error! Bookmark not defined.**
- Gambar 31. Irisan otak dengan pewarnaan TTC..... **Error! Bookmark not defined.**
- Gambar 32. Alur Uji Memori Spasial dengan *Morris Water Maze* (MWM). **Error! Bookmark not defined.**
- Gambar 33. Deskripsi Hewan Coba Tahap 1..... **Error! Bookmark not defined.**
- Gambar 34. Hasil Pewarnaan TTC..... **Error! Bookmark not defined.**
- Gambar 35. Rerata volume iskemia otak tikus tahap 1..... **Error! Bookmark not defined.**
- Gambar 36. Deskripsi hewan coba tahap 2. **Error! Bookmark not defined.**
- Gambar 37. Hasil Pewarnaan TTC tahap 2..... **Error! Bookmark not defined.**
- Gambar 38. Rerata volume iskemia tahap 2..... **Error! Bookmark not defined.**
- Gambar 39. Uji waktu tempuh (*Escape latency*) dan pajang lintasan fase latihan (*Training*). **Error! Bookmark not defined.**
- Gambar 40. Uji waktu tempuh dan panjang lintasan fase uji sensorimotor..... **Error! Bookmark not defined.**
- Gambar 41. Lintasan TQT dan panjang lintasan pada uji probe. **Error! Bookmark not defined.**
- Gambar 42. Uji TQT, panjang lintasan dan frekuensi melintas pada uji probe. . **Error! Bookmark not defined.**
- Gambar 43. Rerata Kadar RAGE dan BDNF Hippocampus. **Error! Bookmark not defined.**
- Gambar 44. CA1 Hippocampus..... **Error! Bookmark not defined.**
- Gambar 45. CA2-CA3 Hippocampus.. **Error! Bookmark not defined.**
- Gambar 46. Volume dan estimasi jumlah neuron hippocampus yang didapatkan dengan metode hitung titik pada sediaan histologi..... **Error! Bookmark not defined.**



UNIVERSITAS
GADJAH MADA

PENGEMBANGAN TEKNIK TRANSIENT BILATERAL COMMON CAROTIS ARTERY OCCLUSION (tBCCAO) SEBAGAI MODEL ISKEMIA OTAK GLOBAL PADA TIKUS MODEL DIABETES YANG DIINDUKSI STREPTOZOTOCIN NICOTINAMIDE Kajian
Volume Iskemia Otak, Ekspresi Advanced Glycation End products Receptor (RAGE) Hippocampus, Ekspresi Brain-Derived Neurotrophic Factor (BDNF) Hippocampus, Jumlah Neuron CA1, CA2CA3 Hippocampus, dan Fungsi Memori Spasial
ETY SARI HANDAYANI, dr Rina Susilowati, PhD; Dr.dr Ismail Setyopranoto, SpS(K)

Universitas Gadjah Mada, 2021 | Diunduh dari <http://etd.repository.ugm.ac.id/>

Gambar 48. Koefisien korelasi Pearson penelitian tahap 3.....**Error! Bookmark not defined.**

10m10d (10 menit iskemia dengan 10 hari reperfusi), 104
10m3d (10 menit iskemia dengan 3 hari reperfusi), 104
10m7d (10 menit iskemia dengan 7 hari reperfusi), 104
15m10d (15 menit iskemia dengan 10 hari reperfusi), 105
15m3d (15 menit iskemia dengan 3 hari reperfusi), 104
15m7d (15 menit iskemia dengan 7 hari reperfusi), 104
2,3,5 *Tryphenyltetrazolium Clorida* (TTC), 5
20m10d (20 menit iskemia dengan 10 hari reperfusi), 105
20m3d (20 menit iskemia dengan 3 hari reperfusi), 105
20m7d (20 menit iskemia dengan 7 hari reperfusi), 105
4-hydroxynonenal (4-HNE), 31
Acid-sensing ion channels (ASICs), 27
Activator Protein -1 (AP-1), 30
Adenosine Tri Phosphate (ATP), 24
Advanced Glycation EndProducts (AGEs), 7
Advanced Glycation EndProducts Receptor (RAGE), 7
Apoptosis-inducing factor (AIF), 74
arachidonic acid (AA), 32
B-cell lymphoma 2 (Bcl-2), 28
B-cell lymphoma extra large (Bcl-xL), 28
Brain-Derived Neurothropic Factor (BDNF), 8
catalase (CAT), 31
Cedera Iskemia Reperfusi (CI/R), 30
c-Jun N-terminal kinase (JNK), 55
Creatine Kinase (CK), 19
cyclooxygenase-2 (COX-2), 32
cytokine-induced neutrophil chemoattractant (CINC), 45
cytosolic phospholipase A₂ (PLA₂), 29
deoxyribonucleic acid DNA, 28
Diabetes Mellitus (DM), 3
electron transport chain (ETC), 30
extracellular matrix (ECM), 32
Extracellular signal-regulated protein kinase (ERK), 47
FFA, *free fatty acid*, 25
focal cerebral ischemia (FCI), 15
Four Vessels Occlusion (4VO), 1
gamma-Aminobutyric acid (GABA), 37
Glial Fibrillary Acidic Protein (GFAP), 19
global cerebral ischemia (GCI), 15
glutathione (GSH), 31
glutathione peroxidase (GPx), 31
Haematoxylin dan Eosin (HE), 5



UNIVERSITAS
GADJAH MADA

PENGEMBANGAN TEKNIK TRANSIENT BILATERAL COMMON CAROTIS ARTERY OCCLUSION (tBCCAO) SEBAGAI MODEL ISKEMIA OTAK GLOBAL PADA TIKUS MODEL DIABETES YANG DIINDUKSI STREPTOZOTOCIN NICOTINAMIDE Kajian
Volume Iskemia Otak, Ekspresi Advanced Glycation End products Receptor (RAGE) Hippocampus, Ekspresi

Brain-Derived Neurotrophic Factor (BDNF) Hippocampus, Jumlah Neuron CA1, CA2CA3 Hippocampus, dan

Fungsi Memori Spasial

ETY SARI HANDAYANI, dr Rina Susilowati, PhD; Dr.dr Ismail Setyopranoto, SpS(K)

Universitas Gadjah Mada, 2021 | Diunduh dari <http://etd.repository.ugm.ac.id/>

hydroxyl radical (OH[•]), 29

Inducible nitric oxide synthase (iNOS), 32

Intercellular Adhesion Molecule-1 (ICAM-1), 31

Interleukin 1 β (IL - 1 β), 31

interleukin-1 β converting enzyme (ICE), 32

Ischemia and Reperfusion Injury (I/R Injury), 24

Lactate Dehydrogenase (LDH), 19

Long term potentiation (LTP), 60

Low Density Lipid (LDL), 54

LPL, lysophospholipid, 25

Malondialdehid (MDA), 19

matrix metalloproteinase (MMPs), 35

mature-BDNF (mBDNF), 59

megapixel (MP), 124

Membrane Attack Complex (MAC), 39

metalloproteinase gene matrilysin (MMP7), 60

Middle Carotis Artery Occlusion (MCAO), 1

mitochondrial permeability transition pores (MPTPs), 35

Mitogen Activated Protein Kinase (MAPKs), 30

Monocyte Chemoattractant Protein 1 (MCP-1), 38

Morris Water Maze (MWM), 9

Nicotinamide-adenine dinucleotide phosphate (NADPH), 29

nitric oxide syntases (NOS), 30

Nitrite Oxide (NO), 19

N-methyl D-aspartate (NMDA), 25

NOS, nitric oxide synthase, 25

Nuclear Factor kappa B (NF-kB), 30

p75NTR (p75 neurotrophin receptor), 61

PAF, platelet activating factor, 25

pentose phosphate pathway (PPP), 50

peroxynitrite (ONOO⁻), 29

Phosphat Buffered Formalin (PBF), 68

phosphoinositol 3-kinase (PI3K), 55

pro-apoptotic protein (BNIP3), 74

Protein Kinase C (PKC), 28

pyruvate dehydrogenase complex (PDH), 37

reactive oxygen and nitrogen spesies (RONS), 41

Reactive Oxygen Species (ROS), 19

Recombinant Tissue Plasminogen Activator (rt-PA), 1

regulated intramembrane proteolysis (RIP), 62

spent in the target quadrant (TQT), 83

Streptozotocin (STZ), 4

superoxide (O₂⁻), 28



UNIVERSITAS
GADJAH MADA

PENGEMBANGAN TEKNIK TRANSIENT BILATERAL COMMON CAROTIS ARTERY OCCLUSION (tBCCAO) SEBAGAI MODEL ISKEMIA OTAK GLOBAL PADA TIKUS MODEL DIABETES YANG DIINDUKSI STREPTOZOTOCIN NICOTINAMIDE Kajian

Volume Iskemia Otak, Ekspresi Advanced Glycation End products Receptor (RAGE) Hippocampus, Ekspresi

Brain-Derived Neurotrophic Factor (BDNF) Hippocampus, Jumlah Neuron CA1, CA2CA3 Hippocampus, dan Fungsi Memori Spasial

Time Quadrant Target/ROI, 14

transforming growth factor- β (TGF- β), 45

Transient Bilateral Common Carotid Artery Occlusion (tBCCAO), 2

tropomyosin-related kinase B (TrkB), 59

Tumor necrosis factor α (TNF- α), 45

Tumor Necrosis Factor α (TNF- α), 31

Two Vessels Occlusion (2VO), 1

Vascular Adhesion Molecules (VCAMs), 31

α -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA), 26

FTY SARI HANDAYANI, dr Rina Susilowati, PhD; Dr.dr Ismail Setyopranoto, SpS(K)
Universitas Gadjah Mada, 2021 | Diunduh dari <http://etd.repository.ugm.ac.id/>