

P02.101**Reduced neuroglobin (Ngb) level associated with the breakdown of blood brain barrier (BBB) after transient middle cerebral artery occlusion (tMCAO) in aged mice**

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Stroke has been linked to vascular cognitive impairment (VCI) and can potentially affect cognitive function in mid and later life. Until recently, neurovascular impairment after stroke was poorly defined. In the present study, we aim to clarify the role of neuroglobin (Ngb) in neurons as well as cerebrovascular cells in sham or transient middle cerebral artery occlusion (tMCAO) in aged mice.

Reduced levels of Ngb in the ipsilateral cortex were observed via immunohistochemistry (IHC) and western blotting after tMCAO in mice. To investigate the mechanism and role of Ngb in cerebral blood vessels, oxygen glucose deprivation (OGD), an *in vitro* hypoxia, was executed in mice primary neurons and brain endothelial cells (bEnd.3). The results showed that the level of Ngb was also reduced, and condensed in subcellular organs in neurons and endothelial cells in the OGD group, compared to the normoxia group.

Interestingly, aged mice showed higher levels of Ngb overall in brain tissue than young mice. When the distribution pattern and cell types of Ngb expression were compared in the old, mid and young group, levels of Ngb in vascular cells were lower in cortex of old and mid-aged mice than that of young group. Also, to investigate the role of Ngb on the BBB leakage, BBB permeability was measured after tMCAO in mice. BBB permeability was higher in old and mid mice, which is coincident with lower vascular level of Ngb in cortex of old and mid mice, compared to young mice group after tMCAO.

These results suggest that the different functional roles of Ngb depend on the oxidative stress and age. Collectively, these pathological changes of BBB leakage may be related to decreased Ngb expression in old mice after tMCAO.

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P02.102**Dissociation of parvalbumin-positive and somatostatin-positive interneurons' contributions to frequency-selective impairments of synaptic inhibition to hippocampal pyramidal cells induced by A β oligomers *in vitro***Kyerl Park¹, Hyowon Chung¹, Hyun Jae Jang¹, Michael Kohl², Jeehyun Kwag^{1,*}¹ *Korea University, Seoul, Republic of Korea*² *University of Oxford, Oxford, UK*

Abnormal accumulation of amyloid beta oligomers (A β O) in the hippocampus impairs hippocampal theta (3–12 Hz) and gamma (30–90 Hz) oscillations, leading to learning and memory deficits in Alzheimer's disease (AD). Hippocampal somatostatin-positive (SST+) and parvalbumin-positive (PV+) interneurons are involved in the generation of theta/gamma oscillations by providing synaptic inhibitions to pyramidal cells (PCs). However, how A β O affects these synaptic inhibitions, consequently resulting in theta/gamma oscillation impairments in AD is unclear.

To address this, we recorded spontaneous inhibitory postsynaptic currents (sIPSCs) of CA1 PC through whole-cell patch-clamp

recordings during sustained optical stimulation (470 nm, 3 s) of channelrhodopsin-2 (ChR2)-expressing SST+ or PV+ interneurons in the hippocampal slices from DMSO- and A β O-injected mice (10 μ M). In DMSO-injected mice, sustained optical stimulation of SST+ and PV+ interneurons selectively enhanced the power of band-pass filtered sIPSCs at theta or gamma frequency, respectively, suggesting frequency-selective activation of SST+ and PV+ interneurons. Interestingly, A β O reduced the power of SST+ and PV+ interneuron-mediated sIPSC at theta or gamma frequency, respectively, indicating A β O-induced frequency-selective impairments of SST+ and PV+ interneuronal inputs to CA1 PC. To find the synaptic locus of such frequency-selective impairments, we recorded SST+ and PV+ interneuron-evoked IPSCs to CA1 PC using optical stimulation (470 nm, 5 ms, 10 pulses) of ChR2-expressing SST+ or PV+ interneurons at theta (5 Hz) or gamma (40 Hz) frequency. In DMSO-injected mice, SST+ and PV+ interneuron-evoked IPSCs showed paired-pulse depression and short-term depression at both theta and gamma frequency, however A β O selectively enhanced those of SST+ and PV+ interneuron-evoked IPSCs at theta or gamma frequency, respectively, indicating A β O induces presynaptic dysfunction of SST+ and PV+ interneurons in frequency-selective manner.

Our results demonstrate A β O causes frequency-selective presynaptic dysfunction of SST+ and PV+ interneuronal inputs to CA1 PC, which may contribute to theta/gamma oscillation impairments in AD.

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P03.01**Pharmacological and genetic inhibition of astrocytic GABA-transaminase enhances tonic GABA inhibition in the hippocampus**Lee Wonseok¹, Park Min Gu², Woo Junsung³, C. Justin Lee², Yoon Boeun^{1,*}¹ *Dankook University, Cheonan, Republic of Korea*² *Institute for Basic Science (IBS), Daejeon, Republic of Korea*³ *Korea Institute of Science and Technology (KIST), Seoul, Republic of Korea*

γ -aminobutyric acid (GABA) is the major inhibitory neurotransmitter synthesized and released from GABAergic neurons and astrocytes in the brain. It has been shown that astrocytically released GABA activates the high affinity GABA_A receptors to mediate tonic inhibition. GABAergic inhibition, a primary target for anti-epileptic drugs, can be affected by the key enzymes of GABA metabolism, such as GABA-transaminase (GABA-T) encoded by ABAT. GABA-T degrades GABA to succinate semialdehyde and exists both in GABAergic neurons and astrocytes. Previous studies have shown that vigabatrin, an irreversible inhibitor of GABA-T, selectively increases tonic GABA, but not phasic GABA. However, it is still unclear whether the increased tonic GABA by GABA-T inhibition is attributed to GABAergic neurons or astrocytes. Here, we hypothesized that pharmacological and genetic inhibition of GABA-T disrupts GABA degradation, increases cytosolic GABA in astrocytes, and elevates tonic GABA release from astrocytes in hippocampus. We firstly confirmed that vigabatrin increased the tonic GABA currents in CA1 pyramidal neurons. In contrast, vigabatrin had no effect in monoamine oxidase B (MAOB) knockout (KO) mice, in which the astrocytic GABA synthesis is absent. These results suggested that vigabatrin was more likely to target astrocytic