2-LBS-24 Late-Breaking Session

Oral glutathione administration rescues neurons by reduction of neuroinflammation in Alzheimer's disease mice

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[Background] Glutamate-cysteine ligase modifier subunit (GCLM) null mice display a 70-80% reduction in total glutathione (GSH) level (Killoy et al. Exp Neurol 2018 Apr;302:129-135). The GCLM null mice causes motor neuron degeneration in mice like SOD1 mutant mice. We here investigated whether oral GSH administration can rescue neurons form neuroinflammation in Alzheimer's disease model mice.
[Methods] After 3 weeks administration of glutathione (100 or 500 mg/kg/day, p.o.) in 12 month-old wild and *APP-NL-GF* knock-in mice, oxidative stress, neuroinflammation and cognition were investigated. We also assessed the GSH levels in mouse brain.
[Results] *APP-NL-GF* knock-in mouse brain display a 50% reduction in total GSH as compare to wild mouse brain. The lipid oxidation assessed by 4-hydroxy-2-nonenal (4-HNE) was also markedly increased in *APP-NL-GF* knock-in mouse brain. The GSH administration dose-dependently diseased the oxidative stress and suppressed microglial activation in the hippocampus. Likewise, the GSH administration improved cognitive impairment observed in *APP-NL-GF* knock-in mice.
[Conclusion] Taken together, the oral GSH administration rescues neurons from oxidative stress and neuroinflammation in neurodegenerative disorders and should be try in Alzheimer disease patients.