

S19-3 Neurotoxicity of trace elements and the pathogenesis of senile type dementia

○Masahiro KAWAHARA¹, Tetsuya NAGATA¹, Isao OHTSUKA¹, Keiko KONOHA¹,
Yutaka SADAKANE¹, Shoko YOKOYAMA¹

¹Kyushu Univ. of Health & Welfare

Increasing evidence has suggested the involvement of trace elements in the pathogenesis of senile type dementia including Alzheimer's disease, vascular type of dementia, Lewy body diseases. It is widely believed that neurotoxicity of β -amyloid protein (A β P) is based on the neurodegeneration observed in Alzheimer's brain. Trace elements such as Al, Zn, Cu, Fe induce the conformational changes of A β P and enhance the neurotoxicity. Zinc co-released with glutamate in the ischemic condition plays crucial roles in the pathogenesis of vascular type dementia. Furthermore, prion protein in prion diseases has the ability to bind to Cu or Zn. We have investigated the molecular mechanism of neurotoxicity of A β P, prion protein, Al, Zn on cultured neurons using pharmacological studies, Ca²⁺ imaging, patch-clamp, DNA microarray analysis, atomic force microscopy. Our and other numerous studies have suggested the implication of trace elements and the disruption of Ca²⁺ homeostasis in the pathogenesis of these dementia. These results may aid for the further understanding of the molecular mechanism of these dementia and for the development of new therapeutic drugs for the treatment or the prevention of the diseases.