

Elucidation of Endemic Neurodegenerative Diseases – a Commentary

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Recent investigations of scrapie, Creutzfeldt-Jakob disease (CJD), and chronic wasting disease (CWD) clusters in Iceland, Slovakia and Colorado, respectively, have indicated that the soil in these regions is low in copper and higher in manganese, and it has been well-known that patients of ALS or Parkinson's disease were collectively found in the New Guinea and Papua islands, where the subterranean water (drinking water) contains much Al^{3+} and Mn^{2+} ions. Above facts suggest that these neurodegenerative diseases are closely related with the function of a metal ion.

We have investigated the chemical functions of the metal ions in detail and established the unique mechanism of the oxygen activation by the transition metal ions such as iron and copper, and pointed out the notable difference in the mechanism among iron, aluminum and manganese ions. Based on these results, it has become apparent that the incorporation of Al(III) or Mn(II) in the cells induces the “iron-overload syndrome”, which is mainly due to the difference in an oxygen activation mechanism between the iron ion and Al(III) or the Mn(II) ion. This syndrome highly promotes formation of hydrogen peroxide, and hydrogen peroxide thus produced can be a main factor to cause serious damages to DNA and proteins (*oxidative stress*), yielding a copper(II)- or manganese(II)-peptide complex and its peroxide adduct, which are the serious agents to induce the structural changes from the normal prion protein (PrP^{C}) to abnormal disease-causing isoforms, PrP^{Sc} , or the formation of PrP 27–30 (abnormal cleavage at site 90 of the prion protein).

It seems reasonable to consider that the essential origin for the transmissible spongiform encephalopathies (TSEs) should be the incorporation and accumulation of Al(III) and Mn(II) ions in the cells, and the sudden and explosive increase of scrapie and bovine spongiform encephalopathy (BSE) in the last decade may be partially due to “acid rain”, because the acid rain makes Al(III) and Mn(II) ions soluble in the subterranean aquifers.

Key words: Endemic Neurodegenerative Diseases, Aluminum and Manganese Ions, Iron-Overload