Brain metals: Methods of analysis and their role in epilepsy

The human brain is abundant in metals which are an essential part of brain biochemistry, structure and, by extension, cognitive functions. Changes to the level of metals in the brain occur in typical brain development and aging, but may also result in, or be the consequence of, neurological conditions. Some conditions are well known to involve etiologies of large shifts in brain metal distribution and concentrations (both increases and deficiencies). Examples include: Menkes disease (Cu deficiency), Wilson's disease (Cu accumulation) and neuroferritinopathy (Fe accumulation). However, it is not always recognized that many common conditions may have forms that are linked to changes in brain metals and metal-metabolism. In this presentation we focus on the possible roles of metals in epilepsy. These include idiopathic and pharmacoresistant epilepsies. We survey historical and recent evidence of "deficiencies" and "surplus" in various metals, as (i) possible causal mechanisms and (ii) the results of seizures. We further describe the historical advancements in methodologies used to examine brain metals, from histology to neuroimaging and novel optical and x-ray techniques. These include recent examples of synchrotron x-ray fluorescence imaging from our laboratory. Finally, we suggest that multi-scale, spatial and temporal characterizations of metal distributions in the brain may be critical for developing treatments for certain forms of epilepsy as well as for a deeper understanding of cognitive function in the healthy brain conditions.

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