Brain Iron Deposition

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The presence of iron in the brain was reported as early as 1886 by the German pathologist, S. S. Zaleski. His early report suggested that deposits of iron in the brain have several distinctive properties: (i) the majority of brain iron is not present as inorganic iron salts such as iron chloride, but is bound to organic molecules, (ii) unlike in the blood, the iron is not bound to hemoglobin, (iii) the iron is predominately in the ferric not the ferrous oxidation state and (iv) the iron is more concentrated in the gray matter than in the white matter. These results were confirmed and extended by Hugo Spatz in 1922.[1,2] He used the Perls' staining technique to produce bright blue precipitates in brain regions with high iron concentrations and demonstrated strong concentrations of ferric iron in the deep brain nuclei of the extrapyramidal motor system including the globus pallidus, the caudate nucleus, the red nucleus, the dentate nucleus and the substantia nigra. Subsequent investigators demonstrated that iron deposits with this specific distribution are present in all normal brains[3,4] and that alterations in the pattern of brain iron deposition are characteristic of several rare, inherited neurological disorders.[5-7] Furthermore, substantial evidence has been found that associates brain iron abnormalities with common neurodegenerative disorders including Alzheimer's and Parkinson's diseases as well as multiple sclerosis.[8-10] Iron may also have a role in brain aging and cognitive ability.[11,12]

The introduction of high-field (1.5 tesla) MR imaging in the early 1980s led to a major advance in the study of brain iron. In 1986 B. P Drayer and his colleagues reported that T2-weighted MR images showed markedly decreased signal intensities (hypointensities) in the same brain regions that had previously been identified in autopsy studies as having high iron concentrations.[13] It was soon demonstrated that this iron-dependent contrast mechanism became more prominent at higher field strengths. The availability of high-field MRI has made it possible to study brain iron non-invasively in living human subjects and has greatly expanded the knowledge of its role in brain physiology and pathology.[14-17]

In recent years brain iron has become a very active area of neuroscience research. The PubMed database for 2010 includes approximately 400 papers containing the phrase 'brain iron.' This high rate of publication, more than one research paper published every day, partly reflects the intensive activity in applying high field MRI to the study of brain pathology and physiology. [18-23] However, it also reflects the large current interest in the cell biology community in identifying and characterizing the proteins and the biochemical pathways responsible for brain iron metabolism.[24]

The role of iron in brain function and brain disease is under active study in the fields of clinical medicine, neuropathology, magnetic resonance imaging, biochemistry and cell biology. New insights and discoveries are rapidly accumulating even though much of the natural history of iron in the brain remains shrouded in mystery. The rapid increase in our understanding of brain iron physiology suggests that exciting new scientific advances and medical applications are likely to occur in the near future.

Disorders of iron metabolism have been established as major aspects of several relatively uncommon brain diseases and they are also suspected of playing a major role in common neurodegenerative diseases that have devastating consequences for millions of people. The ability of MRI to measure non-invasively the accumulation of iron in the brain will give it a prominent position in the future management of iron-dependent brain disorders.

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