Interaction of the Pathogenic Prion Protein with Iron Salts

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Copper, zinc and iron play an important role in neurodegenerative diseases and have an impact on both protein structure (misfolding) and oxidative stress. Homeostasis of these metal ions usually involves a great number of proteins which regulate the proper metal biology. Iron is involved in multiple biological processes within the human brain, including neurotransmitter function, myelin synthesis along with energy production via its ability to change valence states. Also, labile iron is free to participate in the Fenton reaction resulting in the generation of reactive oxygen species (ROS) which go on to induce oxidative stress and neuronal damage. A link between increased levels of iron in brain areas of Alzheimer’s disease (AD) and Parkinson disease (PD) has been recognized. Also, was observed during the evolution of Alzheimer’s disease (AD), Parkinson disease (PD) and Creutzfeldt-Jacob disease (CJD) an elevated levels of non-enzymatic protein glycation and formation of crosslinks via stable advanced glycation end products (AGEs) [1].

Neurodegenerative disorders of the central nervous system are slowly developing, insidious conditions that contribute first to neuronal cell degeneration and later cell death. During the development of the spongiform encephalopathies in human and animals the surface cell degeneration and later cell death. During the development of the spongiform encephalopathies in human and animals the surface cell degeneration and later cell death. During the development of the spongiform encephalopathies in human and animals the surface cell degeneration and later cell death. During the development of the spongiform encephalopathies in human and animals the surface cell degeneration and later cell death. During the development of the spongiform encephalopathies in human and animals the surface cell degeneration and later cell death. During the development of the spongiform encephalopathies in human and animals the surface cell degeneration and later cell death. During the development of the spongiform encephalopathies in human and animals the surface cell degeneration and later cell death. During the development of the spongiform encephalopathies in human and animals the surface cell degeneration and later cell death. During the development of the spongiform encephalopathies in human and animals the surface cell degeneration and later cell death. During the development of the spongiform encephalopathies in human and animals the surface cell degeneration and later cell death. During the development of the spongiform encephalopathies in human and animals the surface cell degeneration and later cell death. During the development of the spongiform encephalopathies in human and animals the surface cell degeneration and later cell death. During the development of the spongiform encephalopathies in human and animals the surface cell degeneration and later cell death. During the development of the spongiform encephalopathies in human and animals the surface cell degeneration and later cell death. During the development of the spongiform encephalopathies in human and animals the surface cell degeneration and later cell death. During the development of the spongiform encephalopathies in human and animals the surface cell degeneration and later cell death. During the development of the spongiform encephalopathies in human and animals the surface cell degeneration and later cell death. During the development of the spongiform encephalopathies in human and animals the surface cell degeneration and later cell death.

The results in Figure 1 showed that a fraction of the PrPres were present in the supernatant non-interacting with the iron oxide as no increase of its molecular weight was evident where most of the prion protein were heavily precipitated by the iron oxide compared to PrPres control lane 8.

The results in Figure 2a were observed after electrophoresis of
denaturing buffer, vortexed, heated 5 min. at 100°C, centrifugation at 12,000 g for 5 minutes, recovered supernatants (P) were loaded in lanes 9 to 14 respectively. The PrPres control were loaded in lane 8 and 15 and were prepared by added 5 µl PrPres and 10 µl distilled water, vortexing, heating 5 min. at 100°C, centrifugation at 12,000 g for 5 minutes and recovering the supernatants. After loading the collected supernatants on 15% SDS PAGE, then electrophoresis, transfer and immunodetection were done using monoclonal antibodies [4] (Figure 3a).

The results in Figure 3a presented a zone phenomenon where the supernatants of the first dilutions of iron citrate induced an increase of the molecular weight of the PrPres bands (lane 1 and 2) indication an interaction of the iron citrate with the prion protein then a drop of the detected bands sizes at the dilution 1/8 and 1/16 (lanes 3 and 4) and thereafter reappeared the normal PrPres bands (lanes 5 and 6). Iron citrate induced also degradation of the precipitated PrPres bands at the dilution 1/2 to the dilution 1/8 then the degradation decreased thereafter.

Figure 3b showed a degradation area due the interaction at the higher iron citrate concentration and the PrPres at lanes 1 and 2 and no more after. Where in the precipitation zone (9 to 13) existed a degradation zone due to the iron citrate-PrPres interaction from the dilution 1:2 and lesser degradation from lanes 10 to 13.

The results obtained showed that the three iron salts interacted each one with the PrPres resulting in the precipitation of this amyloid protein. The precipitation capacity varied from week precipitation as do the iron oxide, to high precipitation capacity solon the concentration employed as do the iron sulfate and finally a higher precipitation capacity with a zone phenomenon as produced with the iron citrate. This precipitation activity was probably due to an ion exchange between the amino acids of the PrPres peptide and the iron salt.

Also, was observed a chemical reduction of the iron sulfate and the iron citrate to a lower iron grade content as evidenced by the presence of dark brown color produced after the suspension of the produced PrPres precipitates induced by these two iron salts. The intensity of the produced color was proportional to the iron salt concentration used.

Figure 1: Immune blot.

References

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