

Neuronal deficiencies studied by Synchrotron-assisted Infrared Microspectroscopy

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Several human diseases, ranging from Alzheimer's to prion disease, have now been identified to be caused by proteins which auto-assemble into high molecular weight aggregates. There is a subgroup of ten such diseases that are related to abnormal polyglutamine (polyQ) repeats, one of which is Huntington's Disease (HD). Its symptoms are progressive deterioration of cognitive and motor functions, along with extensive loss of neurons primarily in the striatum. We used a rat model of HD to examine the chemical makeup of the brain slices. Traditional histochemical staining, shows sequential appearance of htt aggregates and the beginning of cell death on the timescale of over 3 months. We have investigated the striatum with synchrotron-assisted Fourier transform infrared microspectroscopy (SIRMS). One brain hemisphere was infected with HD while keeping the second one as a control. The two types of matter in the striatum are affected in different manners: in neuron-rich gray matter exposed to the disease, a higher content of aggregated protein is detected as early as 6 weeks after infection, but no signs of cell death up to 8 weeks. In contrast, myelin-rich white matter does not show any aggregates, but surprisingly shows a significant increase in phosphorylation. We interpret this as the activation of the cellular response to stress which leads in the end to cell death.

The drastic changes in the white matter were detected in the case of multiple sclerosis. We have studied its animal model, the experimental autoimmune encephalomyelitis (EAE). It is characterized by heavy loss of the insulating lipid-layer, the myelin around axons. This has been clearly confirmed by SIRMS and FTIR. Analysis of spatially resolved maps by both unsupervised principal component analysis and chemical signatures show additional features of this disease.

Both studies indicate that SIRMS is a powerful tool of detecting complex chemical processes in biological tissue in a relatively easy way.

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