Session 6: Biomarkers and function measures

This session focused on studies which further our understanding of biomarkers, allowing us to measure certain indicators of ataxia more precisely. It also included some interesting presentations on the clinical scales and assessment methods that are used to determine a patient's severity of ataxia.

Prof. David Lynch, from the University of Pennsylvania, presented his talk on the use of peripheral frataxin protein levels as a biomarker for FA. Using cells taken from cheek swabs and blood, he found that when frataxin levels in these peripheral cells were decreased, the severity of the symptoms observed increased, as measured by the Friedreich's Ataxia Rating Scale (FARS). As these peripheral cells are easily available, this could prove to be a very useful diagnostic tool but also a potential biomarker for clinical trials.

Dr. Mark Payne, from Indiana University in the US, found that in the heart, Friedreich's ataxia (FA) patients had a decreased ability to metabolise fatty acids and an increased ability to metabolise glucose. These changes were also shown in the heart of a mouse model of FA lacking the expression of the frataxin protein. This contrasted with the results of Prof. Ian Blair from the University of Pennsylvania who found that in platelets (blood cells) from FA patients, glucose metabolism was decreased and fatty acid metabolism was increased. This could suggest that metabolic processes are different depending on the tissue type, but could also be related to the stage of the disease.

Dr Pierre-Gilles Henry (University of Minnesota, US) presented his research on the use of high field magnetic resonance imaging (^{1}H-MRS) which measured neurometabolites (brain-specific molecules) as potential markers for nervous system degeneration. Measuring neurometabolites gives us an indication of neuronal damage as they are produced during essential metabolic processes. Using this technique, this group was the first to report neuronal damage in the spinal cord of FA patients.

Dr Louise Corben discussed her team's research using functional magnetic resonance imaging (fMRI) on people with Friedreich's ataxia. Using fMRI to measure brain activity in people with FA who undertook a memory task, the team from the Murdoch Children's Research Institute in Australia was able to show that the participants displayed reduced

brain activations in cognitive regions of the cerebellar cortex. This suggests that Friedreich's ataxia degeneration spans a greater area of the brain than previously thought.

Dr Martin Delatycki, also from the Murdoch Children's Research Institute, investigated the clinical relevance of the Friedreich's ataxia Impact Scale (FAIS) over a period of one or two years. He found that this assessment tool worked well when taking into account the age of onset and disease duration; however it did not correlate well with the length of GAA repeats. In addition, speech was the only subscale that demonstrated significant change over one and two years, suggesting that the use of the FAIS should be reassessed.

Biomarkers are also important in other ataxias, for example, imaging markers can be used as diagnostic tools. Dr Parkinson reported a study done at UCL Institute of Neurology (London, UK) on the autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS) which is a rare neurodegenerative disorder caused by mutations in the SAC gene. Measuring the changes of retinal nerve fibre layer thickening at the back of the eye by ocular coherence tomography (OCT), they observed that the thickening of retinal nerve fibre is a specific marker to distinguish ARSACS from patients affected with ataxia including FA. This suggests that OCT measurement could be part of routine pre-genetic screening; this finding is even more important as genetic testing for ARSACS is not routinely available.

A number of measurements were also developed to identify ataxia-specific movement dysfunction in both pre-clinical and clinical stages of the disease and how such dysfunction impacted the quality of life of affected individuals. Dr Fleszar reported her study on SCA1, 2, 3 and 6, showing that deficits of balance like body sway and a detailed analysis of gait differentiated healthy controls not only from patients at early stages of the disease, but also from pre-clinical ataxia individuals (before the symptoms develop). These movement features correlated with the estimated time of disease onset and were sensitive to the disease progression before this time, suggesting a potential disease progression marker for the preclinical phase of the SCAs.

Conclusively, session 6 provided a vast and varied update on all of the latest research involving improved markers for FA and SCA, the use of the newest imaging techniques to find biochemical markers and suggestions for improving clinical scales used to measure ataxia symptoms. Ultimately, this will lead to more precise clinical research in the future by following the progression of the disease and measuring the severity of the ataxia symptoms in a way that is more accurate.

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