NHGRI

Disability due to Neuromuscular disease

Francois van der Westhuizen reports on South African participation in the International Centre for Genomic Medicine in Neuromuscular Disease

Neuromuscular diseases (NMDs) affect approximately 20 million children and adults globally. They either result in premature death or are chronic diseases causing lifelong disability with economic impact. They include many different disorders affecting muscle and nerve function and account for 20% of all neurological diseases. Examples include muscular dystrophies, motor neurone diseases and mitochondrial diseases.

Most NMDs are genetic single-gene disorders, with many different causative genes being discovered. In developed countries, precise genetic diagnoses and gene discoveries are already having an important impact on patient care and health outcomes. Unfortunately in developing countries, such as South Africa, this is not the case and the great strides in research that are required to develop such genetic diagnoses in our country have not been forthcoming in recent decades.

The newly established International Centre for Genomic Medicine in Neuromuscular Disease (ICGNMD) – partly funded by the MRC (UK) for five years from July 2019 – has the mission to harness genomics to understand disease mechanisms and improve the health outcomes of children and adults with serious NMDs on a global scale. It is led by the University College London and Cambridge University, and includes partners from five developing countries: South Africa, Brazil, India, Zambia and Turkey.

The main objectives are to build NMD cohorts in these countries, identify the genes involved in the disease in each population, and build human capacities in each country as well as international networks that are sustainable. Reaching these objectives will greatly help to address the treatment of the various NMDs.

For South Africa's participation, experienced researchers and clinicians at the following universities have formed a core team:

- Prof. Francois H van der Westhuizen (coordinator and NMD researcher), Centre for Human Metabolomics, North-West University: Potchefstroom
- Prof. Izelle Smuts (paediatric neurologist), Department of Paediatrics, University of Pretoria
- Prof. Jo Wilmshurst (paediatric neurologist), School of Child and Adolescent Health, Red Cross War Memorial Children's Hospital, University of Cape Town
- Dr Franclo Henning (neurologist), Division of Neurology, Stellenbosch University
- Prof. Jeannine Heckmann (neurologist), Division of Neurology, Groote Schuur Hospital, University of Cape Town
- Prof. Soraya Bardien (geneticist), Division of Molecular Biology and Human Genetics, Stellenbosch University.

The success of this ambitious study for South Africa will greatly depend on the extent to which patients can be recruited and how well the complex, population-specific clinical and genomic data can be scrutinised. It will also depend on collaborations with all stakeholders in South Africa. The centres already participating have a database of patients visiting these clinics, as well as established networks and collaborations (e.g. contact with local branches of the Muscular Dystrophy Foundation of South Africa). We would like to expand the knowledge of this study so that broader access of patients with an NMD, and other collaborations with these clinics, can be established over the next five years.

Prof. Francois H. van der Westhuizen heads the Mitochondria Research Laboratory at North-West University: Potchefstroom, where he is Professor of Biochemistry and Deputy Director of the School of Physical and Chemical Sciences.

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A brief history

of a life lived with MND

The late Professor Stephen Hawking – the most famous disabled scientist of modern times – had a rare, early-onset and slow-progressing form of motor neurone disease (MND). He was diagnosed when he was 21 years old and given only a few years to live, but survived for more than 50 years before dying in March 2018 at the age of 76.

MND destroys motor neurons, the nerve cells that control the movement of the voluntary muscles. Hawking had the most common type of MND called amyotrophic lateral sclerosis (ALS), which affects both upper motor neurons in the brain and lower motor neurons in the brain stem and spinal cord. Signals to all voluntary muscles are disrupted, and muscles weaken and waste away over time, so affected individuals lose their ability to move their arms and legs or even to speak, swallow or chew. Death is usually due to respiratory failure as the muscles responsible for breathing weaken. The average life expectancy is three to five years after diagnosis, but about 10% of affected individuals survive for at least 10 years.

Hawking remained active until shortly before his death, working with colleagues on a scientific paper on black holes, the subject for which he was best known. He gave his final public lecture in Cambridge just a few months earlier, being able to communicate using a voice synthesiser. Although he was British, this computer-generated 'voice' had a slightly American accent, but Hawking refrained from changing it as it had become recognisable as his own.

The communication system was provided by Intel from 1997, with upgrades made every few years as technological advances allowed. Initially Hawking was able to use his thumb to operate a clicker switch,

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The viral Ice Bucket Challenge of 2014 was designed to raise money and awareness for ALS. Although there were concerns that the message was lost along the way, a report released in mid-2019 showed that the campaign raised $115 million in donations.

NASA/Paul E Alers

The communication system used by Prof. Stephen Hawking relied on the Assistive Context-Aware Toolkit (ACAT), which has been made available as free, open-source software to assist others with severe speech problems. The ACAT page on the Intel Open Source website features a recorded message from Hawking about how science and technology can help people with disabilities. https://01.org/acat/.

highlighting characters and words on a keyboard displayed on his computer screen to type out sentences, which were then sent to the voice synthesiser. By 2005 he had lost the ability to use the clicker, so an infrared sensor was attached to his spectacles, and Hawking used his cheek muscles to control the cursor on the screen. The Assistive Context-Aware Toolkit (ACAT) software developed by Intel included a SwiftKey predictive text algorithm, which used machine learning trained on Hawkings books and lectures. It also allowed him to control his mouse in Windows, so he could use email, internet and word-processing software. A webcam meant that he could even make Skype video calls.

This technology is an advanced form of Augmentative and Alternative Communication (AAC), but low-tech options, such as word- and picture-boards with mouth-stick or laser pointers, are used by many people with speech disabilities.

- ALS is also known as Lou Gehrig's disease, after a New York Yankees baseball player who had to retire from the game in 1939 and died from the disease two years later. There is evidence to suggest that concussive head and neck trauma associated with sporting activities increases the risk of developing ALS. Former Springbok rugby players Joost van der Westhuizen and Tinus Linee both died from ALS.