I had several positions in the World Federation of Neurology, including Co-Chair of a Research Committee on Migration and Neurology.

I think that both national and international scientific societies have a very important role in the development of neurologic medicine and stimulating and organising neurologic care and research in clinical neurosciences, either at a political level or by stimulating the networking of people. Finally, they have a very important role in the education of not only the new generations, but all members about the field, and societies are crucial for providing their members with objective information on new approaches to neurologic disorders.

You have >500 published articles listed on PubMed, as well as having authored and edited several medical books. What drives you to continue research and share your findings with the medical world and how important do you feel accurate communication of science is to a field's progression?

This continuous scientific activity is a basic mechanism for remaining mentally young and maintaining my enthusiasm for the field; this is only possible if you have contact with young collaborators, as they often stimulate you to continue. The professor–student relationship is a bidirectional equation that is very important for both subjects and leads to mutual growth.

What advice do you have for aspiring medical students who wish to become accomplished neurological researchers?

To find a good mentor, to have the economic possibility to spend time on research, and to have the capacity to pursue a research and a life project. Furthermore, you must preserve your enthusiasm for scientific progress as well as maintaining your competence.

"It is important to learn more about the natural history of the disorders and to learn more about their mechanisms on the basis of clinical heterogeneity."

Dr Giuseppe Lanza @LinkedIn

Oasi Institute for Research on Mental Retardation and Brain Aging (I.R.C.C.S.), Italy

Firstly, why did you choose to pursue a medical career? Was there a particular person or event that inspired you?

Firstly, I chose to become a doctor because of how keen I was to know the enigmatic functioning of the human body and, in particular, the nervous system. Secondly, I like to deal with intriguing and challenging cases, manage the unmet needs of people for their diseases, and try to relieve the suffering of patients and their families. In addition, I chose to become a doctor to have the opportunity to conduct clinical research within the exciting field of neuroscience. There was not a particular event that inspired me in this choice, although an emotional aspect behind this was that my mother wanted me to be a doctor when I grew up!

Your medical training was based in both Italy and the UK. Were there any differences between neurology practice in these countries?

They both provide an excellent theoretical background and a high level of professional skills. Neurology training appears to be generally longer in the UK, but the fully-trained specialists

seem to enjoy a higher independence and better job opportunities than in Italy. The interaction between preclinical and clinical neurological research is probably more powerful in the UK, although, from a strictly clinical point of view, the opportunities for university staff to become involved in the organisation and delivery of neurology health care appear to be greater in Italy.

You currently work at the Oasi Institute for Research on Mental Retardation and Brain Aging (I.R.C.C.S.). Can you describe your role and responsibilities during a normal day at the institute?

As a clinician, my daily routine involves examining patients, suggesting diagnostic tests, and interpreting the results of these tests to determine the best treatment. I work in a team with medical staff and other health professionals, and I also take part in multidisciplinary meetings involving specialists from other departments. As a researcher, I participate in clinical studies and other research projects, write or revise articles for medical journals, and give presentations at local and external meetings, courses, and seminars.

As a consultant neurologist and clinical researcher, what part of your job do you enjoy the most?

As a consultant neurologist, I always keep in mind that a career in neurology will suit you if you love complex problem-solving, the diagnostic process, and the idea of working with a diverse range of patients. At the same time, I also love to couple clinical duties with research interests, although I am aware that this field is highly competitive. Moreover, research in neurology allows for the discovery of new diagnostic markers and the ability to keep up to date with advances in diagnosis and treatments; this often has crucial translational implications in the daily management of neurological patients.

"TMS was originally introduced for evaluating the excitability in the primary motor cortex and the conductivity along the cortical-spinal tract."

The I.R.C.C.S. is a collaborating centre of the World Health Organization (WHO). What does this relationship with the WHO entail and why, in your opinion, is it important to collaborate with large international healthcare organisations?

The I.R.C.C.S. is a long-lasting collaborating centre of the WHO, specialising in research and training in neuroscience. More recently, the institute has also been invited to contribute to the update and revision of the International Classification of Diseases 11th revision (ICD-11), the most important manual of international classification of diseases and related problems. A multidisciplinary working group, including myself, is actively working on this exciting project, especially in the field of intellectual disability, brain ageing, and neuromuscular disorders. In my opinion, the final goal of any collaboration with large international healthcare organisations, such as the WHO, is to offer the best healthcare system and scientific research in co-operation with other international groups; indeed, we are promoting a number of clinical and scientific events involving operators, patients, families, associations, and other institutions, particularly focussing on the needs of patients and their families.

One of your key interests concerns the application of noninvasive neurophysiological techniques during the diagnosis of neurological disorders, particularly transcranial magnetic stimulation (TMS). Can you briefly explain the science behind this technique?

TMS was originally introduced for evaluating the excitability in the primary motor cortex and the conductivity along the cortical-spinal tract. Nevertheless, today, the applications go well beyond the simple assessment of the pyramidal tract. Indeed, TMS can be used to provide novel insights into the pathophysiology of the circuitries underlying neurological and psychiatric diseases, to probe the *in vivo* excitability and plasticity of the human brain, and to assess the functional integrity of intracortical neuronal and callosal fibres. TMS is well-suited for studies aimed at exploring and monitoring motor system impairment during the preclinical

phase of several neurological disorders or systemic diseases involving the central nervous system. Moreover, when integrated with other electrophysiological techniques (e.g., electroencephalography [EEG]) or structural and functional neuroimaging, TMS also allows the exploration of connectivity across motor and nonmotor areas. Finally, because it can be used to evaluate the effects of drugs that are agonists or antagonists for specific neurotransmitters, TMS can selectively test the activity of glutamatergic, GABAergic, monoaminergic, and cholinergic central circuits (e.g., so called pharmaco-TMS). Briefly, TMS is based on Faraday's law of electromagnetic induction to activate cortical neurons: a transducing coil attached to a high-voltage, high-current discharge system produces a strong time-varying and short-lasting magnetic field at right angles to the stimulation coil. When the stimulation coil is placed tangential to the head, the magnetic field penetrates the scalp and skull with minimal attenuation and induces a secondary eddy current in conductive intracranial tissue.

TMS has also been shown to be an effective treatment for some neurological conditions, such as neuropathic pain and depression. What further studies need to be performed to evaluate the long-term safety and frequent use of TMS?

The feasible application of TMS in restoring altered excitability and disrupted plasticity may lead to the development of specific stimulation protocols as a potential therapeutic and rehabilitation tool in patients with drug-resistant pain or major depression. However, longer follow-up studies and larger cohorts of patients are needed to explore the length of remission produced by the TMS. Moreover, studies combining TMS with other investigations, such as the EEG, will provide direct measures of the synaptic plasticity and functional connectivity, as well as how neural network changes occur in different disorders. Finally, the long-term benefits favoured by metaplastic phenomena induced by chronic drug exposure should be further explored.

"The feasible application of TMS in restoring altered excitability and disrupted plasticity may lead to the development of specific stimulation protocols as a potential therapeutic and rehabilitation tool..."

You have recently published research that investigated the connection between the brain and conditions of the gut, including coeliac disease (CD). Can you explain the reasons behind the intriguing findings of neurophysiological involvement in gastrointestinal diseases?

We have recently reviewed that the majority of electrophysiological changes in CD are often subclinical (the so-called 'coeliac iceberg'), and these need to be strictly monitored because of the possibility of progression into clinically visible neurological syndrome, in both young and adult patients. From a purely neurophysiological perspective, findings from different techniques (EEG, TMS, and other evoked potentials) seem to converge on an overall profile of the 'hyperexcitable coeliac brain'. In particular, regarding humoral autoimmunity to neuronal antigens, CD-related antibody deposits have been found not only in the small intestine but also in different central nervous system sites. Furthermore, a possible blood–brain barrier lesion, secondary to diffuse infiltration of T lymphocytes and inflammatory cells within the perivascular cuffing, might expose cerebral tissues to antibodies. The result may be a vicious cycle that eventually leads to a prevailing synaptic hyperexcitation and a weaker inhibition at the cortical level. The increased excitability may also be the correlate of a glutamate-induced cortical rearrangement or a dysfunctional control of GABAergic inhibitory interneurons. In particular, because glutamate is of pivotal importance in synaptic plasticity, it is speculated that immune system dysregulation triggered by gluten ingestion might result in a long-standing activation of postsynaptic glutamate receptors, which would account for the enhanced hyperexcitability. The eventual

identification of neurophysiological markers might be useful in the diagnosis and monitoring of CD, aiming to improve the healthcare of both single subject and global communities.

What advances would you like to see in the next 5 years for the management of patients with neurological conditions?

The amount of scientific research in neuroscience has recently increased, providing a greater understanding of several disorders, especially those based on the neuroinflammation and disruption of the neurovascular unit. However, this was not paralleled by a similar growth of pharmacological strategies, which currently do not change the course of dementing processes or Parkinsonian syndromes but do manage to slow down progression. In my opinion, promising evidence has come from investigations on new neuroprotective agents and innovative disease-modifying drugs. In addition, a crucial contribution is given by neurogenetics: the identification of genetic markers allows the discovery of novel therapeutic targets, as well as the development of more personalised treatments. Finally, the possibility to noninvasively and painlessly modulate specific cortical–subcortical circuits implicated in vascular, degenerative, and sleep disorders opens new fascinating windows in the field of translational neurosciences and nonpharmacological options for neurological disorders.

Finally, can you tell us what your career plans are for the next 10 years? What do you hope to achieve during this time?

In the near future, I would like to carry forward investigations based on integration of different neurophysiological methods for the experimental study of the processes underlying neurotransmission and cortical plasticity specifically involved in the regulation of sleep and cognitive functions, in both normal and pathological conditions. I will also be involved in another research project aiming to identify any preclinical markers of disease process and progress in patients with vascular or neurodegenerative dementia and late-life depression, trying to correlate clinical changes with neurotrophic factors and imaging findings. These studies will both disclose relevant clinical insights on the management and treatment of neurological patients. During this time, I will keep studying to learn and continuously ask 'why', question neurobiological phenomena, attend different laboratories and institutes, and share exciting ideas with other colleagues with different areas of interest. The take-home message can be the following: "never give up and always look for cultural growth!"

Dr Alexandr Merkin

Auckland University of Technology, Auckland, New Zealand

Firstly, what first inspired you to pursue your current career in research and, more specifically, in stroke, dementia, and traumatic brain injury (TBI)?

I always had an interest in biomedical science and mental health in particular. I started reading the literature on this topic during the fifth or sixth year of secondary school and also from reading my grandfather's books and materials. My grandfather was a medical doctor and lecturer in clinical psychology, so I did not have to look far for an example of a career in this area. Studying biology throughout high school was very rewarding and enjoyable for me. Several years later, I started studying at a medical university and willingly helped out several of my friends at the institute with revising before tests; I felt I had identified a strength that could well be worth pursuing in the future. My experiences led me to a career in teaching. I always loved helping and explaining things to others, and I