Interview

Alzheimer's disease: new paradigms for neurologists

Elio Scarpini was awarded his degree in Neurology in 1981 and he is now Associate Professor of Neurology at the Department of Neurological Sciences (University of Milan, Italy). His main interests include basic (genetics and molecular biology) and clinical aspects of neurodegenerative disorders, primarily Alzheimer's disease and frontotemporal lobar degeneration. Professor Scarpini is a member of the Executive Committee of the European Neurological Society. He serves as a reviewer for several neurological journals and is a member of the Editorial Board of several journals including *Therapy*. He is author of more that 150 scientific articles in international peer-reviewed journals, eight chapters in international volumes and has made more than 250 contributions to conferences.

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■ What first attracted you to a career researching Alzheimer's disease?

I started out studying the inflammatory mechanisms behind multiple sclerosis (MS), which is a demyelinating disease of the CNS. Considering that the ratio of patients with Alzheimer's disease (AD) and MS is 10:1, AD is becoming a huge health and social issue, a number of MS patients have cognitive dysfunctions and that primary progressive forms of MS show a neurodegenerative component, I started to think about possible common mechanisms between MS and AD.

Therefore, I began the analysis of cytokines, chemokines and other inflammatory factors, both in terms of levels in human samples such as CSF and serum, and genetics.

■ What has been your greatest achievement to date in the field of AD?

I think the demonstration that inflammation is present and is a very early event in the pathogenesis of AD is my greatest achievement. Inflammation was first reported in the early 1980s as a crucial event responsible for the development of AD. Despite these optimistic data, treatment of AD patients with anti-inflammatory drugs failed to provide positive results. We demonstrated that inflammation does not occur during the late stages of AD, but is present exclusively in early phases, when symptoms are still very mild [1]. This explains the failure of clinical trials with anti-inflammatory drugs that were given to patients in late stages of AD when inflammation was likely not present anymore.

■ Could you briefly summarize the aims & achievements of the European Neurological Society?

The main aim of the European Neurological Society (ENS) is to organize annual meetings, including both plenary sessions with experts in different areas of neurology, and oral and poster sessions, in order to allow researchers to discuss and share their own scientific results. In addition, the day prior to the beginning of the meeting there are teaching courses and workshops organized by subcommittees devoted to specific topics. The ENS supports young residents who want to carry out work experience in EU centers, and facilitate their participation in the annual meeting by providing travel grants. Lastly, ENS members can suggest updated guidelines and recommendations on the diagnosis and treatment of neurological disorders.

■ Could you explain your role as part of the executive committee of the ENS?

I am involved in the organization of the annual meetings, contributing to the planning of the scientific program with regard to my specific field. I also collaborate with the European Board of Neurology (EBN), which is a section of the Union Européenne des Médecins Specialistes (UEMS), an organization involved in the promotion of high standards of medical education in

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Europe. In addition, I am a member of the Editorial Board of the *Journal of Neurology*, the official journal of the ENS.

■ Could you tell us more about the galantamine trial that you recently worked on?

This clinical trial on galantamine started a few years ago in 2001, and was conducted to assess whether continuing treatment with galantamine for up to 24 months might result in delaying the cognitive deterioration associated with AD compared with cessation of treatment after 12 months [2].

The results of this study clearly demonstrated that treatment with galantamine could be continued for up to 24 months without a significant decline in cognitive deterioration.

The withdrawal design of the trial could potentially raise an ethical issue, as some subjects positively responding to the drug were randomized to placebo treatment, hence effective treatment was stopped. However, in light of the substantial lack of information in the literature at the time of trial planning, this approach was considered by all Ethical Committees as advisable in order to clarify the real efficacy of galantamine in the long-term treatment of AD.

■ What is your department at The University of Milan currently researching?

I am working at the Department of Neurological Sciences at the University of Milan and the Alzheimer's Unit and Multiple Sclerosis Center of Policlinico Hospital (Italy). My position is peculiar as I am part of both the university, which represents the best public institution for research, and a research hospital, which is involved in treating patients and 'translational' research, meaning the application of novel diagnosis and disease monitoring discoveries to clinical practice. My unit includes a neurobiology and molecular genetics laboratory, directed by my collaborator Daniela Galimberti.

■ Much of your work has focused around genetic associations with AD; which findings do you consider to have had the greatest clinical impact in this field in recent years?

So far, genetic risk factors have not been included in the clinical setting, and probably will not be in the future because they increase risk and cannot be used as biomarkers. The assumption of the role of genetic factors is that each gene contributes in a small way to the development of a particular disease but that only the combination of several polymorphisms influences the risk for the disease. To date, several genome-wide analyses have been carried out and a number of genetic factors identified [3]. The challenge for the future will be to move from genetic associations to altered pathways involved in the pathogenesis of the disease.

■ What advances do you hope to see in AD treatment in the next 5 years?

I am confident we will be able to diagnose early AD and related dementias by using biological markers (i.e., objective measures of an ongoing pathologic process). This will help to untangle clinical symptoms from pathologic events occurring in the brain, and to treat the disease before full-blown dementia occurs.

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