Neurodegenerative and Neuropsychiatric Disorders Research:
A Cerebral Career Choice

As people live longer, the incidence of age-related diseases, such as Alzheimer’s disease (AD), will also increase. By 2050, the number of people living with AD is expected to triple in the United States alone, from 5.2 million up to 16 million. This potential for increased incidence of AD, as well as other neurodegenerative diseases such as Parkinson’s disease (PD) and amyotrophic lateral sclerosis (ALS), introduces a critical need for medical breakthroughs that prevent or slow the progression of these diseases. Likewise, neuropsychiatric disorders such as depression and schizophrenia contribute to a substantial proportion of disability among both younger and older individuals. As a result, the field of neuroscience holds a wealth of career opportunities for graduate students and postdoctoral scientists now and in the decades to come. By Emma Hitt

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“T
he math is inescapable,” says Gregory Petsko, a researcher in neurodegenerative diseases and a professor of biochemistry and chemistry at Brandeis University, in Waltham, Massachusetts. “Unless we find a treatment for the prevention of the major neurodegenerative diseases—including Alzheimer’s, Parkinson’s, Lou Gehrig’s, and so forth—within the next 30 or 40 years, we’re cooked.” According to Petsko, the increasing problem is fueled by not only the extended lifespan of the population but also by the fact that people are having fewer children. These two factors, says Petsko, will recharacterize the population pyramid, such that diminishing numbers of younger people will be supporting an ever-increasing aging population, changing the pyramid into a column or even an inverted pyramid.

According to Michael Ehlers, chief scientific officer for Pfizer Neuroscience, neuroscience-related diseases are “arguably the most significant, unmet medical need in the industrialized world.” As populations age, the burden of Alzheimer’s disease and other dementias grows and is on a trajectory to consume a large percentage of all medical dollars, he says. “Neuropsychiatric diseases represent the largest cause of lost productivity and economic burden—more than all cancers and cardiovascular disease combined—with depression alone being the number one cause of disability. Yet, we have had very few novel therapeutics in this area for many years,” he says. “As our knowledge of brain function explodes, there remains a major need to translate these findings into a meaningful understanding of human brain function in health and disease.”

Not only is there a need for therapies, but there is also a need for research into the underlying causes of neurodegenerative and psychiatric disorders. “For many of these disorders, we still don’t have effective treatments because the origin of these disorders and ways to target them is still under debate,” says Heinz Reichmann, president elect of the European Neurological Society. “We are missing a significantly efficacious treatment, and it will be interesting, for example, to determine whether the alpha-synuclein and tau proteins, which contribute to the pathology of Parkinson’s and Alzheimer’s, respectively, can be targeted to provide more effective treatments,” he said.

ADDRESSING IMPORTANT NEEDS
A key need in the field, Petsko says, will be to train physician scientists to translate basic research findings into clinical practice. According to Petsko, the number of Ph.D.s that have been trained in the last 30 years has increased dramatically, but the number of physician scientists has decreased somewhat. He believes that physicians who complete their M.D. training should be encouraged to go into research rather than having to enter clinical practice immediately for financial reasons (i.e., to pay off school loans). “There’s nothing else we could do that would make more of an impact,” he says. He adds that clinicians who also perform research may be

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Neuroscience

more likely than basic researchers to understand how diseases manifest in people. “They are focused on the idea of cures or treatments in a way that many basic researchers are not,” he says. “We need to bring smart people who are broadly trained into the field.”

J. Timothy Greenamyre, professor and vice-chair of neurology at the University of Pittsburgh Medical Center and director of the American Parkinson Disease Association Advanced Center for Parkinson’s Disease Research at the Pittsburgh Institute for Neurodegenerative Diseases, states that there is a need for students to receive formal training in topics such as “The Neurobiology of Human Disease,” in which they not only learn disease mechanisms, but also interact with individuals affected by these diseases to learn how the disease impacts patients and their families.

Regardless of whether trainees pursue careers in academics or industry, says Greenamyre, most would benefit from formal training in how basic laboratory findings are translated into diagnostics or therapeutics and from learning about topics such as the basics of patents and licenses, the procedures involved in conducting clinical trials, and the U.S. Food and Drug Administration approval process.

Along with adequate training of clinician scientists, research funding must also increase if sufficient headway is to be made in preventing and/or treating the looming increase of age-related disorders. According to Petsko, the total amount of money spent on Alzheimer’s disease research is only about $500 million per year, and is much less for other neurodegenerative disorders. By contrast, about $2.4 billion per year is spent on AIDS, which affects a much smaller number of people. “AIDS provides a very valuable lesson, in that it is no longer considered a ‘terrible’ disease, in part, because of advances in biomedical science,” he said. As the population ages, the same trend will hopefully take place in terms of increased funding in Alzheimer’s disease and other neurodegenerative disorders.

According to David Nutt, president of the British Neuropsychiatric Association and professor at Imperial College London, in the United Kingdom, research opportunities exist in all areas of brain disorder research, but less than 10 percent of research funds are spent on this field even though these disorders cause about 30 percent of all disabilities. He suggests that people in the field should lobby for their discipline.

SPECIFIC OPPORTUNITIES

A recent trend in academia has been for scientists to conduct increasingly collaborative research, and neuroscience-related research is no exception. Thus, graduate students and postdocs who focus on expanding their knowledge base and collaborating with others will create more opportunities for themselves. According to Greenamyre, the Pittsburgh Institute for Neurodegenerative Diseases was conceived and created to eliminate barriers that traditionally impede research on neurodegenerative (or any) disease. “As such, it is composed of about a dozen independent lab groups who share open lab space, and by virtue of both architecture and philosophy, there are no walls between lab groups,” he says. Lab groups from neurology, neurosurgery, continued>

The Massachusetts Neuroscience Consortium—

a Collaborative Model

An Interview with Susan Windham-Bannister, president and CEO of the Massachusetts Life Sciences Center

What do you hope to accomplish with the Massachusetts Neuroscience Consortium?

The Massachusetts Neuroscience Consortium is a pioneering new model for accelerating preclinical research, introducing academic researchers to the challenges of targeted research, and facilitating industry-academic partnerships. The pharmaceutical company sponsors will have facilitated access to all of Massachusetts academic and research institutions and will jointly fund projects that leverage the basic, translational, and clinical research expertise resident in the state—the world’s highest density of neuroscience expertise.

According to Congressman Chaka Fattah (D-PA), an advocate for neuroscience research, “This new consortium...is an exciting development for future advances in brain science and medicine. The consortium can provide us with the model for a major national partnership of government, the pharmaceutical industry, leading academic researchers, and medical schools.”

What are the major areas of need in this field in terms of research that you hope to address with the consortium’s efforts?

Neuroscience is a complex discipline in need of both novel therapeutic targets to treat neurological diseases as well as increased understanding of basic mechanisms of function. Significant breakthroughs still elude us in this field, and millions of patients and their families are waiting to hear that we have developed better treatments for diseases such as Alzheimer’s, multiple sclerosis, Parkinson’s, ALS, chronic pain, and others. Interest has also been expressed by consortium members in projects to address the mechanisms of aging, cognition, and synaptic plasticity. Final priorities will be set by the charter members of the consortium.

What opportunities will the consortium and other similar models present for students or postdocs considering a career in neurodegenerative disease research?

We see the Neuroscience Consortium as an opportunity for academic researchers—such as postdocs and graduate students—to build relationships with industry through funded projects and gain exposure to the industry style of research: short-term and results-oriented projects, industry standards for validation, and resources. These opportunities will help young researchers as they determine their next steps in their careers and will facilitate even more effective and productive collaboration between academia and industry.

Given the cost and time involved with the development of new therapies, collaboration is more vital than ever in life sciences research. Traditional approaches to research and drug development have seen a dramatic decline in the number of new therapies moving through the R&D pipelines to patients. Collaboration is essential to accelerating R&D to make a positive impact on curing human disease and improving patient outcomes, especially in complex areas such as neuroscience.
pharmacology, structural biology, and geriatrics all work together in the same space and on the same diseases.

Another recent effort for collaboration is the Massachusetts Neuroscience Consortium, which was initiated in June 2012. Their goal is to accelerate preclinical research, facilitate industry-academic partnerships, and create “a pioneering new model that is designed to leverage the rich research environment in Massachusetts,” says Susan Windham-Bannister, president and CEO of the Massachusetts Life Sciences Center. The consortium brings together seven major industry partners who are willing to collaborate to develop significant advances in major neurological disorders such as Alzheimer’s, Parkinson’s, multiple sclerosis, and neuropathic pain. The companies contributing to the consortium are Abbott, Biogen Idec, EMD Serono, Janssen Research & Development, Merck, Pfizer, and Sunovion Pharmaceuticals (see sidebar on page 144) for more information about this consortium.

For young scientists interested in translational neuroscience, pursuing research in the pharmaceutical industry is particularly rewarding and challenging, says Pfizer’s Ehlers, and “offers the real potential to make discoveries that make medicines.” His advice for young scientists is to think broadly and look outside of traditional career paths. “Training programs for graduate students and postdocs can be quite one-dimensional, exposing trainees to the academic world but little else,” he says. “There is a universe of scientific opportunities outside of the university.”

At Pfizer Neuroscience, Ehlers says, they look specifically for young scientists with a combination of strong quantitative skills and deep knowledge in a specific area, but also with a broad curiosity about all areas of biology. “We also look for people with strong communication skills and an ability to work well collaboratively in teams,” he says.

Graduate students and postdocs interested in a career in this field should also be on the alert for global opportunities, as these diseases will afflict any modernized nation where lifespans are long. In Europe, says Heinz Reichmann, president elect of the European Neurological Society, each country has its own funding sources, both from industry and government, and there are many foundations that support research in this area.

NEW TECHNOLOGIES PROVIDE HOPE

Neurodegenerative diseases are among the most difficult to understand and treat, says Doug Williams, executive vice president of research and development (R&D) at Biogen Idec, a company that focuses on neurodegenerative diseases, including multiple sclerosis, Alzheimer’s, and ALS. However, we are living in an era where new technologies such as genomic sequencing and advanced imaging will rapidly increase what we know about these diseases, he says. “By investing in translational medicine, including better neuroimaging and biomarker strategies, we will be able to make better decisions earlier in clinical development and improve the productivity of our R&D efforts.” This type of investment, he says, “will also enable us to identify which patients may be more likely to benefit from a particular therapy, to determine if a compound is having the intended biological effect on its target, and to detect the progression of a disease even in the absence of new symptoms.”

Specific types of scientists who will be most sought after, says Williams, include computational biologists, cell biologists who understand modeling of human diseases, and stem cell biologists.

Jonathan Brotchie is founder and president of Atuka, Inc., a company with offices based in Canada, the United Kingdom, and China, that provides contract research and consultancy services for the biopharmaceutical industry, specifically to assist larger companies in developing novel therapeutics and diagnostics for Parkinson’s disease.

According to Brotchie, advances may be slowed down not so much by a lack of ideas about drug targets and new therapies, but rather by a lack of understanding of the technologies and methodologies required to develop and validate these ideas. “There is a need to develop better animal models, to recapitulate and predict effects of agents on the molecular pathology of the disease process, and also to develop better imaging and biomarker technologies to assess, as early and precisely as possible, drug effects in clinical studies,” he says.

According to Brotchie, job opportunities are likely to be plentiful at small companies that develop and use cutting-edge technology and capabilities. For example, a PET imaging company, Molecular Neuroimaging, in New Haven, Connecticut, which provides neuroimaging research services to the pharmaceutical and biotech industries, has sprung out of academia to support drug discovery in the field. “These approaches are not available within the pharmaceutical industry and are typically beyond the capabilities of academic groups,” Brotchie says. The picture is very different now than before, he adds, when industry and academia rarely overlapped, but now “convergence, overlap, and cross-fertilization are all part of the environment today for anyone who wants to define a career with a mix of both approaches,” he says.

The challenge now, says Biogen Idec’s Williams, is to go beyond marginal improvements to making transformational changes in how we think about and treat neurodegenerative diseases. “We believe we are at the cusp of a new era when these advances will be possible, but they will require persistence, collaboration, and passion,” he says.

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DOI: 10.1126/science.opms.r1200124