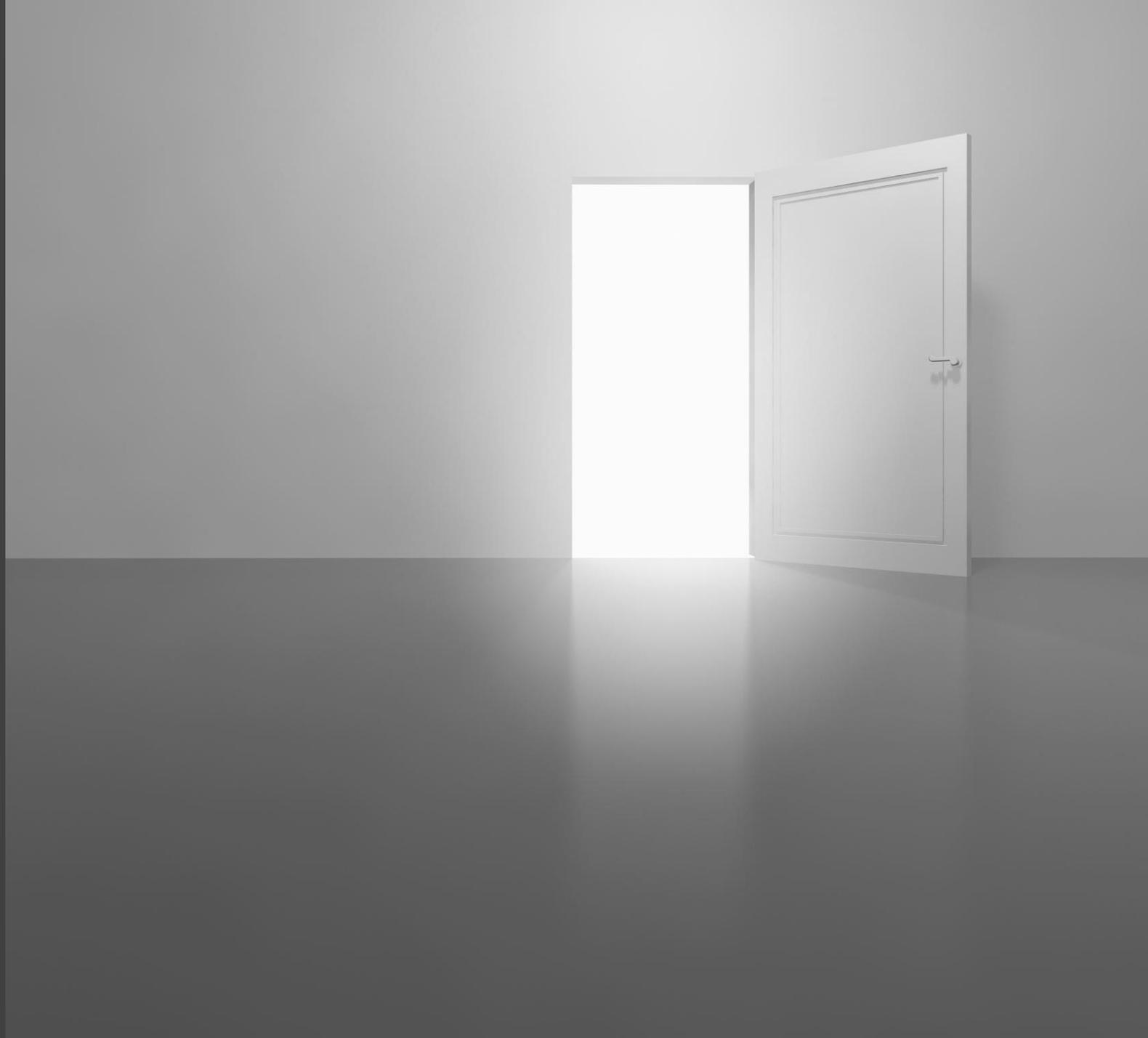
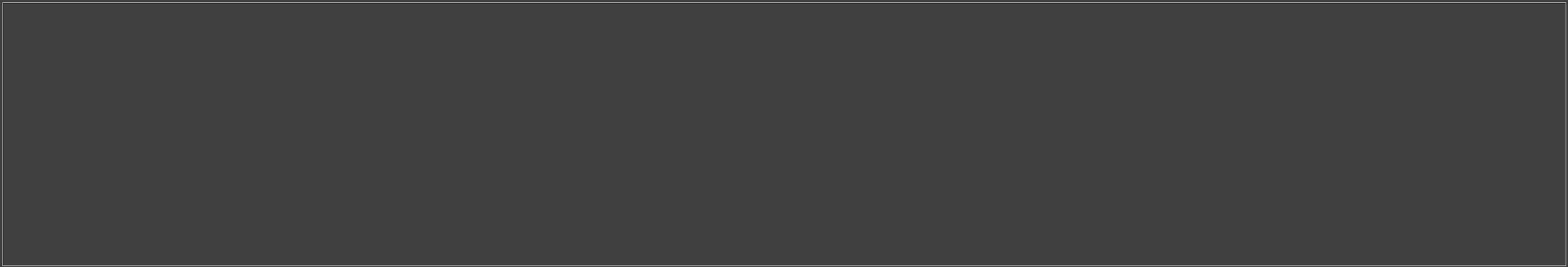


FUELING THE LIGHT OF OPEN SCIENCE

Wilder Penfield Lecture 2019

The Neuro, Montreal





Plan for Our Time Together



HISTORICAL REFLECTIONS ON
THE ROLE OF PHILANTHROPY
IN FOUNDING THE NEURO



NEUROLOGICAL DISORDERS
AND OUR MORAL IMPERATIVE



THE PROMISES AND
CHALLENGES OF OPEN
SCIENCE IN PRACTICE

1932

The Trustees of the Rockefeller Foundation approve the single largest contribution the foundation had made in the field of psychiatry.

The grantee recipient was McGill University.

The purpose was to help establish the Montreal Neurological Institute under the leadership of Dr. Wilder Penfield.

1934

The Montreal Neurological
Institute opens its doors.

Happy 85th Anniversary!

It is, within 2 years, at capacity.

What did Rockefeller fund?

- \$232,652 towards a building and equipment
- \$100,665 in support of an initial planning 2 years of teaching and research
- \$1,000,000 endowment funds to continue support of research and teaching

Why?

Recognition of the great unmet need for treatments

Personal qualities of Dr. Penfield and his bold vision to reorganize and integrate what were typically distinct clinical departments
neurology/neurosurgery/neuropsychiatry.

The promise of progress to come from intertwining research, clinical care and teaching.

The commitments McGill and the city of Montreal were poised and willing to make

1937

A report to the Trustees of Rockefeller states... “the proposed Institute included high values both in men and in ideas; its location in Canada gave promise of influence through out the English-speaking world. The record of the first three years of operation has been distinctly encouraging.”

“The Institute represents a well organized and concentrated attack on the difficult problem of nervous diseases. Mechanisms have been devised for the exchange of information between the three functions of therapy, research and instruction, and for its utilization in the advancement of neurology.”

“The Institute is rightly regarded as the center of neurology and neurosurgery for Canada.”



PART 2:
NEUROLOGICAL
DISORDERS AND OUR
MORAL IMPERATIVE

450 million

The WHO reports that one in four **people in the world** will be affected by **mental** or neurological disorders at **some** point in their lives.

Around 450 million **people** currently **suffer from** such conditions, placing **mental** disorders among the leading causes of ill-health and **disability worldwide**.

50 million

Around 50 million **people** worldwide **have epilepsy**, making it one of the most common neurological diseases **globally**. Nearly 80% of **people** with **epilepsy** live in low- and middle-income countries. It is estimated that up to 70% of **people** living with **epilepsy** could live **seizure-** free if properly diagnosed and treated.

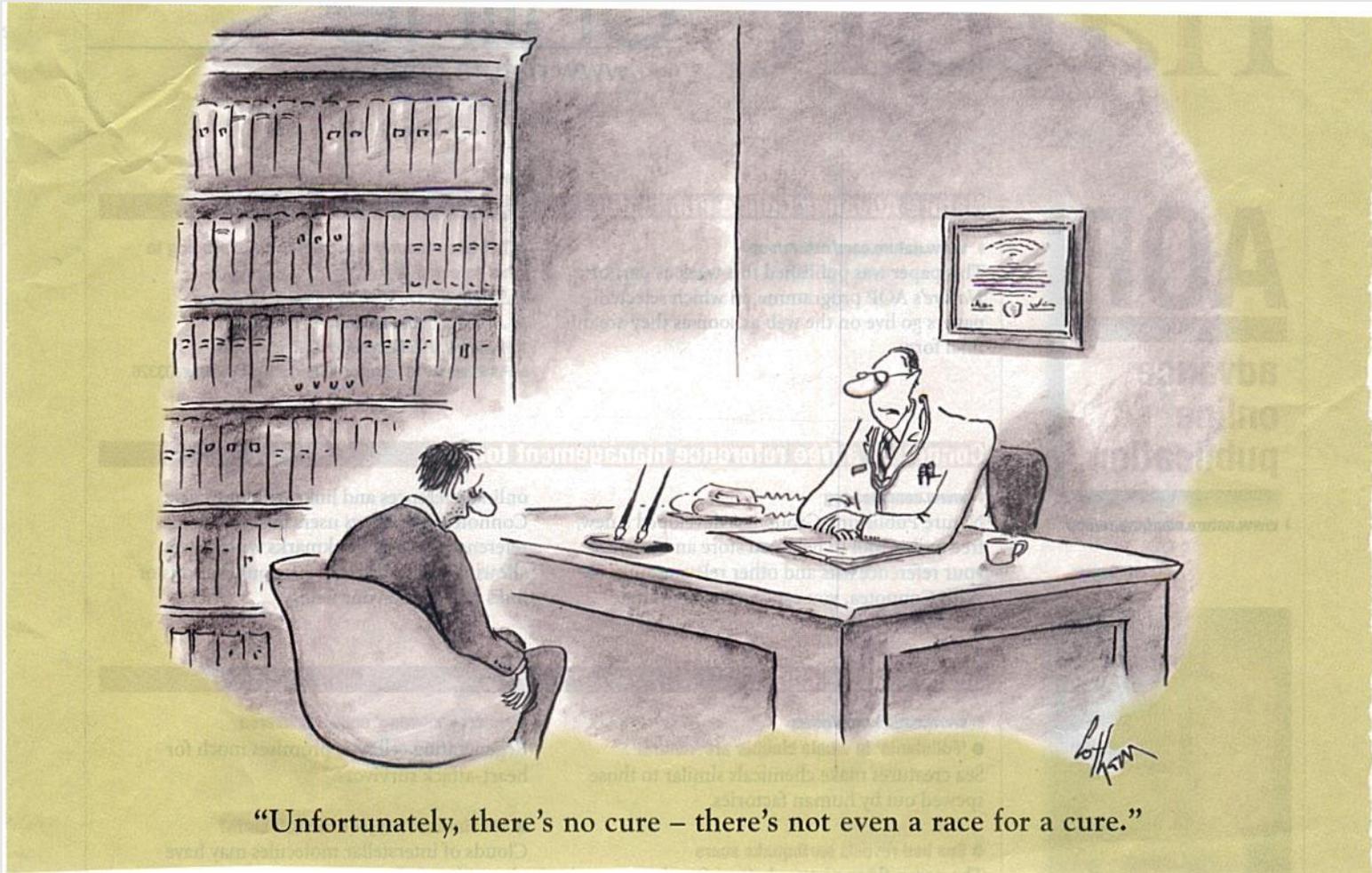
44 million

It is estimated that there are approximately 44 million **people** worldwide living with **Alzheimer's** disease or a related form of dementia.

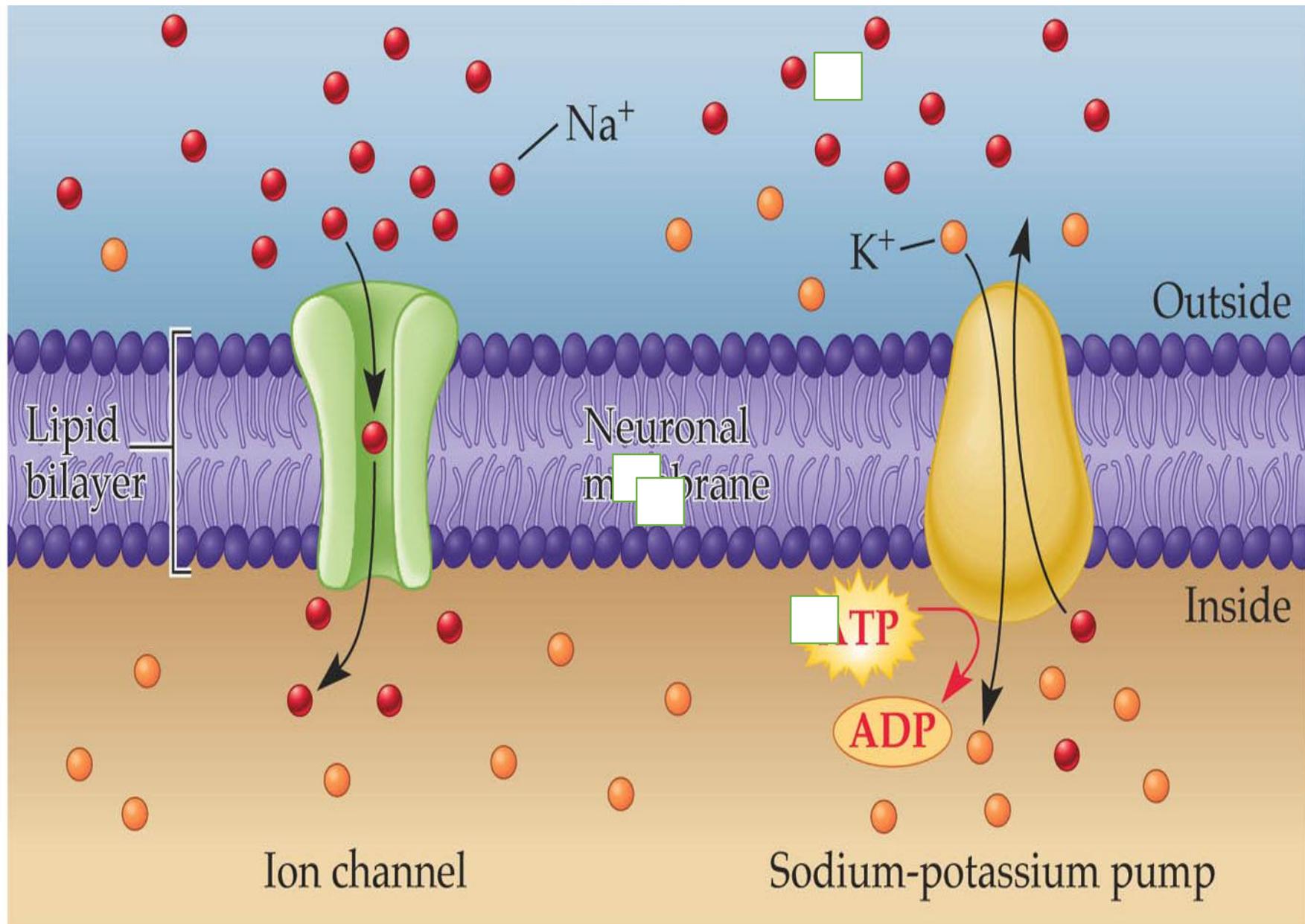
“Upon careful evaluation of our pipeline and the challenges inherent in developing drugs for major neurologic diseases, we’ve made the decision to end our neuroscience research and early development programs with the exception of programs centered on neuro inflammation that will be pursued by our inflammation TA.

This was a very difficult decision and we know it will be a disappointment for our staff and the scientific community.”

David Reese, Executive Vice President of R&D at Amgen, October 30, 2019



“Unfortunately, there’s no cure – there’s not even a race for a cure.”



Private
Fundors:
Advancing
Neurological
Disease
Research and
Care?

Adopt the belief in the serendipitous nature of scientific discovery.

Accept the argument that understanding causative disease mechanisms (simplified in models) are necessary for the development of effective therapies.

Keep the faith that the awards and incentives developed for investing in the acquisition of basic science knowledge will yield applications.

Believe that standard, model organisms are just like us (but, oddly, not enough like us to make experiments unethical).

In the Fall
2018 *Issues in
Science and
Technology*, I
wrote ...

Forty years into a full-on effort to defeat Alzheimer's disease as a major cause of cognitive decline and death— indeed, it is the sixth leading cause of death in the United States, afflicting nearly six million people and wreaking enormous emotional and financial tolls on patients and families—this is where things stand: we have no treatments, and though efforts to improve early-stage diagnosis have had some success, their main impact is to inject enormous new uncertainties and anxieties into a patient's view of the future and sense of self.

Meanwhile, a string of high-profile failures of ALZ therapies based on a dominant scientific hypothesis is the main result of expenditures of huge scientific, corporate, and societal resources. ALZ remains a disease with no known prevention, treatment, or cure.

We must, and we can, start doing better

What would
Dr. Penfield
do?

Resist the lure of beauty versus the mess of reality

Study humans first and then develop disease models versus relying on models of disease

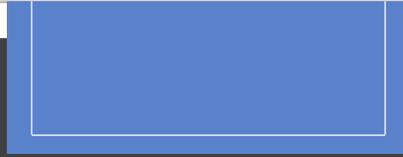
Shift the focus from the worried well to the truly ill

Do not mistake the rare for the common

CON'T FALL 2018 *Issues Science and Technology*

But what of the emerging incredible technological abilities to acquire knowledge directly from humans, whether it's sophisticated and refined cognitive and behavioral testing, or wearables that can track changes in real behavior from such things as the quality and frequency of social interactions or the intricacy of writing and speaking? Why is the revolution in technologies that track our every word and move as whole humans rarely integrated into the biomedical approach?

A richer understanding and characterization of the human disease in the full context of how an organism does or does not accomplish the behaviors needed to thrive in its environment might suggest very different targets for therapeutic interventions. Why wouldn't we at least seriously entertain the possibility that such tools are a more fertile entry point for research on neurodegeneration than utterly abstracted tools such as genes and mouse brains? Yes, there are nascent attempts along these lines, but they represent boutique approaches in the vast enterprise of biomedical science.



PART 3:
THE PROMISES AND
CHALLENGES OF
OPEN SCIENCE IN
PRACTICE



In a 2017 essay appearing in *Brain*, reflecting on the 80th anniversary of the publication of the Penfield and Boldry paper, Marco Catani reflected on the now famous homunculus describing it as -

...arguably the most reproduced yet unreplicated figure in neuroscience.

Cantani goes
on to write...

In their attempt to visually summarize such a large amount of data, the authors faced challenges ...common to modern neuroimaging approaches.

Penfield's historic work raises several issues still vexing contemporary neuroscience that open science practices could address:

- Difficulties relating micro and macro scales
- Complexity of responses with simple stimuli
- Understanding actions and meaningful behaviors
- Presenting summaries of large data sets

At the Center for Open Science, we **believe** an open exchange of ideas accelerates scientific progress towards solving our most persistent problems. The challenges of disease, poverty, education, social justice, and the environment are too urgent to waste time on studies lacking rigor, outcomes that are never shared, and results that are not reproducible.

The Open Research Funders Group (ORFG) is a partnership of funding organizations committed to the open sharing of research outputs. **This will benefit society by accelerating the pace of discovery, reducing information-sharing gaps, encouraging innovation, and promoting reproducibility.**

In the context of neurological disorders this statement immediately raises questions:

- 1. Will open science benefit society?**
- 2. If so, in what ways?**
- 3. How will we know?**
- 4. Who will be the primary beneficiaries?**

120 years ago
Ramon y Cajal
reflected on
the culture of
science in his
*Advice for a
Young
Investigator*

What a wonderful
stimulant it would be ...
if instructors... would
reveal...the origins of
each scientific discovery,
the series of errors and
missteps that preceded
it ...

THOMAS DURCAN is an assistant professor in the department of Neurology and Neurosurgery at McGill University and a member of the Neurodegenerative Disease research group at the Montreal Neurological Institute-Hospital (The Neuro).

I hope to provide some inspiration for others to take what I am doing and make it better. *By being open and doing simple things like putting our protocols, our data, and our notebooks online, we can do research faster, better and more reproducible so that in the next decade, we can have new and better treatments for devastating disorders of the brain.* Patients are frustrated by the lack of progress in developing new therapies and being open will be a new driver that hopefully will bring new and effective treatments into the clinic.

(Profiles in Open; ORFG.org)

Measuring the Impact of Open Science

We have a responsibility to our patients and our researchers to deliver on the promises of Open Science.

By measuring the impact of our efforts, we hope to validate the approach and continue to expand the Open Science movement.

We have mandated an independent Open Science Evaluation Committee to measure the impact of Open Science at The Neuro. This committee is chaired by [Richard Gold](#) from the McGill Centre for Intellectual Property Policy and made up of a team of international social scientists from Biomedical Ethics, Economics and Innovation policy.

The committee will work with organizations such as the Organization for Economic Co-operation and Development (OECD) to define appropriate metrics and evaluate the Open Science model to identify academic, innovation, and research policies that promote global economic and social well-being.

What role should private fundors play?

- Be open minded about Open Science
- Be scientific about Open Science
- Allow academic institutions to take the lead
- Incentivize, reward, recognize, support – not mandate
- Be thoughtful about inequities
- Be realistic about unintended consequences