

# On the application of neuroscience for the treatment of human disease



GIVING LIFE TO POSSIBLE

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Assistant Professor of Neurology  
Baylor College of Medicine

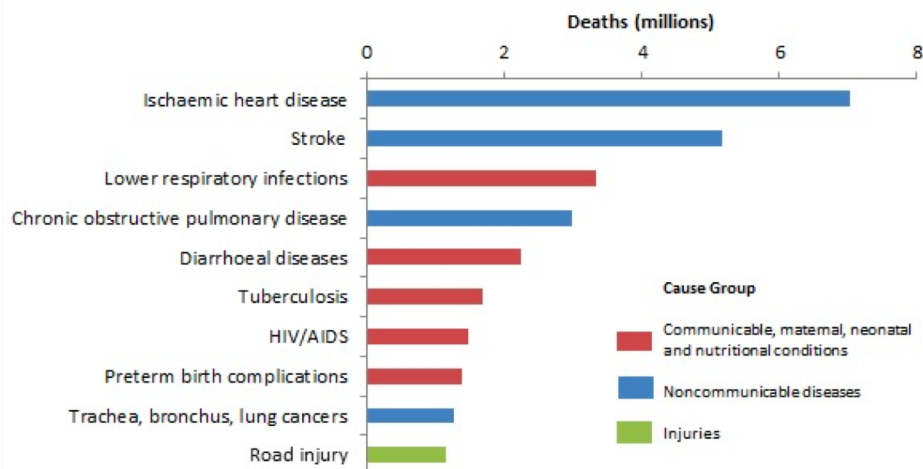
Brain Awareness Week 2019  
Rice Neuroscience Society

## The burden of neuropsychiatric disease

- Approaches to medically oriented careers in neuroscience
- Challenge YOU!
- A bit about a new course offering at Rice Neuroscience

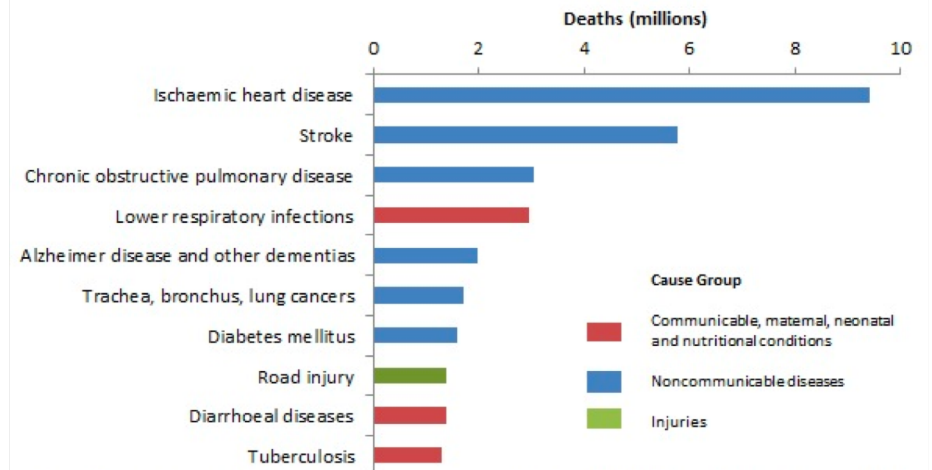
# Things that kill ..

## Top 10 global causes of deaths, 2000



Source: Global Health Estimates 2016: Deaths by Cause, Age, Sex, by Country and by Region, 2000-2016. Geneva, World Health Organization; 2018.

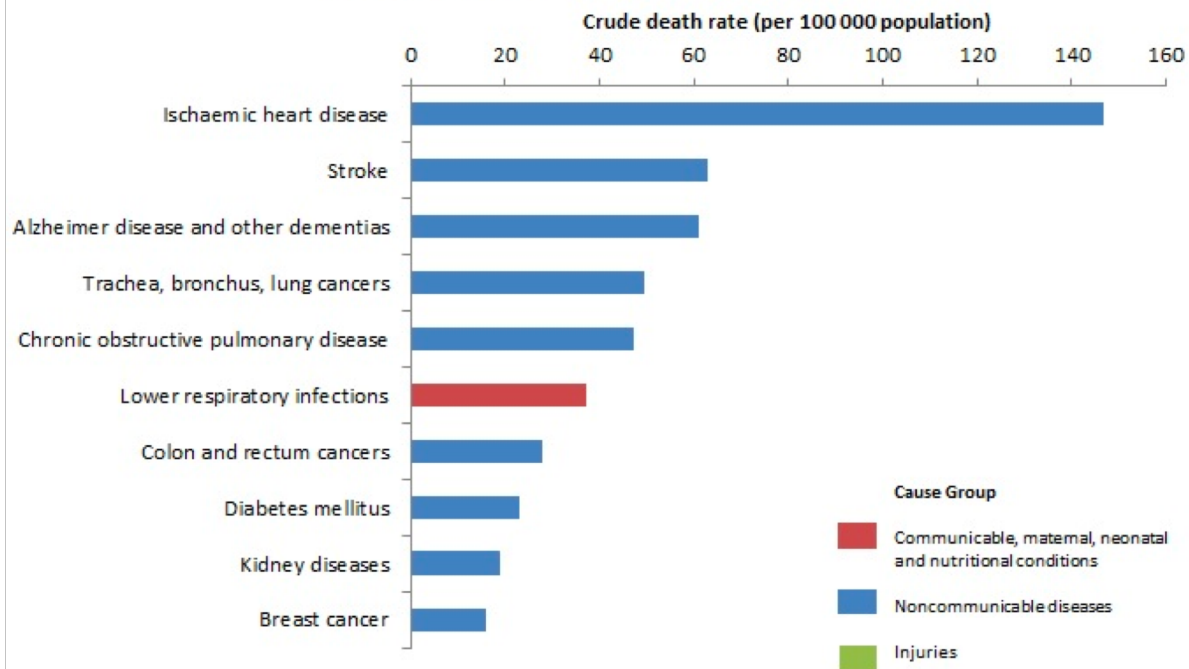
## Top 10 global causes of deaths, 2016



Source: Global Health Estimates 2016: Deaths by Cause, Age, Sex, by Country and by Region, 2000-2016. Geneva, World Health Organization; 2018.



### Top 10 causes of deaths in high-income countries in 2016



Source: Global Health Estimates 2016: Deaths by Cause, Age, Sex, by Country and by Region, 2000-2016. Geneva, World Health Organization; 2018. World Bank list of economies (June 2017). Washington, DC: The World Bank Group; 2017 (<https://datahelpdesk.worldbank.org/knowledgebase/articles/906319-world-bank-country-and-lending-groups>).

# Things that kill impair quality of life and impart disability



187 Countries, 21 world regions, both men and women, and about 20 different age groups

Together: 10.4% of global DALYs, 2.3% of global YLLs and, **28.5% of global YLDs**

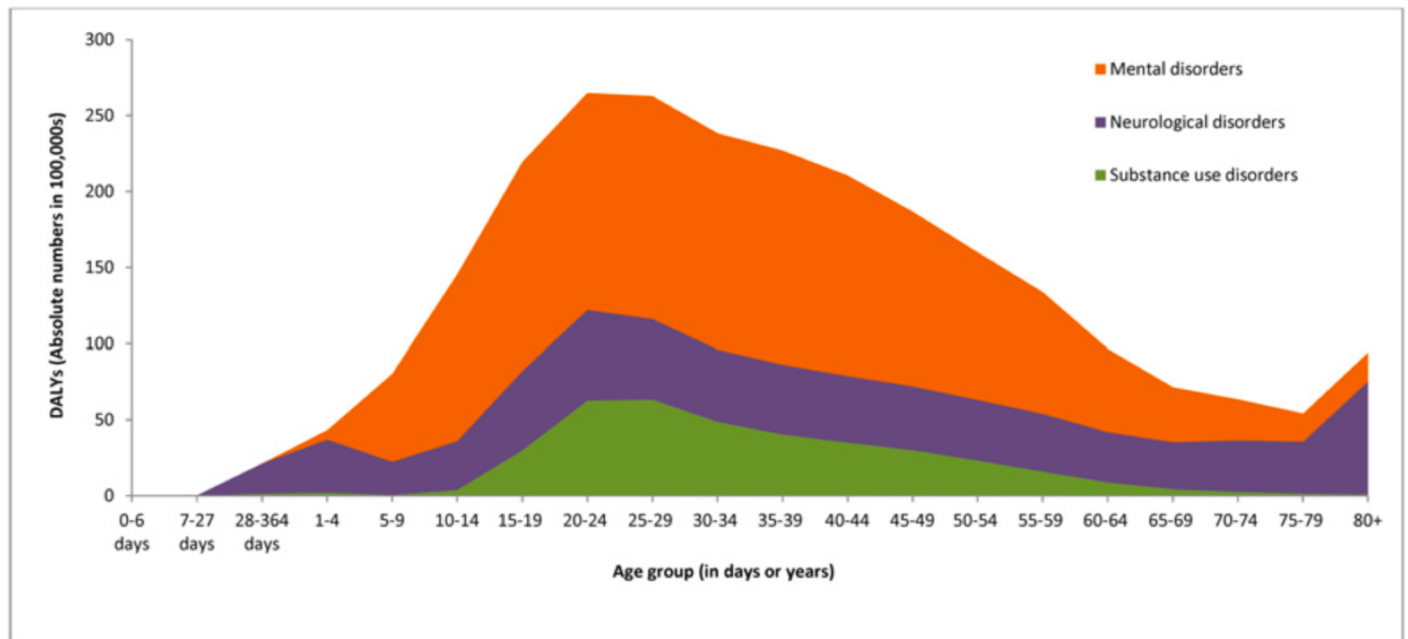
YLD: Years lived with disability

YLL: Years lost to premature mortality

**DALY: the TOTAL number of years lost to disability or early death**

**Table 1. GBD 2010 Mental, Neurological, and Substa**

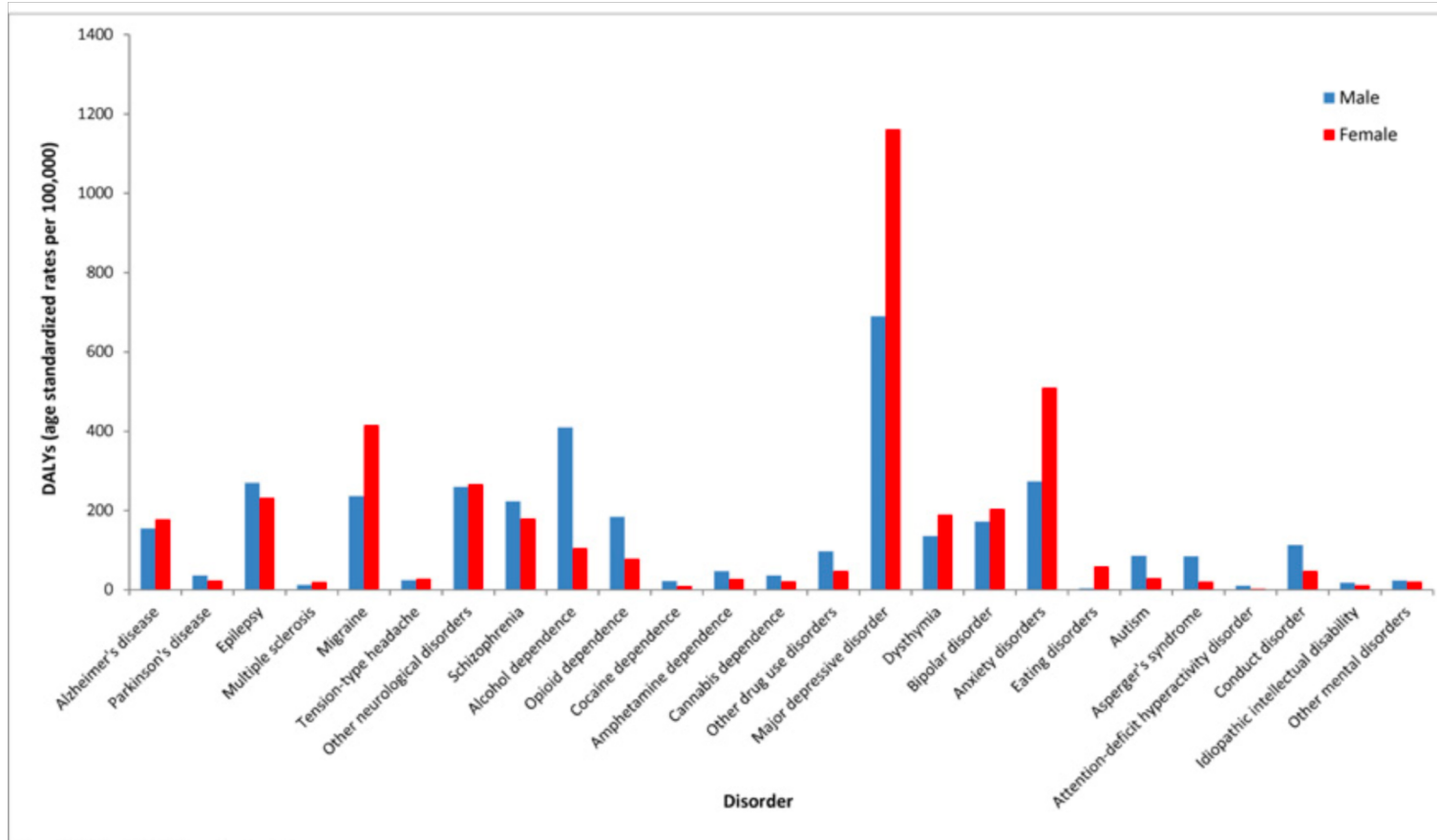
Disorders	Disability weights	
<b>Neurological disorders</b>		
Alzheimer's disease	mild: 0.082 (0.055–0.117);	
Parkinson's disease	mild: 0.011 (0.005–0.021);	
Epilepsy	treated, seizure free:0.072 (0.211–0.445); untreated:0	
Multiple sclerosis	mild: 0.198 (0.137–0.278);	
Migraine	0.433 (0.287–0.593)	
Tension-type headache	0.04 (0.025–0.062)	
<b>Substance use disorders</b>		
Alcohol dependence	mild: 0.25(90.176–0.359);	
Opioid dependence	0.641 (0.459–0.803)	
Cocaine dependence	0.376 (0.235–0.553)	
Amphetamine dependence	0.353 (0.215–0.525)	
Cannabis dependence	0.329 (0.223–0.455)	
<b>Mental disorders</b>		
Major depressive disorder	mild: 0.159 (0.107–0.223);	
Dysthymia	0.159 (0.107–0.223)	
Bipolar disorder	manic: 0.480 (0.323–0.642 (0.021–0.055)	
Schizophrenia	acute: 0.756 (0.571–0.894	
Anxiety disorders	mild: 0.03 (0.017–0.048); n	
Eating disorders	Anorexia nervosa: 0.223 (0	
Autism	0.259 (0.177–0.362)	
Asperger's syndrome	0.11 (0.073–0.157)	
Attention-deficit hyperactivity disorder	0.049 (0.031–0.074)	36,400,000
Conduct disorder	0.236 (0.031–0.074)	48,700,000
Idiopathic intellectual disability	mild: 0.031 (0.018–0.049); moderate:0.08 (0.053–0.114); severe:0.126 (0.085–0.176); profound: 0.157 (0.107–0.221)	30,800,000



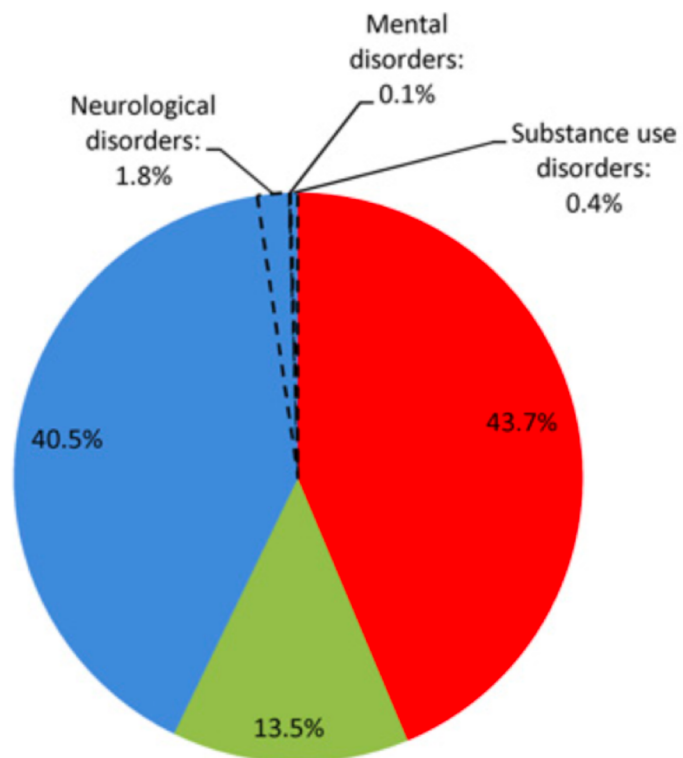
Note: DALYs = disability-adjusted life years.

**Fig 1. Absolute DALYs Attributable to Mental, Neurological, and Substance Use Disorders, by Age, 2010.**

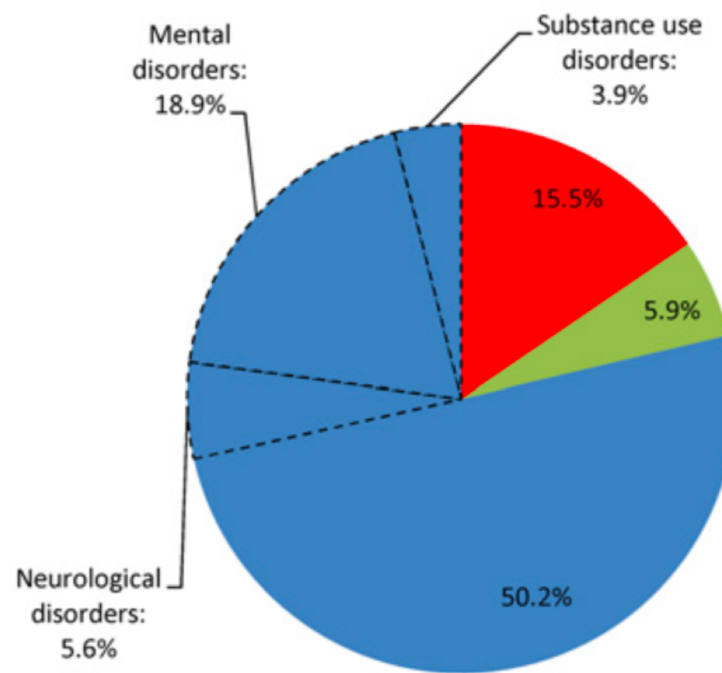
doi:10.1371/journal.pone.0116820.g001



### YLLs



### YLDs



- Communicable diseases
- Injuries
- Non-communicable diseases

Note: YLLs = years lost to premature mortality; YLDs = Years lived with disability



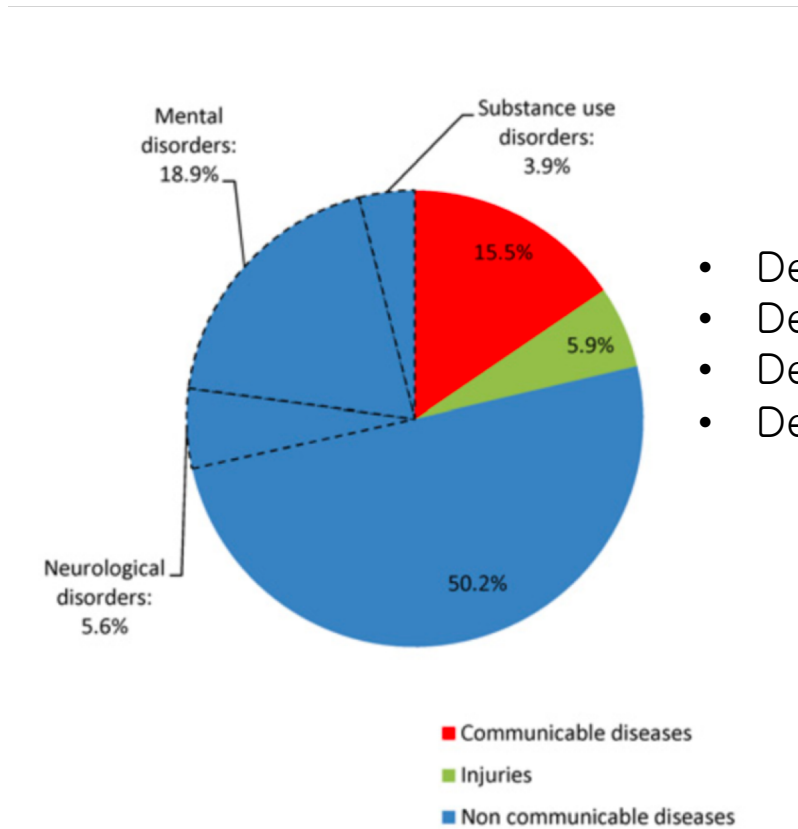
# WHY?

- Neurons, glia and associated cellular populations (glia, neurovasculature) are incredibly complicated
- Neurons are for the most part POST mitotic
- Brain, spinal cord and nerves are anatomically complicated
- We do not have a brain or spinal cord transplant program (yet)
- Many of these conditions are difficult to diagnose (misdiagnosis, underdiagnosis)
- Many of these conditions are associated with incredible societal stigma

SO, do more research!

- The etiology or cause is often unknown
- If etiology is unknown, how do you make an animal model to test a treatment?
- If the gene is known, often mice do not recapitulate the symptoms of disease
- Some human neuropsychiatric symptoms are exquisitely human (and can not be studied in animals)

# Challenge to Future Neuroscientists



- Develop more efficient diagnostic tools
- Develop a better understanding of pathophysiology
- Develop safer and more effective treatments
- Develop better ways of monitoring treatment response

Graduate school?

Medical School?

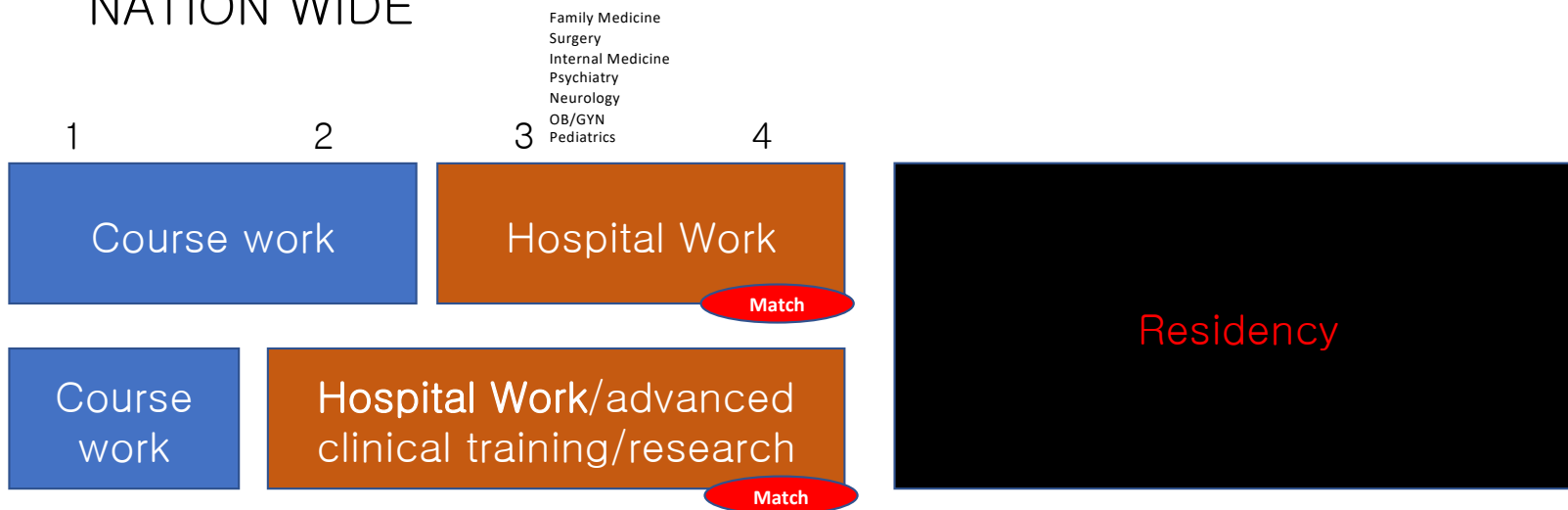


MDPhD?  
Yikes!

Work in industry?

# The MD Route

- Four year program\*
- Requires the MCAT and a comprehensive application process
- Emphasis on well rounded candidates, but will at times substitute **depth** for **breadth**
- You will take the USMLE Step I, II (CS and CK)
- Provides a structured training program that is standardized  
NATION WIDE

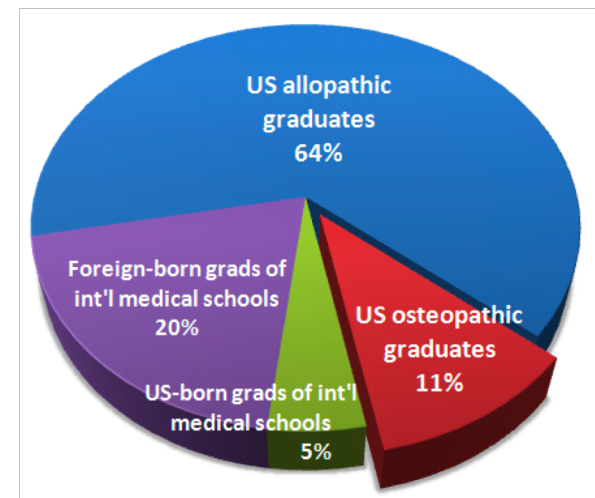


# Osteopathic Medicine (DO)

- Also a four year program
- Originated on techniques where joints and bones were manipulated to diagnose and treat illness (“osteo”)
- Now more mainstream
- Traditionally, less competitive entrance than MD schools
- Traditionally, graduates have gone into primary care
- DO graduates do have more limited choices for subspecialty

## NOTES:

- Highly competitive
- Expensive over four years (loans)
- Overall **low risk**
- Requires further post graduate medical training (**RESIDENCY**) and/or further post-POST-graduate medical training (**FELLOWSHIP**)



# RESIDENCY (in neuroscience-ish fields)

Postgraduate Medical Education (PGY1–X)

Do you want to see patients in a clinic and talk to them and examine them and return their phone calls?

Do you want to be a surgeon? Do you enjoy the OR environment?

Do you prefer to work with a pediatric population or an adult population?

Would you be comfortable with a career where you never physically interact with patients?

Psychiatry

Neurology

Neurosurgery

Anesthesia and Pain Management

Neuroradiology

Neuropathology

# RESIDENCY

Postgraduate Medical Education (PGY1–X)

## Adult Psychiatry

- 4 year residency
- +/- fellowships

## Child Psychiatry

- 3 or 4 year residency
- 2 year fellowship

## Anesthesia and Pain Management

- 4 year residency
- +/- fellowships

## Adult Neurology

- 1 year internship
- 3 year residency
- +/- fellowships

## Child Neurology

- 2 year internship
- 3 year residency
- +/- fellowships

## Neuropathology

- 2 year residency in anatomic pathology
- 2 year fellowship in neuropathology

## Neurosurgery

- 1 year internship
- **6 year residency**
- +/- fellowships

## Neuroradiology

- 1 year internship
- 4 year residency
- 1 year fellowship

# RESIDENCY

Postgraduate Medical Education (PGY1–X)

## NOTES:

- Can be highly competitive
- SALARIED positions: PGY1 \$55K
- Primarily hospital or clinic or laboratory based (often multiple sites)
- **RIGOROUS and front-loaded(80h work week on average)**
- Many enter into different residency programs mid-training
- Can be at academic or community medical centers
- Maybe protected time for research (at the end)

Rounds and team hierarchy

*Morbidity and mortality*

See One, Do One, Teach One

*Attending physician*





Graduate school?

Medical School?

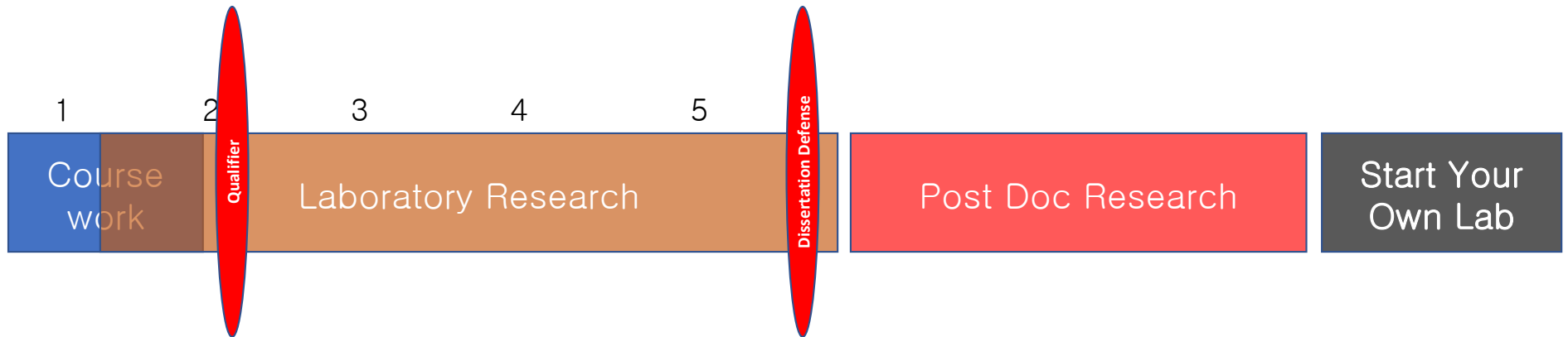


MDPhD?  
Yikes!

Work in industry?

# Graduate School: PhD

- Lasts 4–X years
- Stipended (G1 earn about ~\$30K)
- Poorly standardized, often structured based on historical norms
- Formal introduction into the scientific method: Observation, Hypothesis, Experimentation
- Publication Requirements (some)
- All students assign a THESIS COMMITTEE



# PhD at a Medical School?

The screenshot shows the NYU Langone Health website. The top navigation bar includes 'Patient Care', 'Education & Research', and 'NYU Langone Health'. Below this, there are links for 'Education', 'Research', 'Faculty', 'Departments & Institutes', and 'Our Community'. The main content area features a large image of two people in a lab setting with the heading 'PhD Program' and the text 'Our PhD program prepares aspiring scientists for careers in biomedical research.' A sidebar on the left lists various programs under 'Sackler Institute of Graduate Biomedical Sciences', including 'PhD Program', 'Admissions', 'PhD Training Programs', 'Academics', 'Life at Sackler Institute of Graduate Biomedical Sciences', 'MD/PhD Program', 'MS in Biomedical Informatics', 'Summer Undergraduate Research Program', 'PhD Training Faculty', and 'Administration'. The main text describes the PhD program as a career in biomedical research, mentioning interdisciplinary training and combined MD/PhD programs. A video player is embedded, showing students in a lab setting, with a play button and the text '(MUSIC PLAYING)'. Below the video, a small caption reads: 'VIDEO: Students at NYU School of Medicine's Sackler Institute of Graduate Biomedical Sciences talk about why they chose our PhD program. For more videos, please visit the Sackler Institute of Graduate Biomedical Sciences virtual tour.' The bottom navigation bar includes 'Home', 'People', 'Doctoral Program', 'Undergraduate Program', 'Labs & Groups', 'Events', and 'Contact'.

- Greater emphasis on disease models or studying disease tissue
- Many of your collaborators will be MDs or MDPHds
- Potentially more interactions with members of scientific/pharma industry

The screenshot shows the NYU CNS Center for Neural Science website. The top navigation bar includes 'NYU/CNS Center for Neural Science' and 'NEW YORK UNIVERSITY FACULTY OF ARTS & SCIENCE'. Below this, there are links for 'Home', 'People', 'Doctoral Program', 'Undergraduate Program', 'Labs & Groups', 'Events', and 'Contact'. The main content area features a large image of two people in a lab setting with the heading 'Overview of the Doctoral Program'. A sidebar on the left lists various programs under 'NYU/CNS Center for Neural Science', including 'Overview', 'Requirements & Sample Curriculum', 'Facilities', 'Admissions, Financial Aid & Housing', 'Handbook & Guide', 'Training Programs in Neuroscience', 'Courses: Schedules and Links', and 'Neuroscience-related programs at NYU'. The main text describes the Doctoral Program in Neural Science, mentioning its history and the interdisciplinary nature of the program. It also mentions the 'NYU Shanghai track in Neural Science' and the 'New Admission Process - See Below'. A search bar is located at the top right, and a 'CNS Personnel Directory' link is at the bottom left. The bottom navigation bar includes 'Home', 'People', 'Doctoral Program', 'Undergraduate Program', 'Labs & Groups', 'Events', and 'Contact'.

- Greater emphasis on basic neuroscience
- More TA responsibilities
- Closer ties to departments like engineering or physics or mathematics

It's  
about  
the  
people

NYU/CNS  
Center for Neural Science

NEW YORK UNIVERSITY  
FACULTY OF ARTS & SCIENCE

Home **People** Doctoral Program Undergraduate Program Labs & Groups Events Contact

**Core Faculty**

- Global Distinguished Professor**
- Associates**
- Affiliates**
- Research Scientists**
- Visiting Scholars**
- Postdoctoral**
- Predoctoral**
- Administrative Staff**

**Administration**

- Director: **Eric Klann**
- Director of Graduate Studies: **Michael Hawken**
- Director of Undergraduate Studies: **Chiye Aoki**
- Associate Director: **Amala Ankolekar**

**Core Faculty**

- Cristina M. Alberini**, Professor of Neural Science; Ph.D. 1988, University of Genoa. Molecular mechanisms of long-term memory. [Lab homepage](#)
- Dora Angelaki**, Professor of Neural Science and Mechanical and Aerospace Engineering; Ph.D. 1991, University Of Minnesota. Circuitry and models of navigation and multi-sensory integration.
- Chiye Aoki**, Professor of Neural Science and Biology; Ph.D. 1985, The Rockefeller University. Neuronal plasticity in neocortex. [Lab homepage](#)
- Thomas J. Carew**, Anne and Joel Ehrenkrantz Dean of the Faculty of Arts and Science; Professor of Neural Science; Ph.D. 1970, University of California, Riverside. Molecular, cellular, and behavioral architecture of memory formation.
- Adam Carter**, Associate Professor of Neural Science; Ph.D. 2002, Harvard University. Cellular and circuit neurophysiology. [Lab homepage](#)
- Christine Constantinople**, Assistant Professor of Neural Science (starting Sep 2018); Ph.D. 2013, Columbia University. Circuitry underlying decision-making. [Lab homepage](#)
- André A. Fenton**, Professor of Neural Science; Ph.D. 1998, SUNY Health Science Center. Molecular, neural, behavioral, and computational aspects of memory. [Lab homepage](#)
- Paul W. Glimcher**, Silver Professor; Professor of Neural Science, Economics and Psychology; Ph.D. 1989, University of Pennsylvania. The neurobiological, economic, and psychological bases of human and animal decision-making. [Lab homepage](#)
- Michael J. Hawken**, Professor of Neural Science and Psychology; Ph.D. 1979, University of Chicago. Neuronal mechanisms of visual perception.
- David J. Heeger**, Silver Professor; Professor of Psychology and Neural Science; Ph.D. 1987, University of Pennsylvania. Functional imaging of the human brain (fMRI), computational neuroscience, vision, attention. [Lab homepage](#)
- Roozbeh Kiani**, Associate Professor of Neural Science; Ph.D. 2009, University of Washington. Decision making, visual shape and motion processing. [Lab homepage](#)
- Lynne Kiorpes**, Professor of Neural Science and Psychology; Ph.D. 1982, University of Washington. Development of visual function. [Lab homepage](#)
- Eric Klann**, Professor of Neural Science; Ph.D. 1989, Medical College of Virginia. Molecular mechanisms of learning and memory. [Lab homepage](#)
- Joseph E. LeDoux**, University Professor; Henry and Lucy Moses Professor of Science; Professor of Neural Science and Psychology; Director, Emotional Brain Institute; Ph.D. 1977, State University of New York, Stony Brook. Memory and emotion. [Lab homepage](#)
- Wei Ji Ma**, Associate Professor of Neural Science and Psychology; Ph.D. 2001, University of Groningen. Perception, working memory, and decision making. [Lab homepage](#)
- J. Anthony Movshon**, University Professor; Silver Professor; Professor of Neural Science and Psychology; Ph.D. 1976, Cambridge University. Vision and visual development. [Lab homepage](#)
- Simon Peron**, Assistant Professor of Neural Science; Ph.D. 2008, Baylor College of Medicine. Structure and function of cortical representations. [Lab homepage](#)
- Bijan Pesaran**, Associate Professor of Neural Science; Ph.D. 2002, California Institute of Technology. Neuronal dynamics and decision making. [Lab homepage](#)
- Alex D. Reyes**, Professor of Neural Science; Ph.D. 1990, University of Washington. Functional interactions of neurons in a network.
- John Rinzel**, Professor of Neural Science and Mathematics; Ph.D. 1973, New York University. Biophysical mechanisms and theoretical foundations of neural computations.
- Dan H. Sanes**, Professor of Neural Science and Biology; Ph.D. 1984, Princeton University. Development and plasticity of the auditory system.
- Cristina Savin**, Assistant Professor of Neural Science and Data Science; Ph.D. 2010, Goethe University Frankfurt. Learning and memory, neural circuits, probabilistic computation. [Lab homepage](#)
- David Schneider**, Assistant Professor of Neural Science; Ph.D. 2012, Columbia University. Sensory and motor circuits for listening and learning. [Lab homepage](#)
- Malcolm N. Semple**, Professor of Neural Science and Psychology; Ph.D. 1981, Monash University. Neurobiology of hearing.
- Robert M. Shapley**, Natalie Clews Spencer Professor of the Sciences; Professor of Neural Science, Psychology, and Biology; Ph.D. 1970, The Rockefeller University. Visual physiology and perception.
- Eero P. Simoncelli**, Silver Professor; Professor of Neural Science, Mathematics, Data Science and Psychology; Investigator, Howard Hughes Medical Institute; Ph.D. 1993, Massachusetts Institute of Technology. Computational neuroscience, visual/auditory perception, statistical image and signal processing.

**Faculty Interest Map**

Place mouse over dots to identify faculty. Core CNS faculty are within the inner circle.

**Search CNS**

Google Custom:

**CNS Personnel Directory**

## How do you evaluate a potential PhD mentor?

- Talk to them and their lab members
- Read their work
- Appreciate their publication record

The screenshot shows the PubMed search results for the query 'Saper CB'. The search is filtered to 'Summary' format, sorted by 'Publication Date', and shows 342 items. The first item is 'Narcolepsy in orexin knockout mice: molecular genetics of sleep regulation' by RM Chemelli, JT Willie, CM Sinton, JK Elmquist, T Scammell, C Lee, et al. (2004). The second item is 'Hypothalamic regulation of sleep and circadian rhythms' by CB Saper, TE Scammell, J Lu (2005).

The screenshot shows the Google Scholar profile for Clifford B Saper, Professor of Neurology at Harvard Medical School. His profile includes a 'FOLLOW' button and a 'Cited by' section with a bar chart showing citations from 2012 to 2019. The 'Cited by' table shows the following data:

Year	Citations
2012	~3000
2013	~3000
2014	~3000
2015	~3000
2016	~3000
2017	~3000
2018	~3000
2019	~3000

Summary statistics for his work:

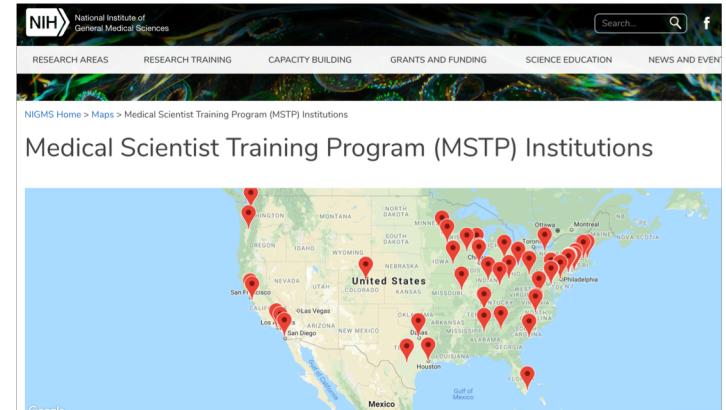
Metric	All	Since 2014
Citations	74419	19001
h-index	138	72
i10-index	315	229

- Understand their funding

The screenshot shows the NIH RePORTER website, which is used for reporting research projects. The page includes a search bar, navigation tabs for 'QUICK LINKS', 'RESEARCH', 'ORGANIZATIONS', 'WORKFORCE', 'FUNDING', 'REPORTS', and 'LINKS & DATA'. The 'FUNDING' tab is selected, and the 'RESEARCHER AND ORGANIZATION' section is visible. This section contains fields for entering the Principal Investigator (PI) name, City, State, Country, Congressional District, and DUNS Number. There are also buttons for 'SUBMIT QUERY', 'CLEAR QUERY', and 'LOOKUP'.

# Medical Scientist Training Programs (MSTP) MDPhD

The goal  
– To train an elite force of physician–scientists



bedside

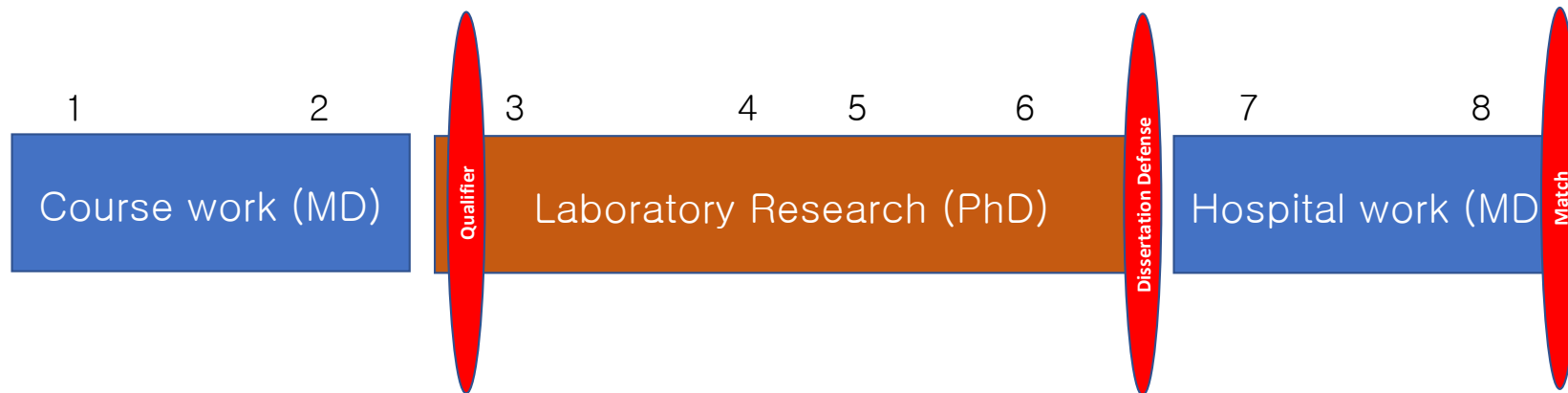


benchside

# Medical Scientist Training Programs (MSTP) MDPhD

Notes:

- MSTP Vs MDPHD programs?
- Accelerated Combined Degree Program
- Stipended from start to finish (MSTP1 ~\$30K) – **NO LOANS**
- Somewhat standardized across institutions
- No concessions for either degree\*

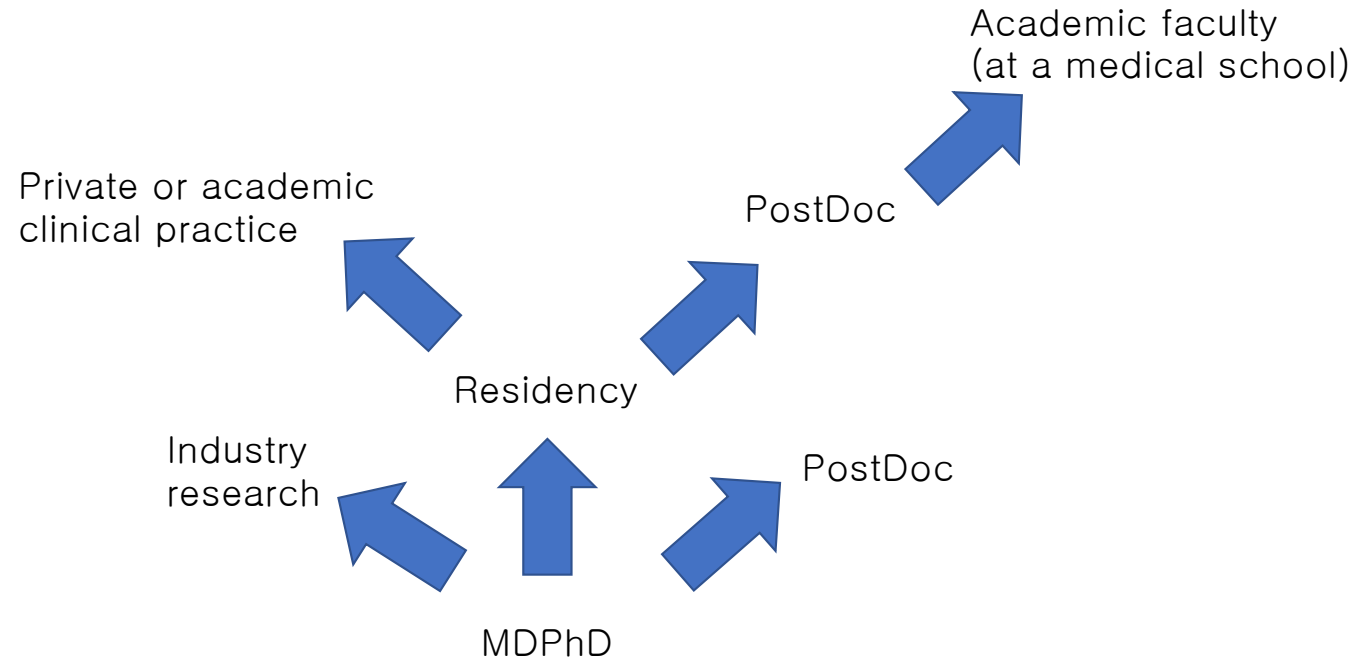


# Medical Scientist Training Programs (MSTP)

## MDPhD

Notes:

- Most graduates go on to residency training, typically nonsurgical specialties
- Outcomes are tracked by the NIH





# IMPORTANT: You do not need to be an MDPHD To function as a physician–scientist

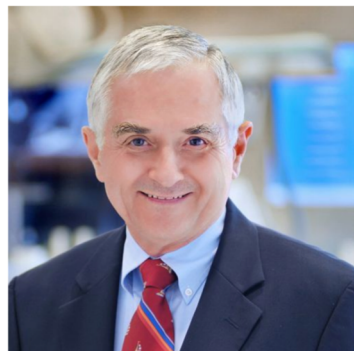
DIVISION OF  
**SLEEP MEDICINE**  
HARVARD MEDICAL SCHOOL

**FACULTY PROFILE**

**Thomas E. Scammell, MD**  
Professor of Neurology, Harvard Medical School  
Physician, Professor, Department of Neurology, Beth Israel Deaconess Medical Center  
Physician, Professor, Department of Neurobiology, Children's Hospital Boston  
[See publications](#)



People > Arthur L. Beaudet, M.D.



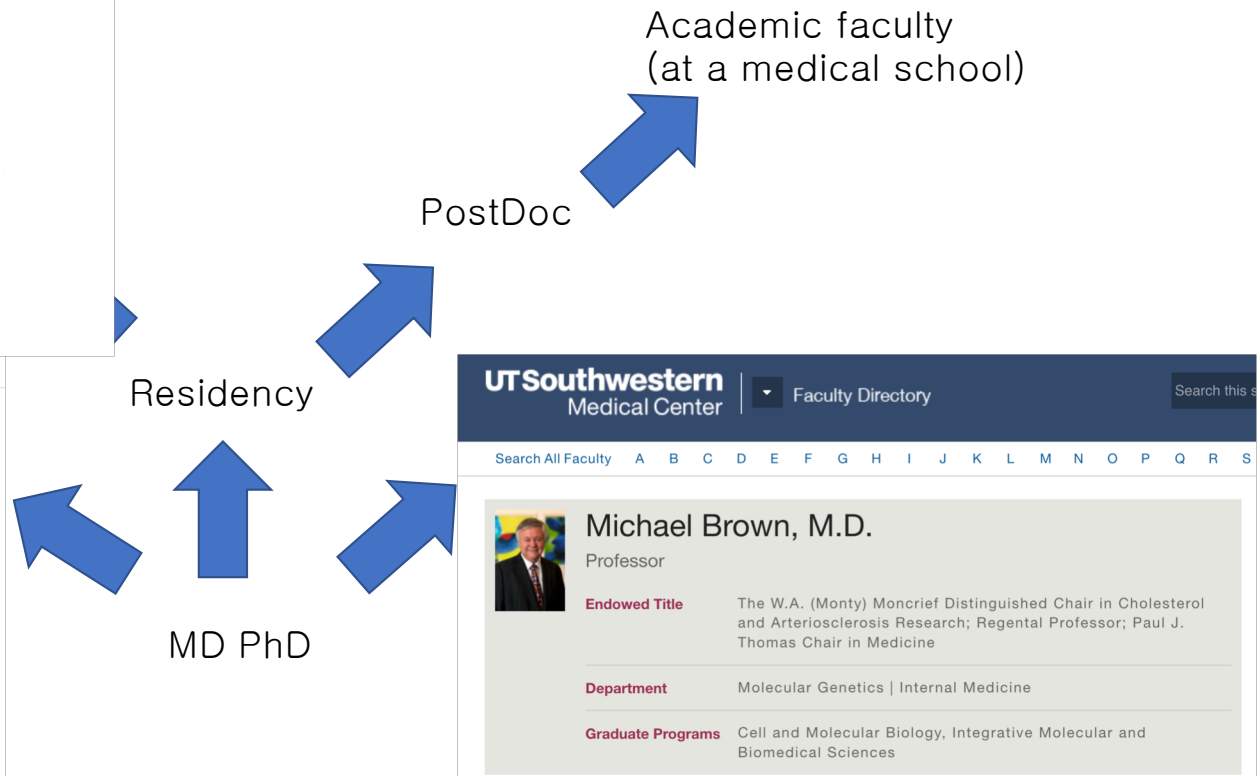
#### POSITIONS

**Henry and Emma Meyer Chair and Professor**  
Molecular and Human Genetics  
Baylor College of Medicine  
Houston, TX, US

**Professor**  
Molecular & Cellular Biology  
Baylor College of Medicine  
Houston, Texas, United States

**Professor**  
Pediatrics  
Baylor College of Medicine  
Houston, Texas, United States

**Faculty Member**  
Program in Integrative Molecular and Biomedical Sciences  
Baylor College of Medicine  
Houston, Texas, United States



- Introduction to myself and my own unique journey
- The burden of neuropsychiatric disease
- Pathways towards medically oriented careers in neuroscience
- A bit about a new course offering at Rice Neuroscience

## Advanced Research Seminar in Translational Neuroscience

**3 Credits**

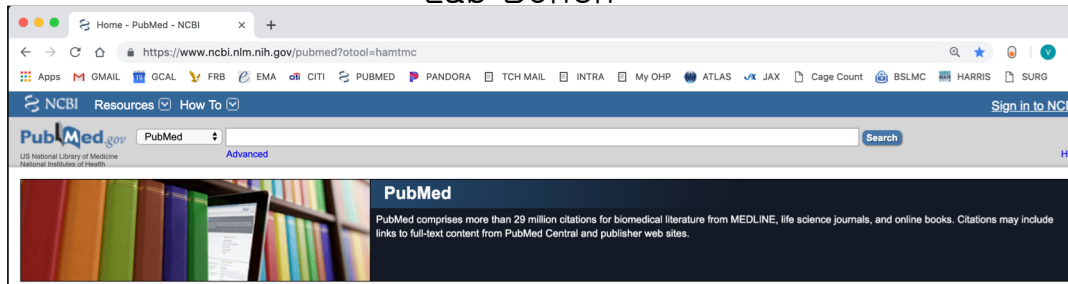
Fall 2019

Course Director: Vaishnav Krishnan MDPH (Baylor Neurology, Rice ECE\*)

### EMPHASIS:

- Identifying a neuropsychiatric **disease or a symptom** that suffers from a treatment gap (i.e., where existing treatments are insufficient)
- Review existing theories on the **pathophysiology** of this problem
- Critically evaluate **preclinical models** in which to study this disease or symptom
- Examine how **candidate treatments** have been tested in those models
- Explore the **barriers to implementing those treatments in humans**

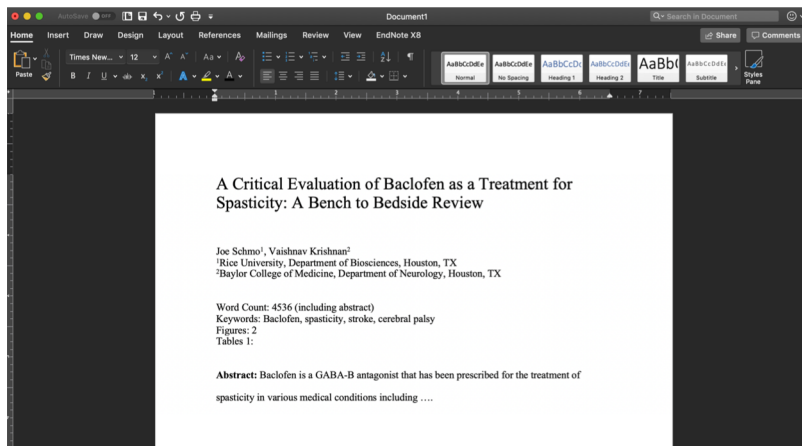
### Lab Bench



### Seek Counsel



## Write a manuscript (review)



The screenshot shows a word processing application window titled "Document1". The title bar includes "Autobackup" and "EndNote X8". The menu bar includes Home, Insert, Draw, Design, Layout, References, Mailings, Review, View, and EndNote X8. The ribbon includes Font, Paragraph, Styles, and a Share/Comments section. The main text area contains the following content:

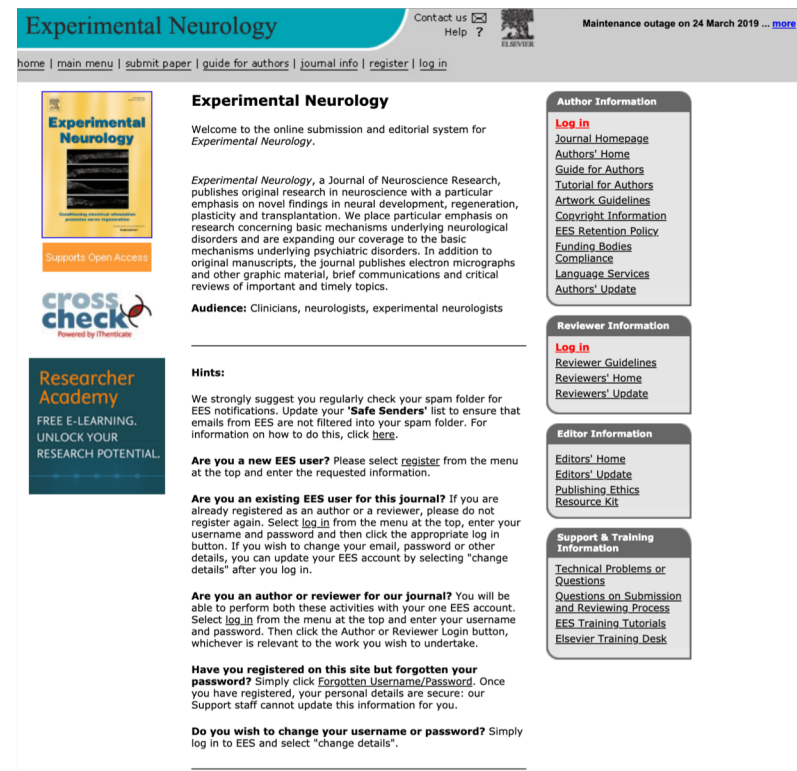
**A Critical Evaluation of Baclofen as a Treatment for Spasticity: A Bench to Bedside Review**

Joe Schmo<sup>1</sup>, Vaishnav Krishnan<sup>2</sup>  
<sup>1</sup>Rice University, Department of Biosciences, Houston, TX  
<sup>2</sup>Baylor College of Medicine, Department of Neurology, Houston, TX

Word Count: 4536 (including abstract)  
Keywords: Baclofen, spasticity, stroke, cerebral palsy  
Figures: 2  
Tables: 1

**Abstract:** Baclofen is a GABA-B antagonist that has been prescribed for the treatment of spasticity in various medical conditions including ...

## Submit a manuscript (review)



The screenshot shows the Experimental Neurology journal website. The header includes the journal name, navigation links (home, main menu, submit paper, guide for authors, journal info, register, log in), and contact information. A maintenance outage notice is visible in the top right corner.

### Experimental Neurology

Welcome to the online submission and editorial system for *Experimental Neurology*.

*Experimental Neurology*, a Journal of Neuroscience Research, publishes original research in neuroscience with a particular emphasis on novel findings in neural development, regeneration, plasticity and transplantation. We place particular emphasis on research concerning basic mechanisms underlying neurological disorders and are expanding our coverage to the basic mechanisms underlying psychiatric disorders. In addition to original manuscripts, the journal publishes electron micrographs and other graphic material, brief communications and critical reviews of important and timely topics.

**Audience:** Clinicians, neurologists, experimental neurologists

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