McGOVERN INSTITUTE

New Frontiers in Addiction Science

McGovern researchers are combining neuroscience and engineering to get at the roots of addiction.

The Toll of Addiction

Addiction takes a devastating toll on the health of millions, with widespread consequences on loved ones, the economy, and society at large.

FINANCIAL STRAIN

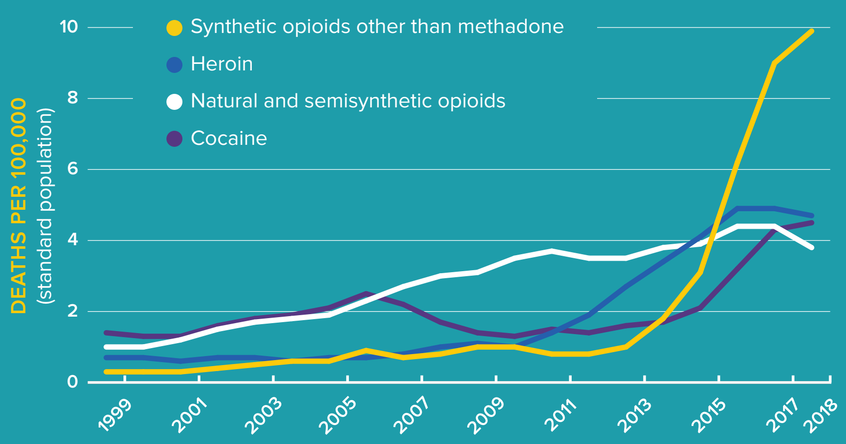
$800B

Annual costs related to crime, lost work productivity, and health care in the US due to the the abuse of prescription and illicit drugs, alcohol, and tobacco.

EMOTIONAL IMPACT

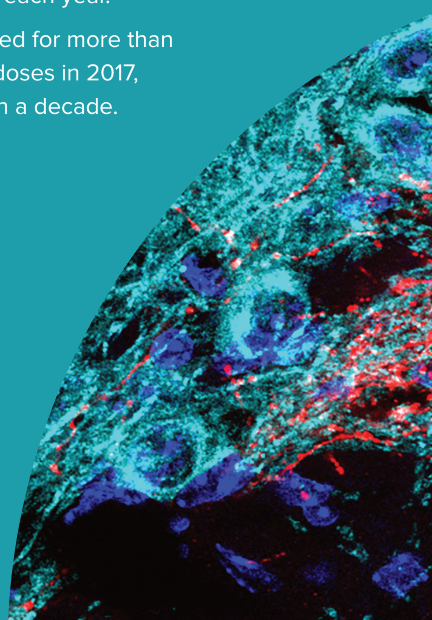
1 in 5 children grow up in a home affected by addiction.

FATALITIES



Tobacco and alcohol are two of the top three preventable causes of death in the US each year.

Addiction accounted for more than 70,200 drug overdoses in 2017, a 2-fold increase in a decade.



These numbers are staggering.
We must do something now.

Source: CDC, NIDA, StatNews, 2016 Surgeon General's Report

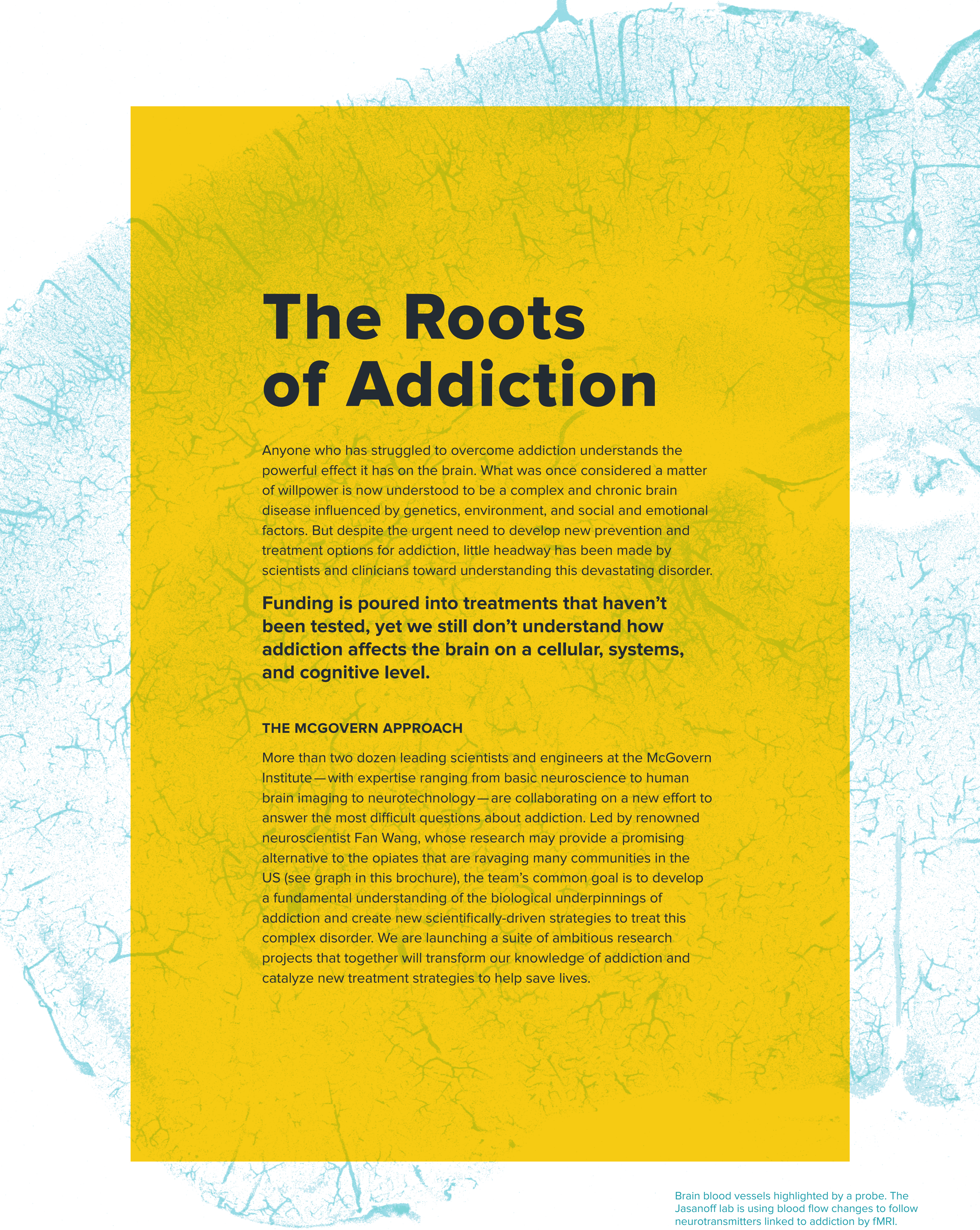
The Roots of Addiction

Anyone who has struggled to overcome addiction understands the powerful effect it has on the brain. What was once considered a matter of willpower is now understood to be a complex and chronic brain disease influenced by genetics, environment, and social and emotional factors. But despite the urgent need to develop new prevention and treatment options for addiction, little headway has been made by scientists and clinicians toward understanding this devastating disorder.

Funding is poured into treatments that haven't been tested, yet we still don't understand how addiction affects the brain on a cellular, systems, and cognitive level.

THE MCGOVERN APPROACH

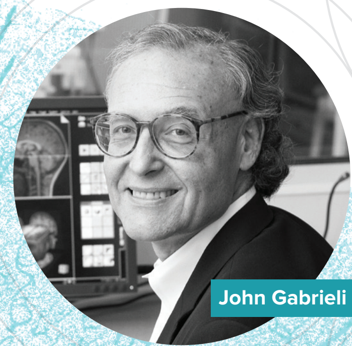
More than two dozen leading scientists and engineers at the McGovern Institute — with expertise ranging from basic neuroscience to human brain imaging to neurotechnology — are collaborating on a new effort to answer the most difficult questions about addiction. Led by renowned neuroscientist Fan Wang, whose research may provide a promising alternative to the opiates that are ravaging many communities in the US (see graph in this brochure), the team's common goal is to develop a fundamental understanding of the biological underpinnings of addiction and create new scientifically-driven strategies to treat this complex disorder. We are launching a suite of ambitious research projects that together will transform our knowledge of addiction and catalyze new treatment strategies to help save lives.



Brain blood vessels highlighted by a probe. The Jasanoff lab is using blood flow changes to follow neurotransmitters linked to addiction by fMRI.

Image: Alan Jasanoff

The Questions We're Asking



Why do some people become addicted while others do not?

It remains a mystery why some people become addicted to drugs, alcohol and other behaviors, while others do not. Studies have found that identical twins are more likely to abuse drugs than non-identical twins, but it is not a given that addiction is hereditary. **Polina Anikeeva** and **Ann Graybiel** are using novel techniques to study variability in addiction.

Self-destructive, drug-seeking behavior has been demonstrated in animal models that continue to seek out cocaine even in the presence of a paired punishment. Using this model, Anikeeva is developing novel fiber-based probes to investigate electrophysiological and neurochemical biomarkers that distinguish addicted subjects from those resistant to addiction.

Graybiel is investigating the direct and indirect dopamine pathways that drive motor behavior as a result of drug use. Differences in these pathways may be linked to an individual's risk of developing addiction. Using their designer mice, the Graybiel lab is assessing new pathways linked to addiction and gene expression in neurons to better understand the circuits themselves, as well as how opioid receptors are expressed.

What are the biological roots of addiction? Can they be fixed?

Fan Wang's lab is pinpointing circuits that play a role in opioid addiction. Wang and her team have identified particular neurons that, when inhibited, cause animals to crave less morphine and undertake non drug-seeking activities. Once these critical brain circuits and clusters of neurons are identified, the Wang lab will examine their connectivity, plasticity, and changes in function when influenced by morphine. Gaining a deeper understanding of how drugs of abuse affect these circuits will help pave the way for future treatments.

Polina Anikeeva is developing tools that are helping us to both understand, and interfere with, circuits linked to reward and addiction. The lab has recently developed new approaches that use light and even magnetic fields to activate neurons in the brain's reward region. By controlling these circuits in mice, Anikeeva will explore the role they play in drug-seeking behavior and how to decrease responses linked to addiction in these circuits and models.

"Preforms" in the Anikeeva lab are drawn into flexible fibers that are compatible with delicate brain tissue. These probes are now being used in Anikeeva lab addiction research.
Photo: Justin Knight

Ed Boyden has recently pioneered a powerful new technology that allows scientists to enlarge tissue and visualize the microscopic connections between neurons, and the nanoscopic molecules at those connections, with unprecedented scale and resolution. The Boyden lab now plans to use this technology, called expansion microscopy, to map the molecular and circuit changes associated with addiction. By using machine learning to help extract meaning from these datasets, Boyden hopes to identify new molecular and circuit-level targets for new addiction treatment strategies.

Can neuroscience predict who will benefit from rehab programs?

More than half of individuals treated for drug or alcohol abuse will relapse within six months, and it is still not clear to scientists why some addicts respond to inpatient treatment programs and others do not. **John Gabrieli's** lab will use brain imaging and machine learning to establish predictors of relapse; understand brain activity before, during, and after treatment; and potentially match individuals with optimal interventions.

How does addiction influence the entire brain?

Drugs including cannabis, alcohol, nicotine, and cocaine trigger a surge of dopamine in the brain. But addiction also influences other neurochemicals, affects multiple brain regions, and disrupts essential processes like decision-making, judgment, memory, and learning. McGovern investigators are exploring these understudied neurochemicals, processes, and brain regions to gain a broad picture of how addiction affects the entire brain.

Alan Jasanoff is renowned for developing magnetic resonance imaging (MRI) sensors that can monitor neural activity deep within the brain. By deploying new sensors that detect neurochemicals, as well as communication between brain regions linked to motivation, reward, and addiction, the Jasanoff lab is learning how addiction alters numerous aspects of brain-wide function.

Ann Graybiel is interested in how addiction influences the brain's "reward circuit" and spreads to other regions of the brain that impact complex cognitive processes like working memory, flexible thinking, and self-control. Leveraging her leading expertise, Graybiel's lab is uncovering dopamine-linked pathways that may be involved in longer-term habit formation, making addictive habits harder to break.

Can we find non-addictive alternatives to opiates for pain relief?

Finding an effective pain relief method that is truly non-addictive could be a breakthrough in stemming the growth of opioid addiction. The **Wang** lab has recently discovered pain-suppressing neurons in the brain that can potentially be harnessed for developing therapies to relieve chronic pain. To move forward, the lab is performing deep single-cell sequencing to identify receptors and/or ion channels uniquely expressed in these cells. This information will help scientists screen for drugs that can activate these natural painkillers. Further electrophysiological characterization of these neurons may lead to the development of non-invasive, drug-free therapies for pain relief.

Groundbreaking insights into the neurobiology of addiction are badly needed to make real progress and save lives.

Over the next five years McGovern researchers will:

REVEAL

+ Some of the complex brain circuitry underlying addiction
+ Why addiction risk varies greatly between individuals

DEVELOP

+ Innovative new tools to study addiction
+ Novel targets for pain relief that don't rely on opiates

DELIVER

+ A deep knowledge base of addiction, from cells to circuits to the whole brain
+ New strategies to predict, prevent, and treat addiction

JOIN US

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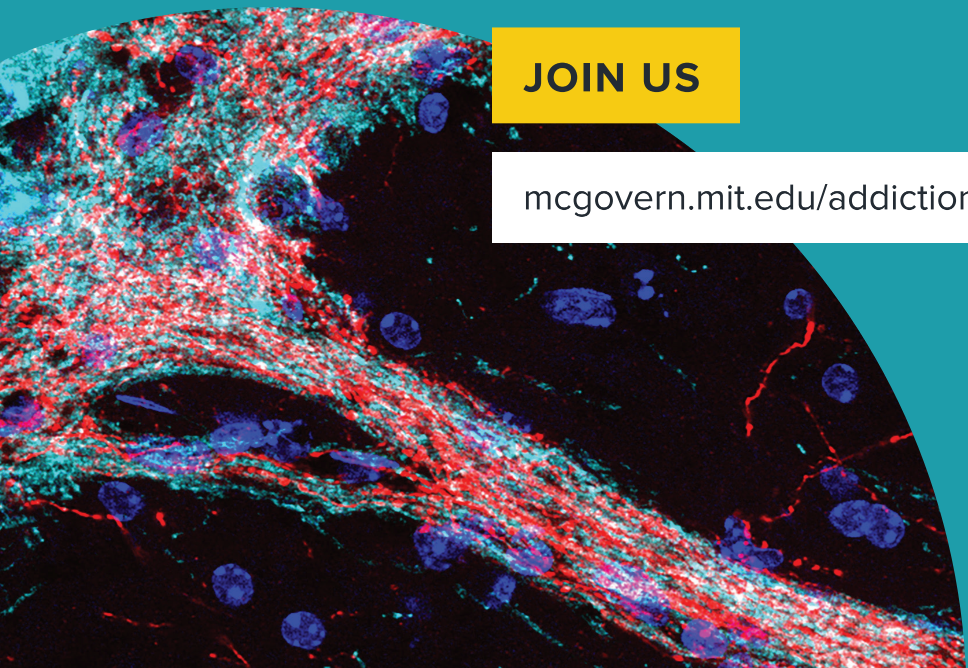

Striosomal neurons (red) reach the substantia nigra (blue), a microscopic view of connections between brain regions linked to addiction.

Image: Jill Crittenden