



National Institute of  
Neurological Disorders  
and Stroke

# National Disability Forum

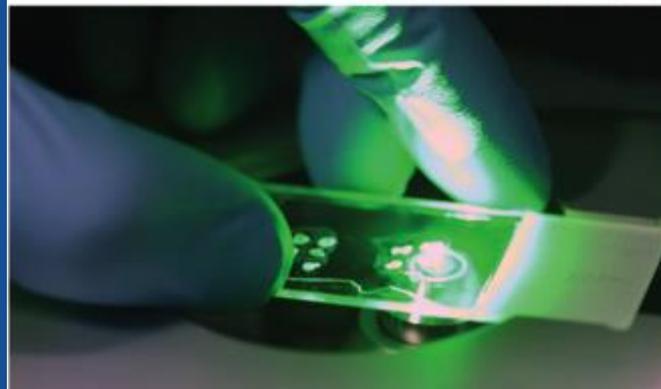
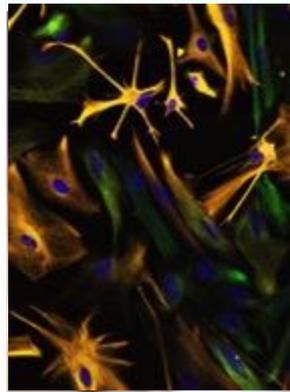
*“What Impairments  
Have a Likelihood  
to Improve?”*

December 3<sup>rd</sup>, 2019

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Associate Director, National Institute of  
Neurological Disorders and Stroke, NIH

**DISCLOSURES: NONE**





# NINDS mission

To seek fundamental knowledge about the brain and nervous system and to use that knowledge to reduce the burden of neurological disease.

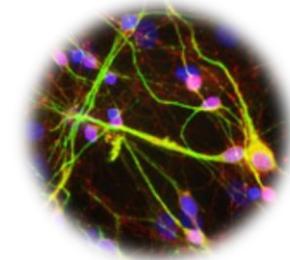
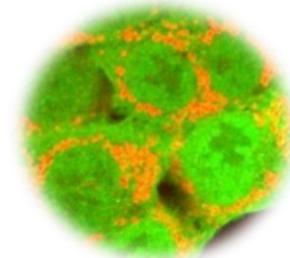
# NINDS Supports Research Across a Wide Disease Spectrum

Absence of Septum Pellucidum  
Acute Disseminated Encephalomyelitis  
Adie Syndrome  
Agnosia  
Aicardi Syndrome  
Aicardi-Goutieres Syndrome  
AIDS – Neurological Complications  
Alexander Disease  
Alpers' Disease  
Alternating Hemiplegia  
**Amyotrophic Lateral Sclerosis (ALS)**  
Anencephaly  
Apraxia  
Arachnoid Cysts  
Arachnoiditis  
Ataxia Telangiectasia  
Barth Syndrome  
Becker's Myotonia  
Behcet's Disease  
Bell's Palsy  
Binswanger's Disease  
Blepharospasm  
Brown-Sequard Syndrome  
CADASIL  
Cerebellar degeneration  
Cerebellar Hypoplasia  
Bell's Palsy  
Binswanger's Disease  
Blepharospasm  
Brown-Sequard Syndrome  
CADASIL

Cerebellar degeneration  
Cerebellar Hypoplasia  
Cerebral Cavernous Malformation  
Cerebral Palsy  
Charcot-Marie-Tooth Disease  
Chiari Malformation  
Choreo-acanthocytosis  
Cockayne Syndrome Type II  
Coffin Lowry Syndrome  
Complex Regional Pain Syndrome  
Corticobasal Degeneration  
Cytomegalic Inclusion Disease  
Dancing eyes-Dancing Feet Syndrome  
Dandy-Walker Syndrome  
Dravet Syndrome  
Dystonias  
Early Infantile Epileptic Encephalopathy  
Empty Sella Syndrome  
Encephalitis Lethargica  
**Epilepsy**  
**Essential Tremor**  
Fabry Disease  
Familial Dysautonomia  
Farber's Disease  
Friedreich's Ataxia  
Frontotemporal Dementia  
Gaucher Disease  
Gerstmann's Syndrome  
Gerstmann-Straussler-Scheinker Disease  
Giant Axonal Neuropathy  
Glycogen Storage Disease  
Guillain-Barre Syndrome  
HTLV-1 Associated Myelopathy  
Huntington's Disease  
Hydranencephaly  
Inclusion Body Myositis  
Joubert Syndrome  
Kearns-Sayre Syndrome  
Kennedy's Disease  
Kuru  
Landau-Kleffner Syndrome  
Lennox-Gastaut Syndrome

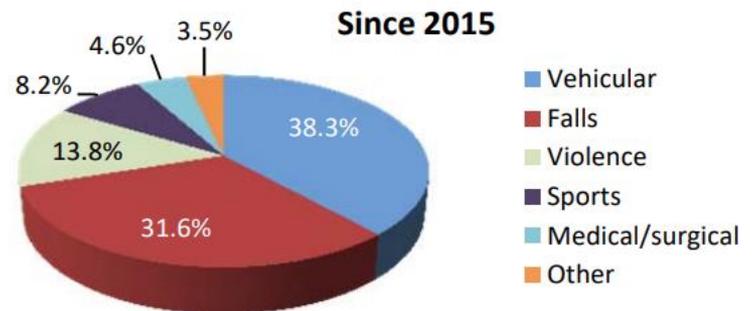
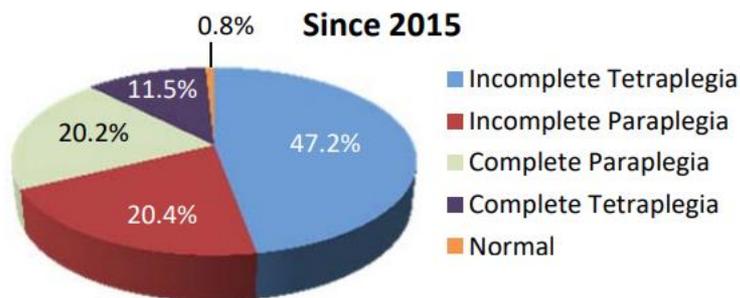
Leukodystrophy  
Lyme Disease-Neurological Complications  
Lewy Body Disease  
Menkes Disease  
Meralgia Paresthetica  
Microcephaly  
Miller-Fisher Syndrome  
Moebius Syndrome  
Myasthenia Gravis  
Narcolepsy  
Neuroleptic Malignant Syndrome  
Niemann-Pick Disease  
Normal Pressure Hydrocephalus  
Olivopontocerebellar Atrophy  
Pantothenate Kinase-Associated Neurodegeneration  
Parkinson's Disease  
Paroxysmal Hemicrania  
Pick's Disease  
Post polio syndrome  
Primary Later Sclerosis  
Progressive Hemifacial Atrophy  
Pseudotumor Cerebri  
Rasmussen's Encephalitis  
Refsum Disease  
Rett Syndrome  
Sandhoff Disease  
Semantic Dementia  
Septo-Optic Dysplasia  
**Spinal Cord Injury**  
Spinal Muscular Atrophy  
Stiff Person Syndrome  
**Stroke**  
Sturge-Weber Syndrome  
Subacute Sclerosing Panencephalitis

Tay-Sachs Disease  
Thoracic Outlet Syndrome  
Tourette Syndrome  
Trigeminal Neuralgia  
Transverse Myelitis  
Tuberous Schlerosis  
Von-Hippel-Lindau Disease  
Wernicke-Korsakoff Syndrome  
West Syndrome  
William's Syndrome  
Wilson Disease  
Wolman's Disease  
Zellweger Syndrome



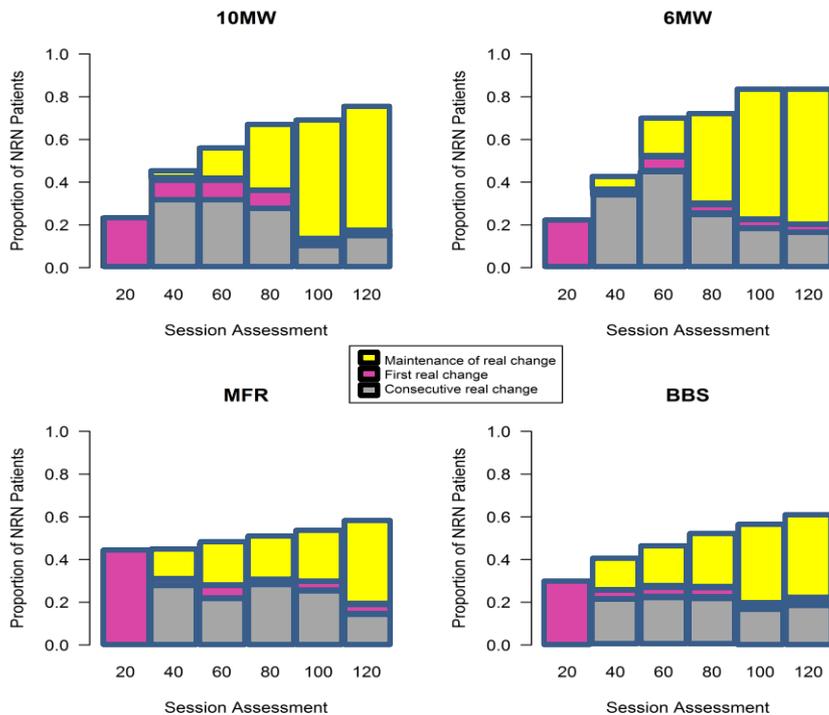
# Spinal Cord Injury

- Roughly 17,000 new cases/year
- About 250,000 living with SCI



# Clinical Expertise Optimizes Neuromodulation

- Used to be standard expectation that recovery after SCI would fully plateau by ~1 year: **Not the case anymore.**
- Clear evidence that incomplete SCI individuals can continue to see small-moderate improvements in ambulation, autonomic function and QOL.



- Chronic Incomplete SCI with 120 clinical treatments of Locomotor Training
- 6 times higher than national PT benefit limit

***Improvement Never Plateaued***  
***Significant Gains were maintained***  
***6-12 months after treatment***  
***ended.***

Morrison S et al 2018 Arch Phys Med Rehab

# Stimulation + Rehabilitation leads to functional recovery \**persisting beyond stimulation*\*

- Electrical stimulation in combination with rehab can greatly increase indices of recovery, and can even be used to improve motor and autonomic parameters long after neurologically motor complete SCI

- Leg function for people with AIS A-D SCI

Harkema...Edgerton *Lancet* 2011, Angeli... Harkema *Brain* 2014, Rejc... Harkema, *Sci Rep* 2017,\* Gill... Zhao *Nature Medicine* 2018, Angeli... Harkema *NEJM* 2018, Wagner... Courtine *Nature* 2018\*, Darrow... Samadina *J Neurotrauma* 2019



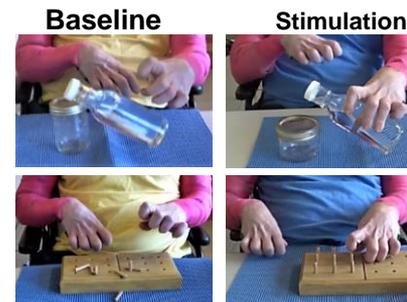
Angeli... Harkema *NEJM* 2018



Gill... Zhao *Nat. Medicine* 2018

- Hand function for people with AIS B-D SCI

Lu... Edgerton *Neurorehab N Repair* 2016,\* Gad... Edgerton *J Neurotrauma* 2018,\* Inanici...Moritz *IEEE TNSRE* 2018,\*



Inanici... Moritz *IEEE TNSRE* 2018\*



Wagner... Courtine *Nature* 2018\*

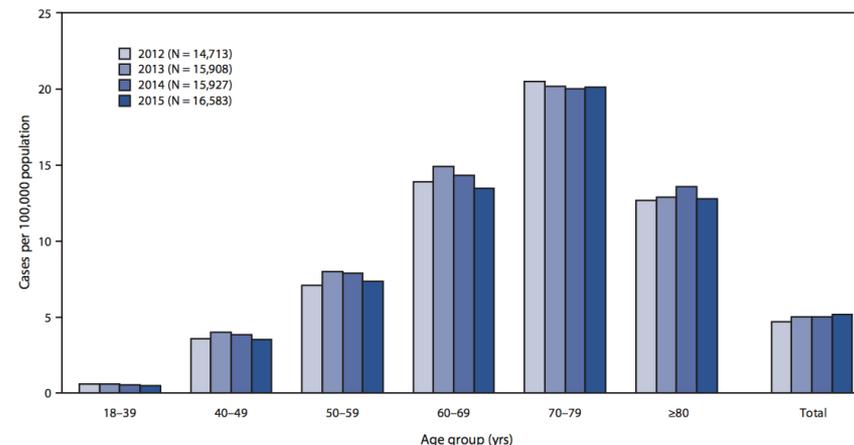
# ALS

## Amyotrophic Lateral Sclerosis

- 2 new cases per 100,000 people per year
- About 16,000 living with ALS

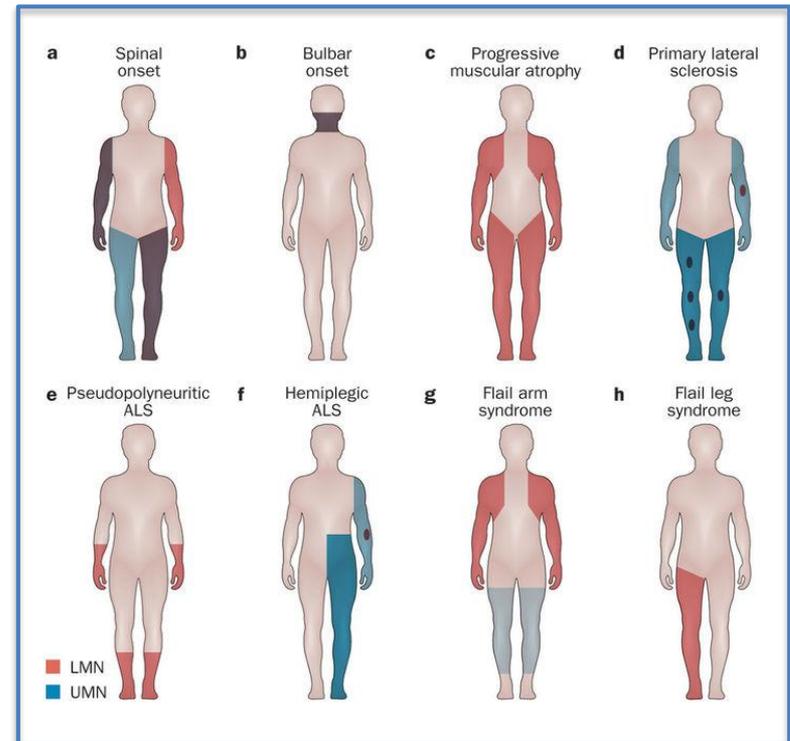
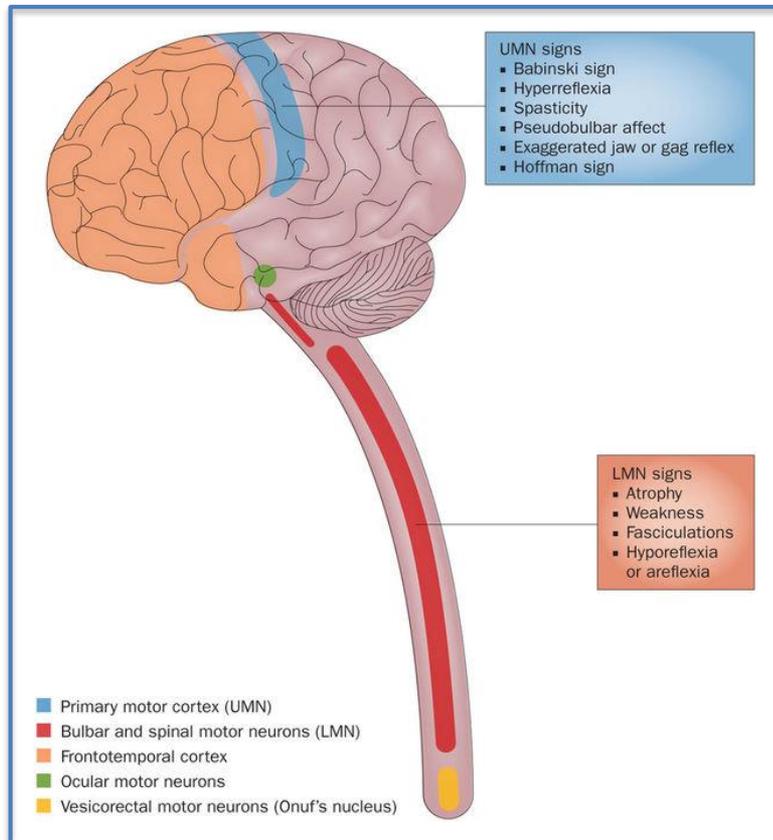
Morbidity and Mortality Weekly Report

FIGURE. Estimated prevalence of amyotrophic lateral sclerosis (ALS), by age group — National ALS Registry, United States, 2012–2015\*



\* Prevalence per 100,000 population using the 2015 U.S. Census estimate.

# The phenotype of ALS is highly variable



[Swinnen and Robberecht, Nature Reviews Neurology, 2014]

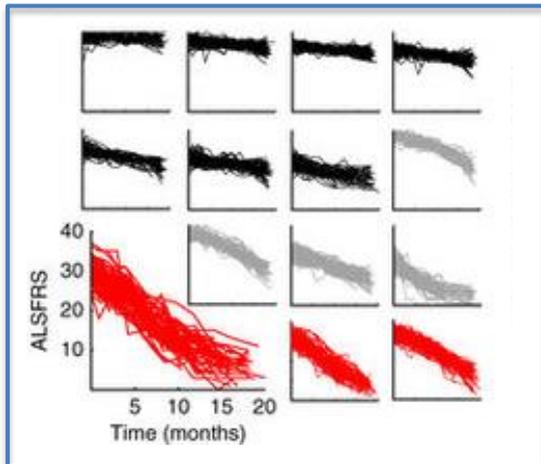
# Can ALS scores improve?



Open-Access Database - completed clinical trials  
(contains data from > 10,000 ALS patients!)

Pooled Resource Open-Access  
ALS Clinical Trials Database

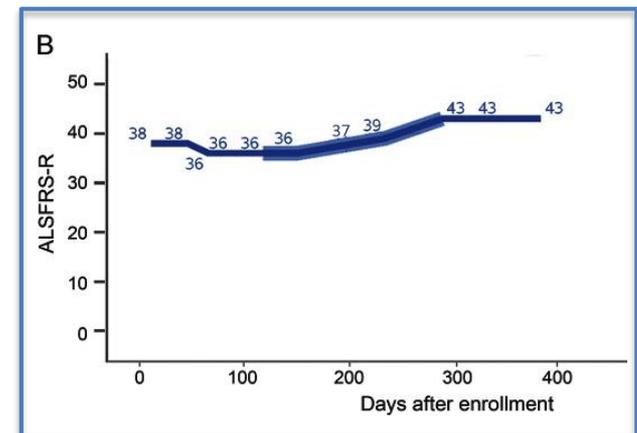
## Patterns of ALSFRS-R decline



[Kuffner et al., Nat Biotech, 2015]

**Fewer than 1%** of patients with ALS ever experienced an increase of 4 or more points

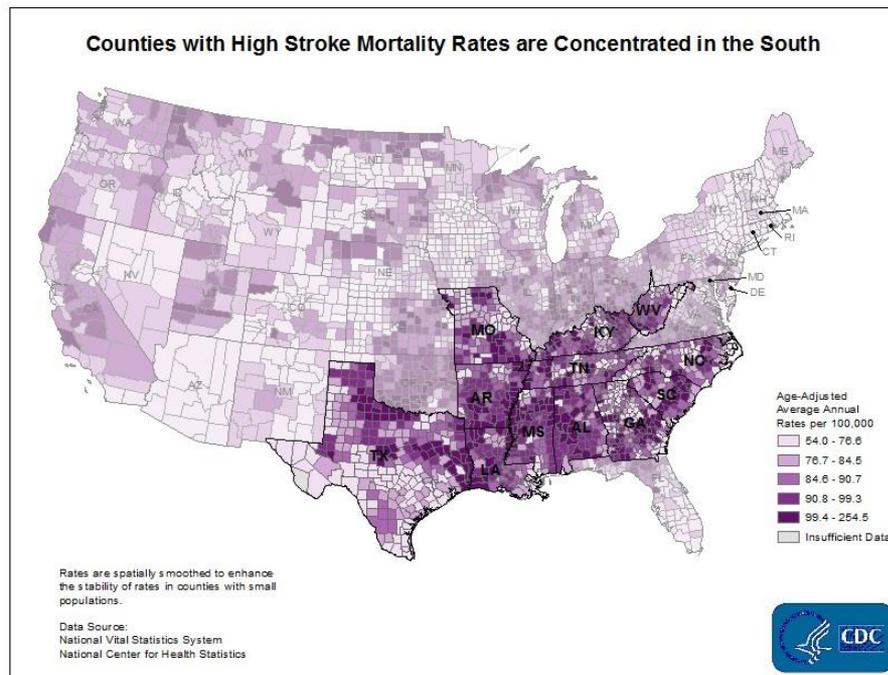
***Not a cure!*** May reflect response to treatment of certain symptoms or variability of the measure



[Bedlack et al., Neurology, 2016]

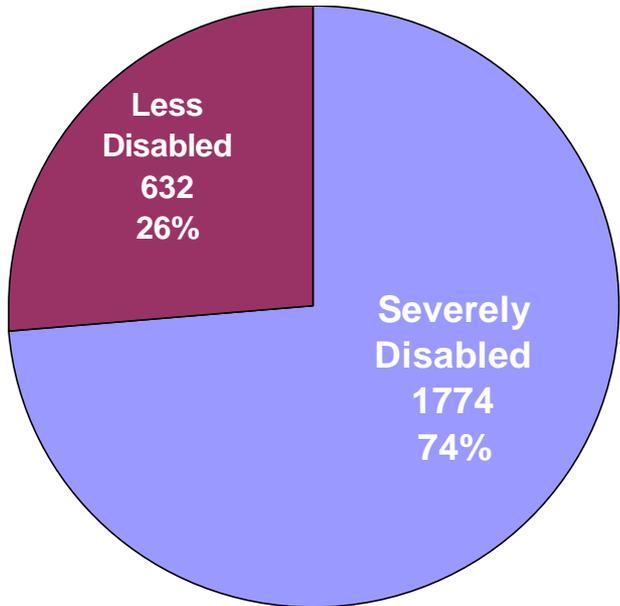
# Stroke

- About 800,000 new strokes/year
- Prevalence of about 3% of US population



# The General Rule is that Stroke Victims Recover Function over Weeks to Months

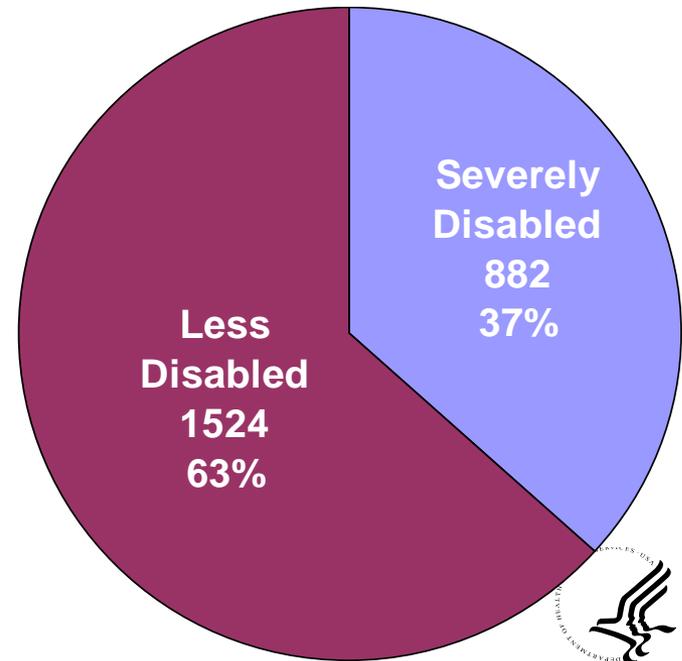
Severely Disabled Strokes – defined by FIM score < 77



On admission to Spaulding Rehab, almost three-quarters of strokes were severely disabled

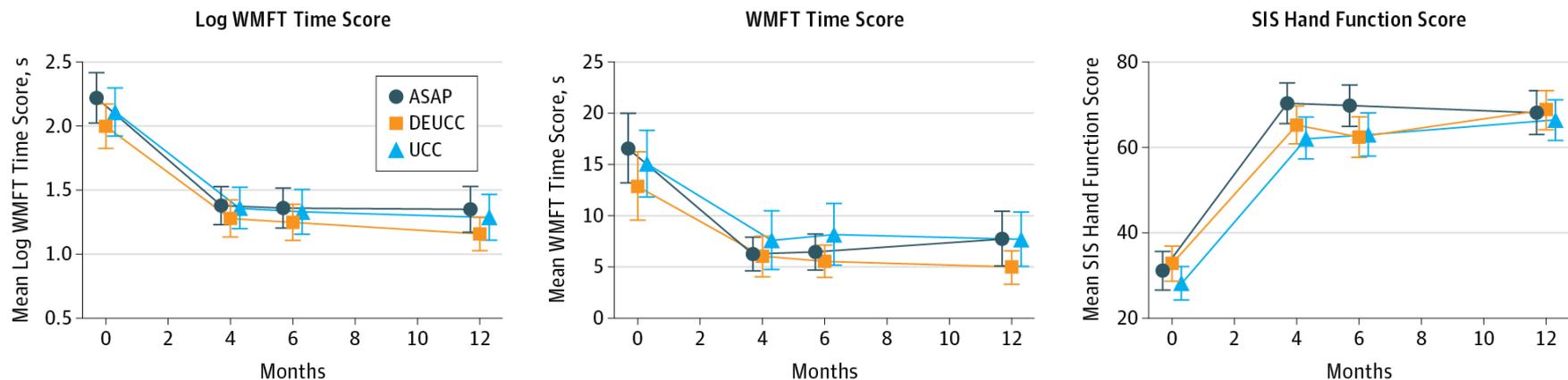
On discharge from Rehab, only about a third remained severely disabled

Age is a major determinant of the degree of recovery after stroke.



# Motor Stroke Recovery

From: **Effect of a Task-Oriented Rehabilitation Program on Upper Extremity Recovery Following Motor Stroke: The ICARE Randomized Clinical Trial**

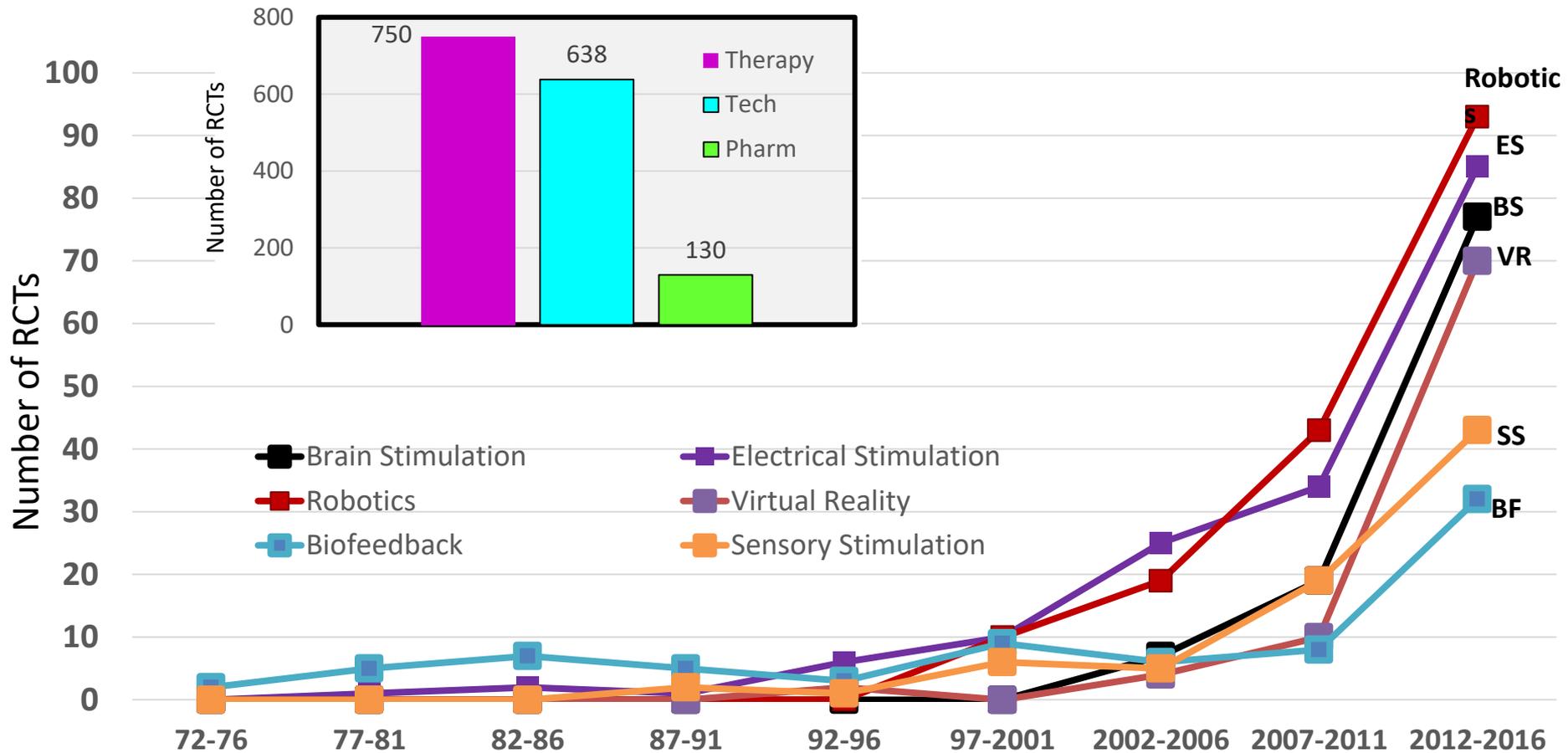


## Figure Legend:

Longitudinal Changes in Unadjusted Imputed Mean Scores Across Months for the Primary and Secondary Outcomes Primary outcome, log-transformed Wolf Motor Function Test (WMFT) time score (left) and secondary outcomes, WMFT time score (center) and patient-reported Stroke Impact Scale (SIS) hand function subscale score (right). N=119 in the Accelerated Skill Acquisition Program (ASAP) group; n = 120 in the dose-equivalent usual and customary care (DEUCC) group; and n = 122 in the monitoring-only usual and customary care (UCC) group. Timing of each assessment after randomization was as follows: 0 months = baseline; 4 months = end of therapy; 6 months = follow-up; and 12 months = end of study. Statistical analyses were performed on the imputed intention-to-treat data set. Error bars represent 95% CIs.

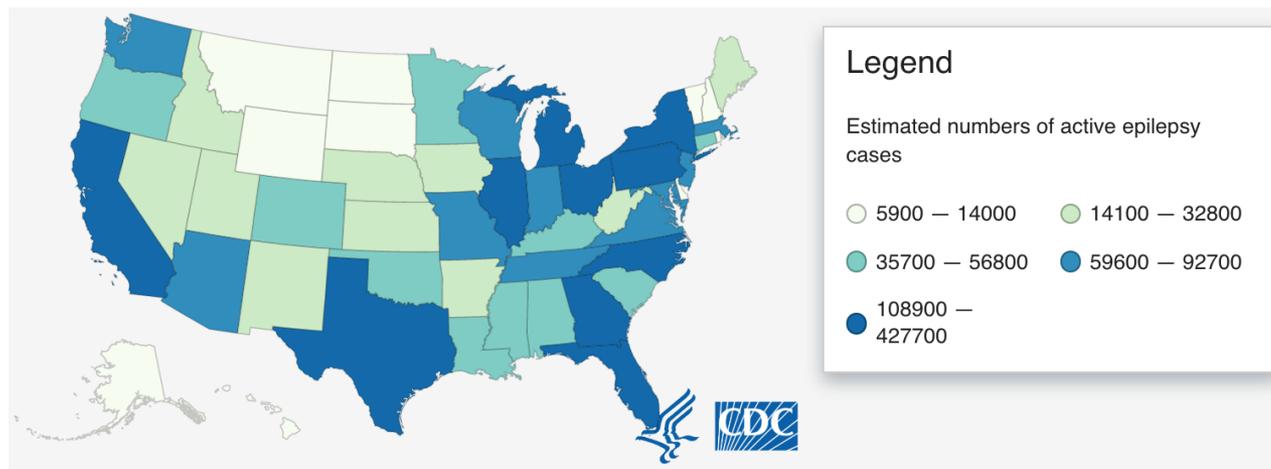
JAMA. 2016;315(6):571-581. doi:10.1001/jama.2016.0276

# Stroke Rehab Motor RCTs: Trends in Technology Interventions



# Pediatric Epilepsy

- About 500,000 in US have active epilepsy and is the most frequent chronic neurologic condition
- Incidence rate: 144 per 100 000 person-years in the first year of life and 58 per 100 000 for ages 1 to 10 years



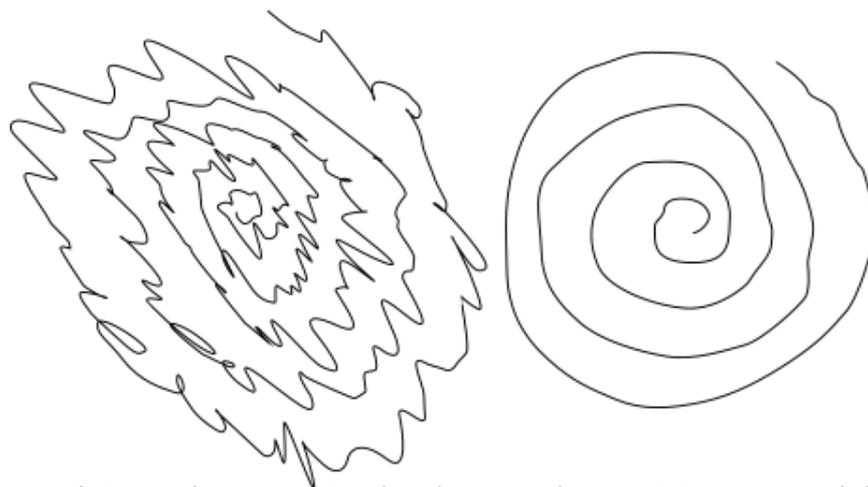
# Example: Pediatric Epilepsy

## Getting an accurate diagnosis is critical

- Some pediatric syndromes have natural history of recovery before adulthood (e.g., childhood absence, Rolandic)
- Others do not (e.g., juvenile myoclonic – there are some more malignant forms)
- For all ages, even after successfully controlling seizures with medicine, devices, or surgery, people with epilepsy might still not be able to be gainfully employed because of adverse reactions from medicines, post-op effects (e.g., transient aphasia or worse – like a big stroke), ongoing comorbidities (e.g., anxiety, depression), or other reasons
- Key is ongoing reassessments

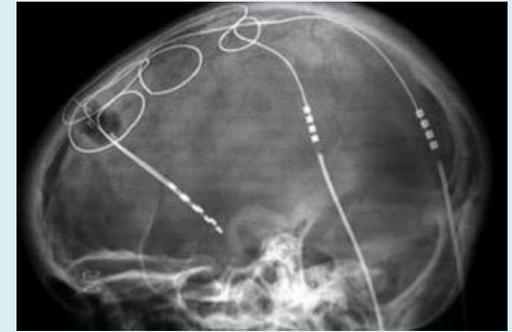
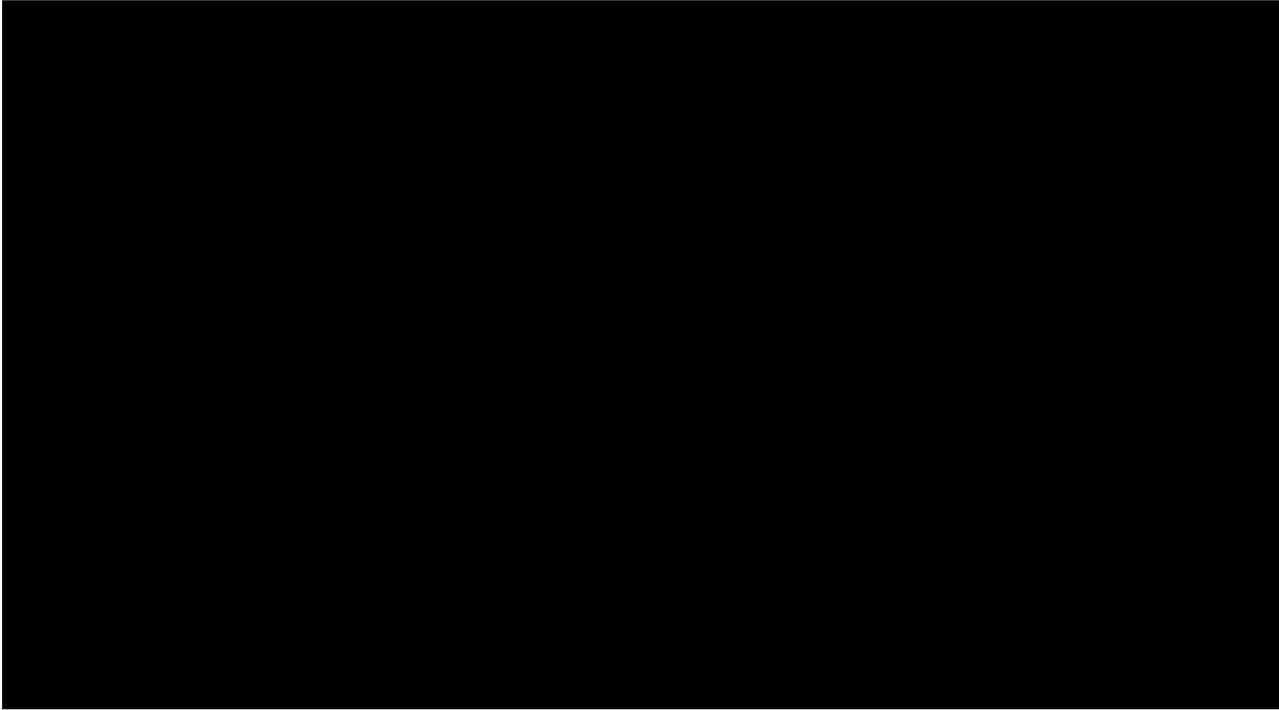
## Essential Tremor

- Approximately 4% of adults 40 years of age and older are affected by ET
- Annual incidence of ~24 per 100,000



Archimedean spirals drawn by a 22-year-old male suffering with unilateral essential tremor.

# BRAIN Researchers Improve Treatment Options for Chronic Disorders



*Researchers are improving on FDA-approved Deep Brain Stimulation to incorporate feedback from brain to automatically adjust brain stimulation from pacemaker*

## Other videos

<http://www.youtube.com/watch?v=xejclvw3wsk>  
<http://www.youtube.com/watch?v=IOHtUzW02cg>

# NINDS

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