National Disability Forum

“What Impairments Have a Likelihood to Improve?”

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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-Squard Syndrome
CADASIL
Cerebellar degeneration
Cerebellar Hypoplasia
Cerebral Cavernous Malformation
Cerebral Palsy
Charcot-Marie-Tooth Disease
Chiari Malformation
Chorea-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
LLyme 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
Tubercous Sclerosis
Von-Hippel-Lindau Disease
Wernicke-Korsakoff Syndrome
West Syndrome
William’s Syndrome
Wilson Disease
Wolman’s Disease
Zellweger Syndrome

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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

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**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

- 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,*
ALS

Amyotrophic Lateral Sclerosis

– 2 new cases per 100,000 people per year

– About 16,000 living with ALS
The phenotype of ALS is highly variable.
Can ALS scores improve?

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

Patterns of ALSFRS-R decline

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

[Kuffner et al., Nat Biotech, 2015]

[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.
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.

Stroke Rehab Motor RCTs: Trends in Technology Interventions

In the graph, the number of RCTs is plotted against time (1972-2016) for different technology interventions:

- **Brain Stimulation**
- **Electrical Stimulation**
- **Robotics**
- **Virtual Reality**
- **Biofeedback**
- **Sensory Stimulation**

The graph shows a significant increase in the number of RCTs for each category over time, particularly noticeable in the 2000s and 2010s.

The inset chart provides a breakdown of the number of RCTs for each technology category over distinct time periods:

- **72-76**: 750 Therapy, 638 Tech, 130 Pharm
- **77-81**: 72-76 Therapy, 638 Tech, 130 Pharm
- **82-86**: 72-76 Therapy, 638 Tech, 130 Pharm
- **87-91**: 72-76 Therapy, 638 Tech, 130 Pharm
- **92-96**: 72-76 Therapy, 638 Tech, 130 Pharm
- **97-2001**: 72-76 Therapy, 638 Tech, 130 Pharm
- **2002-2006**: 72-76 Therapy, 638 Tech, 130 Pharm
- **2007-2011**: 72-76 Therapy, 638 Tech, 130 Pharm
- **2012-2016**: 72-76 Therapy, 638 Tech, 130 Pharm

The data highlights a trend of increasing RCTs in technology interventions over the years, with a notable rise in recent decades.
Pediatric Epilepsy

- About 500,000 in US have active epilepsy and is the most frequent chronic neurologic condition

- Incidence rate: \(144 \text{ per } 100,000\) person-years in the first year of life and \(58 \text{ per } 100,000\) for ages 1 to 10 years
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.
Researchers are improving on FDA-approved Deep Brain Stimulation to incorporate feedback from brain to automatically adjust brain stimulation from pacemaker.
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