NINDS Contributions to Approved Therapies

NINDS invests in and conducts research across the spectrum of neuroscience and neurology research, from basic studies on fundamental biological mechanisms, to clinical trials to test new treatments in patients. Here, we describe the path leading to the development and approval of one therapy for a neurological disorder, and we highlight contributions enabled by NINDS and NIH support.

Optimizing Endovascular Therapy for Ischemic Stroke

Overview

Nearly 800,000 people in the U.S. have a stroke each year. Most of these strokes are ischemic strokes, caused when a clot in a brain artery blocks blood flow, leading to permanent impairment if blood flow is not restored promptly. The clot-busting drug tPA (tissue plasminogen activator) was the first treatment approved for acute ischemic stroke and is an important front-line therapy. However, intravenous (IV) tPA must be given within four and a half hours after stroke onset, and it has limited effectiveness in patients with strokes due to clots in large brain arteries, which account for over a third of ischemic strokes and a disproportionately larger fraction of stroke-related death and disability.

With major contributions from NINDS-supported research, a procedure called endovascular thrombectomy offers another way to restore blood flow and save at-risk brain tissue in people with large artery strokes. In a typical version of the procedure, a device called a stent-retriever is guided through a catheter to the site of a clot in a brain artery. There, the operator opens the stent and retrieves the clot into the catheter to restore blood flow. Several endovascular thrombectomy devices are cleared by the FDA for removing clots from the brain, and clinical guidelines provide criteria for their use in carefully selected patients up to 24 hours after stroke symptom onset.

Endovascular thrombectomy has developed alongside advances in brain imaging methods that help physicians determine which patients are most likely to benefit from this treatment. NINDS-supported research was essential to understanding stroke injury progression, developing the first device approved for endovascular thrombectomy, applying novel imaging methods to acute stroke evaluation, and defining brain imaging profiles that, together with time since symptom onset, guide treatment decisions for acute stroke.

Urgent medical attention remains imperative for stroke, as increasing numbers of brain cells die for every minute of blocked blood flow. However, endovascular therapy with sophisticated brain imaging enables good outcomes for more stroke patients and at later times after stroke onset than was once thought possible.

Learn more at: https://www.ninds.nih.gov/About-NINDS/Impact/NINDS-Contributions-Approved-Therapies
Studies of brain injury progression after stroke in animal models show that the core lesion is initially surrounded by a penumbra of vulnerable tissue with reduced blood flow. Magnetic resonance angiography and computed tomographic angiography are developed and applied to acute stroke diagnosis, offering faster, non-invasive alternatives to conventional angiography.

FDA approves IV tPA as the first treatment for acute stroke, based on a clinical trial led by NINDS. Stroke is recognized as a treatable emergency, transforming systems of care and paving the way for additional therapies.

Researchers define a brain imaging profile in stroke patients called mismatch, in which the area of damaged tissue is smaller than the area at risk. They predict that patients with this profile will benefit most from treatment to restore blood flow.

Diffusion-weighted imaging (DWI) detects early stroke lesions in in experimental animals. DWI is used in stroke patients and combined with perfusion imaging to rapidly detect brain tissue already damaged by stroke, as well as surrounding areas with low blood flow. Studies show variable injury expansion after stroke.

A second NINDS-funded study, DEFUSE 2, finds that patients with the mismatch profile had better outcomes after endovascular therapy than patients without mismatch. DEFUSE 2 used software developed by the investigators for fast, automated analysis of brain imaging scans.

Industry-sponsored clinical trials show a benefit for endovascular therapy over medical therapy alone in stroke patients with LAO.

The Diffusion and Perfusion Imaging Evaluation For Understanding Stroke Evolution (DEFUSE) study finds patients with the target mismatch profile had the best rates of good clinical outcomes after IV tPA treatment. The Mechanical Embolus Removal in Cerebral Ischemia (MERCI) is the first FDA-approved endovascular thrombectomy device for use in stroke patients who are ineligible for or fail to benefit from IV tPA. Additional improved devices follow.

Two clinical trials, including DEFUSE 3, support the use of endovascular thrombectomy for large artery stroke as late as 16-24 hours after onset, when combined with MRI or CT perfusion imaging for patient selection.

The CT Perfusion to Predict Response to Recanalization in Ischemic Stroke Project (CRISP) uses CT imaging to identify patients with the target mismatch profile and finds good clinical outcomes with endovascular treatment up to 18 hours after symptom onset.

A group of clinical trials fails to show better outcomes for endovascular therapy compared to standard medical therapy. These trials did not require imaging evidence of large artery occlusion (LAO) or mismatch.

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