Science Advancement & Outreach
A DIVISION OF PETA

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Request for Information (RFI): Extending the Response Date for Inviting Feedback on the Proposed NIH Research Plan on Rehabilitation Scientific Themes FY26-FY30 (NOT-HD-25-029)

Submitted by email to Rehabilitation1@mail.nih.gov on August 28, 2025

Overall, the proposed themes and objectives for NIH's Research Plan on Rehabilitation FY26-FY30 appropriately capture the priorities and needs of the rehabilitation research field and its stakeholders. However, it is critical that the "-omics, cellular, and systems-level research" supported under Theme 1 prioritizes non-animal methods. Rehabilitation research must be grounded in human-relevant approaches, as studies of disabling conditions requiring rehabilitation, including stroke, spinal cord injury, and Parkinson's disease, cannot be faithfully modeled in animals.

For stroke experiments that use animals, key species differences, such as brain composition,[1] blood–brain barrier function,[2,3] and inflammatory responses,[4,5,6] significantly limit translatability and hinder the ability to predict individual recovery in humans. Moreover, variability across animal strains introduces confounding factors—for instance, different rat strains have been shown to respond differently to post-stroke treatments. The frequent use of young animals, despite stroke primarily affecting elderly populations, adds another layer of mismatch.[7]

A major challenge in stroke rehabilitation experiments that use animals is subject motivation. For instance, constraint-induced movement therapy (CIMT), a widely used rehabilitation model, often causes distress in animals, leading to reduced engagement with the impaired limb and compromising the model's validity.[8]

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[1] Krafft PR, Bailey EL, Lekic T, et al. Etiology of stroke and choice of models. *Int J Stroke*. 2012;7(5):398-406. doi:10.1111/j.1747-4949.2012.00838.x
[2] Chen ZQ, Mou RT, Feng DX, Wang Z, Chen G. The role of nitric oxide in stroke. *Med Gas Res*. 2017;7(3):194-203. doi:10.4103/2045-9912.215750
[3] Syvänen S, Lindhe O, Palner M, et al. Species differences in blood-brain barrier transport of three positron emission tomography radioligands with emphasis on P-glycoprotein transport. *Drug Metab Dispos*. 2009;37(3):635-643. doi:10.1124/dmd.108.024745
[4] Lin S, Lin Y, Nery JR, et al. Comparison of the transcriptional landscapes between human and mouse tissues. *Proc Natl Acad Sci U S A*. 2014;111(48):17224-17229. doi:10.1073/pnas.1413624111
[5] Johnson S, Dwivedi A, Mirza M, McCarthy R, Gilvarry M. A Review of the Advancements in the *in-vitro* Modelling of Acute Ischemic Stroke and Its Treatment. *Front Med Technol*. 2022;4:879074. doi:10.3389/fmedt.2022.879074
[6] Roth S, Liesz A. Stroke research at the crossroads - where are we heading?. *Swiss Med Wkly*. 2016;146:w14329. doi:10.4414/smw.2016.14329
[7] Livingston-Thomas JM, Tasker RA. Animal models of post-ischemic forced use rehabilitation: methods, considerations, and limitations. *Exp Transl Stroke Med*. 2013;5(1):2. doi:10.1186/2040-7378-5-2
[8] *Ibid.*

The “early-stage technology development for rehabilitation” supported under Theme 3 should also be conducted exclusively with non-animal models. Rehabilitation research after cartilage defect repair illustrates why: rodents and goats, two of the most used animals in these experiments, differ significantly from humans in cartilage thickness, growth plate maturity, gait mechanics, and joint biomechanics, making outcomes untranslatable.[9]

Finally, under Theme 5, training programs for researchers and clinician scientists must be centered on cutting-edge non-animal approaches. As these methods expand and mature, robust training initiatives are needed to build workforce expertise and confidence in their use.

In conclusion, future NIH rehabilitation research should shift decisively toward non-animal, human-centered methods to maximize translatability, overcome current limitations, and improve rehabilitation outcomes for patients.

[9] Moran CJ, Ramesh A, Brama PA, O'Byrne JM, O'Brien FJ, Levingstone TJ. The benefits and limitations of animal models for translational research in cartilage repair. *J Exp Orthop*. 2016;3(1):1. doi:10.1186/s40634-015-0037-x