

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2. Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Randolph S. Marshall		POSITION TITLE Professor of Neurology	
eRA COMMONS USER NAME (credential, e.g., agency login) MARSHALLR			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
Harvard College, Cambridge, MA	B.A.	1982	Biology
Univ. California, Berkeley, CA	M.S.	1986	Sociolinguistics
Univ. California, San Francisco, CA	M.D.	1988	Medicine
Cornell New York Hospital, New York, NY	Internship	1989	Internal Medicine
Columbia Presbyterian Medical Center, NY, NY	Residency	1992	Neurology
Columbia Presbyterian Medical Center, NY, NY	Fellowship	1994	Cerebrovascular

A. Personal Statement

My research program: PI on a study of Blood Flow and Cognition in patents with asymptomatic carotid artery stenosis, PI of a multi-center clinical trial investigating hemodynamic variables affecting cognition in large vessel carotid artery disease. Principles being studies in these grants are directly relevant to the current work being proposed. I am also PI of a Regional Coordinating Center for NINDS-sponsored StrokeNet, for which I serve as Co-Chair of the Education and Training Core at the national level. As co-director of the Cerebral Localization Lab, established in 1994, my research goals are centered on the investigation of brain function in the acute and chronic phase and the underlying physiology that determines brain injury and recovery. Much of the work I have done has involved brain imaging, including new MRI techniques, fMRI and the transcranial Doppler-based hemodynamic studies. Correlations between cerebrovascular physiology, hemodynamics and behavior are sought with the collaboration of investigators in neuroanesthesiology, neurosurgery and interventional neuroradiology.

B. Positions and Honors

Professional Positions:

1994-2001	Assistant Professor of Neurology, Columbia University College of Physicians and Surgeons, Department of Neurology, NY.
1992-2001	Clinical Assistant Neurologist, New York Presbyterian Hospital
2001-2007	Associate Professor of Clinical Neurology, Columbia University College of Physicians and Surgeons, Department of Neurology, NY
2001-2007	Clinical Associate Neurologist, New York Presbyterian Hospital
2007-2008	Acting Director, Stroke Division, Department of Neurology
2007-present	Professor of Neurology, Columbia University College of Physicians and Surgeons, Department of Neurology, NY
2007-present	Clinical Neurologist, New York Presbyterian Hospital
2008-present	Chief, Stroke Division, Department of Neurology

Other Experience and Professional Memberships:

1990-	American Academy of Neurology (Science Committee Vice-Chair, 2017-present)
1993-	American Heart Association, NY Chapter.
1999-	American Heart Association Stroke Council.
1997-	American Medical Association, New York.
2003-	American Neurological Association

1994- Diplomat, American Board of Psychiatry and Neurology
2008- Diplomat, ABPN, Vascular Neurology

Honors and Awards:

1995-2000 Clinical Investigator Development Award (NINDS K08)
1996 Clinical Trials Pilot Study Award, Columbia University, 1996.
1999-2004 Independent Scientist Award (NINDS K02),
2013 C Miller Fisher Lectureship, MGH
2018 A.L. Sahs Lectureship, University of Iowa
2019 C Miller Fisher Neuroscience Visionary Award (American Heart Association)

C. Contributions to Science

1. Discovery of the role of cerebral hemodynamics in brain function.

Beginning with a seminal paper in 2001 using a natural experimental model of human, awake carotid artery balloon test occlusions, we established cerebral blood flow thresholds for sustained attention at 37 cc/110g/min for reversible deficit, and 27cc/100g/min for irreversible impairment (until the condition of the balloon test occlusion was removed. Thresholds had only been established in animal models to that point. Our discovery led to 2 major NIH grants to study this phenomenon, and several publications which explored the relationship between cerebral blood flow and cognition. Other labs internationally have pursued this question as cited below. One phase-3 multi-center clinical trial on this topic has been completed (RECON), and another (CREST-H) is now funded. The clinical implications of a “reversible dementia” are far-reaching.

1. **Marshall RS**, Lazar RM, Pile-Spellman J, Young WL, Duong DH, Joshi S, Ostapovich N. Recovery of brain function during induced cerebral hypoperfusion. *Brain* 2001;124: 1208-1217.
2. **Marshall RS**, Krakauer JW, Matejovsky T, Zarahn E, Barnes A, Lazar RM, Hirsch J, Hemodynamic Impairment as a stimulus for functional brain reorganization, *J Cereb Blood Flow Metab* 2006;26:1256-62.
3. **Marshall RS**, Festa JR, Cheung YK, Chen R, Pavol MA, Derdeyn CP, Clarke WR, Videen TO, Grubb RL, Adams HP, Powers WJ, Lazar RM. Cerebral hemodynamics and Cognitive Impairment; baseline data from the RECON trial. *Neurology* 2012 Jan 24;78(4):250-5. Epub 2012 Jan 11 PMID: 22238418
4. **Marshall RS, Asllani I**, Pavol MA, Cheung YK, Lazar RM. Altered cerebral hemodynamics and cortical thinning in asymptomatic carotid artery stenosis. *PLoS One*. 2017 Dec 14;12(12):e0189727. PMID: 29240808

2. Discovery of the principle of “proportional recovery” after stroke.

Arising from an NINDS grant for which I was PI, the novel principle of “proportional recovery” was initially published in 2008 by Prabhakaran S et al. The finding was extended to recovery of language function in the paper by Lazar et al, confirmed with functional imaging in the paper by Zarahn et al. The finding has now been replicated in several labs, and is emerging as an important biological benchmark of potential recovery that may be used in randomized clinical trials.

1. Prabhakaran S, Zarahn E, Riley C, Speizer A, Chong J, Lazar RM, **Marshall RS**, Krakauer J. Inter-individual variability in the capacity to recover motor function after ischemic stroke. *Neurorehabil Neural Repair* 2008 Jan-Feb;22(1):64-71.
2. Lazar RM, Minzer B, Antoniello D, Festa J, Krakauer JW, **Marshall RS**. Improvement in aphasia scores after stroke is well predicted by initial severity, *Stroke* 2010, 2010 Jul;41(7):1485-8. Epub 2010 Jun 10.
3. Zarahn E, Alon L, Ryan SL, Lazar RM, Vry MS, Weiller C, **Marshall RS**, Krakauer JW. Prediction of Motor Recovery Using Initial Impairment and fMRI 48 h Poststroke. *Cereb Cortex*. 2011 Dec;21(12):2712-21. Epub 2011 Apr 28. PMID: 21527788.
4. Byblow WD, Stinear CM, Barber PA, Petoe MA, Ackerley SJ. Proportional recovery after stroke depends on corticomotor integrity. *Ann Neurol*. 2015 Jul 7. doi: 10.1002/ana.24472. [Epub ahead of print], PMID: 26150318

3. Discovery of the contribution of alternative pathways in stroke recovery.

Until the year 2000 there was little understanding of the role of non-infarcted brain regions in recovery of motor function after stroke. Our publication in *Stroke* in 2000 was one of the seminal papers in the field, leading to many follow up studies, both in our lab and others, furthering of knowledge about neuroplasticity. Our original paper was cited by Thompson's Essential Scientific Indicators in 2006 as one of the most frequently referenced articles in its field.** That paper is cited below. The finding was confirmed by an analogous study in an animal model followed by a White Paper published from the First International Workshop on Neuroimaging and Stroke Recovery that I co-organized in New York with JC Baron, SC Cramer, and BH Dobkin. A subsequent manuscript was chosen in 2010 by Faculty of 1,000 Medicine as a major contribution in the field***. A large and burgeoning literature on functional neuroplasticity that accompanies stroke recovery followed.

1. ****Marshall RS**, Perera GM, Lazar RM, Krakauer JW, Constantine RC, DeLaPaz RL. Evolution of cortical activation during recovery from corticospinal tract infarction. *Stroke* 2000;31:656-661.
2. Dijkhuizen RM1, Ren J, Mandeville JB, Wu O, Ozdag FM, Moskowitz MA, Rosen BR, Finklestein SP. Functional magnetic resonance imaging of reorganization in rat brain after stroke. *Proc Natl Acad Sci U S A*. 2001 Oct 23;98(22):12766-71. Epub 2001 Oct 16.
3. Baron JC, Cohen LG, Cramer SC, Dobkin BH, Johansen-Berg H, Loubinoux I, ***Marshall RS**, Ward NS. First International Workshop in Neuroimaging and Stroke Recovery. Neuroimaging in Stroke Recovery: A Position Paper from the First International Workshop on Neuroimaging and Stroke Recovery. *Cerebrvasc Dis* 2004;18:260-67.
4. *****Marshall RS**, Zarahn E, Alon L, Minzer B, Lazar RM, Krakauer JW. Early imaging correlates of subsequent motor recovery after stroke. *Ann Neurol* 2009, 65(5):596-602.

4. Contributions to clinical trials and clinical management in Stroke.

Leadership roles in the NINDS SPOTRIAS network and now the NIH StrokeNet consortium have generated contributions to the advance in clinical management. The recently changing landscape of acute stroke management has required thought leadership to put clinical trial advances in context.

1. Willey JZ, Ortega-Gutierrez S, Petersen N; Khatri P, Ford AK, Rost NS, Ali LK, Gonzales NR, Merino JG, Meyer BC, **Marshall RS**. Impact of acute ischemic stroke treatment in patients over age 80: the SPOTRIAS consortium experience. *Stroke* 2012. 43(9):2369-75. doi: 10.1161/STROKEAHA.112.660993. Epub 2012 Jul 12. PMID: 22798327
2. Kidwell CS, Jahan R, Gornbein J, Alger JR, Nenov V, Ajani Z, Feng L, Meyer BC, Olson S, Schwamm LH, Yoo AJ, **Marshall RS**, Meyers PM, Yavagal DR, Wintermark M, Guzy J, Starkman S, Saver JL, for the MR RESCUE Investigators. A trial of imaging selection and endovascular treatment for ischemic stroke. *NEJM* 2013 Mar 7;368(10):914-23. doi: 10.1056/NEJMoa1212793
3. **Marshall RS**, Festa JR, Cheung YK, Pavol MA, Derdeyn CP, Clarke WR, Videen TO, Grubb RL, Slane K, Powers WJ, Lazar RM; RECON Investigators. Randomized Evaluation of Carotid Occlusion and Neurocognition (RECON) trial: Main results. *Neurology* 2014 4;82:744-51. PMID: 24477109
4. Rostanski SK, **Marshall RS**, Precision Medicine for Ischemic Stroke. *JAMA Neurol*. 2016 May 2. doi: 10.1001/jamaneurol.2016.0087. [Epub ahead of print] No abstract available. PMID: 27135837

Complete list of my published work in My Bibliography:

<http://www.ncbi.nlm.nih.gov/myncbi/collections/bibliography/48101148/>

D. Research Support

Ongoing Research Support

1R01NS080168

Brott (PI)

4/1/2014 – 3/31/2021

NINDS: Carotid Revascularization and Medical management for Asymptomatic Carotid Stenosis (CREST2). Multicenter Phase 3 randomized clinical trial to determine whether carotid stenting or carotid endarterectomy is better than medical management alone in patients with asymptomatic high grade carotid stenosis.
Role: Site PI

1R01NS097876 (Marshall) 4/1/2016 – 3/31/2021
NINDS: Carotid Revascularization and Medical Management for Asymptomatic Carotid stenosis-Hemodynamics (CREST-H)
This is an ancillary physiological cohort study on the CREST-2 study to determine whether a subset of patients with asymptomatic carotid artery stenosis who have flow failure will benefit from revascularization to improve cognition.
Role: MPI

1U01 NS086872-01 Broderick (PI) 05/01/18 – 04/30/23
NINDS
NIH StrokeNet National Clinical Coordinating Center
Stroke Trials Network will be managed centrally for the purpose of enrolling stroke patients in Phase II clinical trials of acute stroke treatment, prevention and recovery, and to provide a training environment for next generation of Stroke Physician Scientists.
Role: Co-I

1U24 NS107237-01 Marshall (Co-PI) 05/01/18 – 04/30/23
NINDS Stroke Trials Network of Columbia and Cornell (NYCCSTN)
Regional Stroke Trials Network hub for the purpose of enrolling stroke patients in Phase II clinical trials of acute stroke treatment, prevention and recovery, and to provide a training environment for next generation of Stroke Physician Scientists.
Role: PI

Completed Research Support (last 3 years)

1R01NS076277-01A1 (Marshall/Lazar, Co-PIs) 4/1/2012-3/31/2018
NINDS
Blood Flow and Cognition. Cross-sectional and longitudinal human physiology study to determine how blood flow regulation in the brain affects cognition in patients with asymptomatic high-grade carotid artery stenosis. ASL-MRI and transcranial Doppler used to correlate cerebral autoregulation with disease-specific measures of cognitive function.
Role: Co-PI

1U10 NS086728-01 Marshall (Co-PI) 05/01/13 – 04/30/18
NINDS Stroke Trials Network of Columbia and Cornell (NYCCSTN)
Regional Stroke Trials Network hub for the purpose of enrolling stroke patients in Phase II clinical trials of acute stroke treatment, prevention and recovery, and to provide a training environment for next generation of Stroke Physician Scientists.
Role: PI

R21NS096972 (Lazar) TAVR and Cognition 10/1/16 -- 09/30/18
This prospective observational outcomes study will examine the relationship between global cerebral hypoperfusion and cognition in patients before and after implantation of a transcatheter aortic valve replacement (TAVR).
Role: Co-I

NIA R56AG034189 Brickman (PI) 09/01/2016 – 08/31/2017
White Matter Hyperintensities in Aging and Dementia
This project will examine the degree to which small vessel cerebrovascular contributes independently or interactively to the development and clinical expression of AD across racial and ethnic groups. It will provide novel mechanistic insight into the disease and help identify new targets for intervention.

Program Director/Principal Investigator (Last, First, Middle):

Role: Co-I