OMB No. 0925-0001 and 0925-0002 (Rev. 10/15 Approved Through 10/31/2018)

BIOGRAPHICAL SKETCH

**DO NOT EXCEED FIVE PAGES**.

NAME: Robert Scott Fisher, MD, PhD

eRA COMMONS USER NAME (credential, e.g., agency login): Fisher991

POSITION TITLE: Maslah Saul MD Professor of Neurology

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)

| INSTITUTION AND LOCATION | DEGREE  (if applicable) | Completion Date  MM/YYYY | FIELD OF STUDY |
| --- | --- | --- | --- |
| California Institute of Technology | B.S. | 06/71 | Biology |
| Stanford University School of Medicine | Ph.D. | 06/76 | Neuroscience |
| Stanford University School of Medicine | M.D. | 06/77 | Medicine |
| California Institute of Technology | B.S. | 06/71 | Biology |

# A. Personal Statement

My skill set includes animal models of epilepsy, clinical epilepsy, EEG, development of devices to treat epilepsy and clinical trial design. I have designed and been national PI for pivotal brain stimulation trials to treat epilepsy (e.g., the SANTE anterior thalamus DBS trial and the pivotal trial for the Aspire SR Cyberonics heart rate-sensing vagus nerve stimulator. I direct a transcranial magnetic stimulation (TMS) laboratory at Stanford. I have worked with Dr. Lee on optogenetic circuitry in rat models of epilepsy and epilepsy circuitry. My role in the project will be related to EEG and clinical epilepsy networks.

Weitz A†, Fang Z†, Lee HJ†, Fisher RS†, Smith WC†, Choy M, Liu J, Lin P, Rosenberg M, Lee JH\*, Optogenetic fMRI reveals distinct, frequency-dependent networks recruited by dorsal and intermediate hippocampus stimulations, Neuroimage, 2015;107:229-241.

Liu J, Lee HJ, Weitz AJ, Fang Z, Lin P, Choy M, Fisher R, Pinskiy V, Tolpygo A, Mitra P, Schiff N, Lee JH. Frequency-selective control of cortical and subcortical networks by central thalamus. Elife. 2015 Dec 10;4. pii: e09215. doi: 10.7554/eLife.09215.

Fisher RS, Cross JH, French JA, Higurashi N, Hirsch E, Jansen FE, Lagae L, Moshe SL, Peltola J, Roulet Perez E, Scheffer IE, Zuberi SM. Operational classification of seizure types by the International League Against Epilepsy: Position Paper of the ILAE Commission for Classiﬁcation and Terminology. Epilepsia 2017; 58(4):522–530, 2017.

Fisher R, et al. Electrical stimulation of the anterior nucleus of thalamus for treatment of refractory epilepsy.

Epilepsia, 2010; 51:899–908.

# B. Positions and Honors

## Positions and Employment

Neurology Assistant Prof Johns Hopkins 07/83 ‑ 12/87

EEG Lab Acting Director Johns Hopkins 04/85 - 09/85

Neurology Associate Prof Johns Hopkins 12/87 - 12/91

Epilepsy Center Director Barrow Institute 01/92 - 10/00

Neurology Professor Clinical Univ of Arizona 01/96 - 10/00

Neurology Chairman Barrow Neuro Institute 10/98 - 10/00

Neurology Named Professor Stanford 10/00 - now

## Other Experience and Professional Memberships

NSF Traineeship, Caltech, with Dr. Roger Sperry; 1971; 1972 Medical Scientist Training Program Fellowship (NIH GM01922); 1982 President, American Society for Neurolo­gical Investigation; 1983 Fellow, Epilepsy Foundation of America; 1985 Klingenstein Fellowship in Neur­osciences; 1985 Member, Professional Advisory Board, Epilepsy Association of Maryland; 1986 Associate Editor of the journal Epilepsia; 1986 Chair NIH-NINCDS Committee to review anticonvulsants; 1987 Member Professional Advisory Board of Epilepsy Association of America; 1988 NINCDS Neurosciences Study Section A; Membership American Neurological Association; National Secretary, American Epilepsy Society; Chair Epilepsy Foundation Research Committee, Chair American Epilepsy Society Research Committee, Chairman, Neurology, Barrow Neurological Institute; President Epilepsy Society of Arizona; Past-President, American Epilepsy Society, Executive Committee of the Board, International League Against Epilepsy; International, Editor-in-Chief, Epilepsia, Endowed Professorship, Stanford. Editor-in-Chief, epilepsy.com.

## Honors

1967 Valedictorian, Nova High School; George Green Memorial Award: "outstanding research", Caltech.;; 1976 Hans Berger Award, American EEG Society; 1977 Roland P. Mackay Award, American Academy of Neurology; 1984 Frank Ford Award for Clinical Teaching, Johns Hopkins University; International League Against Epilepsy; International Ambassador for Epilepsy Award, Int. League Against Epilepsy, American Epilepsy Society Annual Service Award 2004, American Epilepsy Society Award for Best Clinical Research (annual for 2006, international); Castle Connolly, America Top Docs, 1996-2012, Neurology Departmental teaching award 2006. Gloor Award from the American Society of Clinical Neurophysiology (EEG Society annual research award).

# C. Contribution to Science

1. Deep brain stimulation for epilepsy. Electrical stimulation of the brain to treat refractory epilepsy was first described by Heath, Delgado and Cooper, but my work validated it as a new type of therapy and brought it into worldwide use ([Fisher 2013](file:///H:\_Docs\Biosketch%20Fisher%202-21-2016.docx#_ENREF_8)). Starting with animal studies ([Mirski and Fisher 1994](file:///H:\_Docs\Biosketch%20Fisher%202-21-2016.docx#_ENREF_16); [Mirski, Rossell et al. 1994](file:///H:\_Docs\Biosketch%20Fisher%202-21-2016.docx#_ENREF_17)), I showed that stimulation could reduce chemically and electrically-induced seizures. I performed pilot trials in patients, and then led a multicenter, randomized trial in patients ([Fisher, Salanova et al. 2010](file:///H:\_Docs\Biosketch%20Fisher%202-21-2016.docx#_ENREF_6)). As a consequence, deep brain stimulation at the anterior thalamus is now approved in 35 countries.

* Fisher, R., V. Salanova, et al. (2010). "Electrical stimulation of the anterior nucleus of thalamus for treatment of refractory epilepsy." Epilepsia 51(5): 899-908.
* Fisher, R. S. (2013). "Deep brain stimulation for epilepsy." Handb Clin Neurol 116C: 217-234.
* Mirski, M. A. and R. S. Fisher (1994). "Electrical stimulation of the mammillary nuclei increases seizure threshold to pentylenetetrazol in rats." Epilepsia 35(6): 1309-1316.
* Mirski, M. A., L. A. Rossell, et al. (1994). "Electrical-stimulation of thalamic anterior nucleus raises seizure threshold in an experimental-model of generalized epilepsy." Neurology 44(4): A235-A235.

2. Vagus nerve stimulation for epilepsy. I led the national trial of the latest generation vagus nerve stimulator, which stimulates at time of ictal tachycardia. The trial was successful, presented at a national meeting and a manuscript is being prepared for publication. I reviewed the rationale for this approach ([Eggleston, Olin et al. 2014](file:///H:\_Docs\Biosketch%20Fisher%202-21-2016.docx#_ENREF_5); [Fisher, Eggleston et al. 2015](file:///H:\_Docs\Biosketch%20Fisher%202-21-2016.docx#_ENREF_11)) and developed the Academy of Neurology Therapeutics and Technology assessment ([Fisher and Handforth 1999](file:///H:\_Docs\Biosketch%20Fisher%202-21-2016.docx#_ENREF_12)).

* Eggleston, K. S., B. D. Olin, et al. (2014). "Ictal tachycardia: The head-heart connection." Seizure-European Journal of Epilepsy 23(7): 496-505.
* Fisher, R. S., K. S. Eggleston, et al. (2015). "Vagus nerve stimulation magnet activation for seizures: a critical review." Acta Neurol Scand **131**(1): 1-8.
* Fisher, R. S. and A. Handforth (1999). "Reassessment: vagus nerve stimulation for epilepsy: a report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology." Neurology **53**(4): 666-669.
* Fisher RS, et al. Automatic vagus nerve stimulation triggered by ictal tachycardia: clinical outcomes and device performance-the U.S. E-37 trial. Neuromodulation 2016; 19: 188–195.

3. Definition and Classification of Epilepsy. The International League Against Epilepsy appointed me Chair of the Task Force to provide a formal definition of epilepsy and a second Task Force to update the classification of types of seizures. This resulted in two highly cited articles ([Fisher, Boas et al. 2005](file:///H:\_Docs\Biosketch%20Fisher%202-21-2016.docx#_ENREF_10); [Fisher, Acevedo et al. 2014](file:///H:\_Docs\Biosketch%20Fisher%202-21-2016.docx#_ENREF_9)). The most beneficial aspect of the re-definition is the possibility to “outgrow” epilepsy after being seizure-free for 10 years. I also led the re-classification of seizure types for the world.

* Fisher, R. S., W. V. Boas, et al. (2005). "Epileptic seizures and epilepsy: Definitions proposed by the International League against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE)." Epilepsia 46(4): 470-472.
* Fisher, R. S., C. Acevedo, et al. (2014). "ILAE official report: a practical clinical definition of epilepsy." Epilepsia 55(4): 475-482.
* Fisher RS, Cross JH, French JA, Higurashi N, Hirsch E, Jansen FE, Lagae L, Moshe SL, Peltola J, Roulet Perez E, Scheffer IE, Zuberi SM. Operational classification of seizure types by the International League Against Epilepsy: Position Paper of the ILAE Commission for Classiﬁcation and Terminology. Epilepsia 2017; 58(4):522–530, 2017.
* Fisher RS, Cross JH, D’Souza CD, French JA, Haut SR, Higurashi N, Hirsch E, Jansen FE, Lagae L, Moshe SL, Peltola J, Roulet Perez ER, Scheffer IE, Schulze-Bonhage A, Somerville E, Sperling M, ia Yacubian EM, Zuberi SM. Instruction manual for the ILAE 2017 operational classification of seizure types. Epilepsia, 58(4):531–542, 2017.
* Brodie MJ, Zuberi SM, Scheffer IE. The 2017 ILAE classification of seizure types and the epilepsies: what do people with epilepsy and their caregivers need to know? Epileptic Disord 2018; 20(2) 77-87.

4. Direct drug perfusion on a seizure focus. Working in rodent models of epilepsy, I was one of the first to show efficacy of perfusion of anti-seizure drugs directly onto a seizure focus. ([Eder, Jones et al. 1997](file:///H:\_Docs\Biosketch%20Fisher%202-21-2016.docx#_ENREF_3); [Eder, Stein et al. 1997](file:///H:\_Docs\Biosketch%20Fisher%202-21-2016.docx#_ENREF_4); [Stein, Eder et al. 2000](file:///H:\_Docs\Biosketch%20Fisher%202-21-2016.docx#_ENREF_18); [Anschel, Ortega et al. 2004](file:///H:\_Docs\Biosketch%20Fisher%202-21-2016.docx#_ENREF_1)). Planning for human clinical trials are now underway.

* Anschel, D. J., E. Ortega, et al. (2004). "Diazepam prophylaxis for bicuculline-induced seizures: a rat dose-response model." Neurosci Lett 356(1): 66-68.
* Drazkowski, J. F., R. S. Fisher, et al. (2003). "Seizure-related motor vehicle crashes in Arizona before and after reducing the driving restriction from 12 to 3 months." Mayo Clin Proc 78(7): 819-825.
* Eder, H. G., D. B. Jones, et al. (1997). "Local perfusion of diazepam attenuates interictal and ictal events in the bicuculline model of epilepsy in rats." Epilepsia 38(5): 516-521.
* Eder, H. G., A. Stein, et al. (1997). "Interictal and ictal activity in the rat cobalt/pilocarpine model of epilepsy decreased by local perfusion of diazepam." Epilepsy Res 29(1): 17-24.

5. Seizures and driving. I have published several studies and position papers on guidelines for driving in people with a history of epilepsy ([Fisher and Krumholz 1988](file:///H:\_Docs\Biosketch%20Fisher%202-21-2016.docx#_ENREF_13); [Krumholz, Fisher et al. 1991](file:///H:\_Docs\Biosketch%20Fisher%202-21-2016.docx#_ENREF_15); [Fisher, Parsonage et al. 1994](file:///H:\_Docs\Biosketch%20Fisher%202-21-2016.docx#_ENREF_14); [Fisher 1999](file:///H:\_Docs\Biosketch%20Fisher%202-21-2016.docx#_ENREF_7); [Drazkowski, Fisher et al. 2003](file:///H:\_Docs\Biosketch%20Fisher%202-21-2016.docx#_ENREF_2)). DMV regulations in Maryland and Arizona and the National Transportation Safety Administration rules were altered in part because of my research.

* Fisher, R. S. (1999). "Commercial driving and epilepsy in the United States." Epilepsia 40: 73-73.
* Fisher, R. S. and A. Krumholz (1988). "Driving and epilepsy." Md Med J 37(10): 795-798.
* Fisher, R. S., M. Parsonage, et al. (1994). "Epilepsy and driving: an international perspective. Joint Commission on Drivers' Licensing of the International Bureau for Epilepsy and the International League Against Epilepsy." Epilepsia 35(3): 675-684.
* Krumholz, A., R. S. Fisher, et al. (1991). "Driving and epilepsy. A review and reappraisal." JAMA 265(5): 622-626.

# <https://www.ncbi.nlm.nih.gov/sites/myncbi/1bAvAgsndiU5w/bibliography/52671530/public/?sort=date&direction=ascending.D>

# Additional Information: Research Support and/or Scholastic Performance

## Ongoing Research Support

Stimulation Anterior Nucleus of Thalamus for Epilepsy. Fisher (Multicenter Overall PI) 01/1/13 - 12/31/18

Medtronic. This study is a pivotal multicenter randomized trial of anterior nucleus of thalamus stimulation to treat refractory epilepsy. Role: Overall PI and designer of the trial

Treatment of the Seizure Focus Fisher (PI) 1/1/2013 – 12/31/2018

Source: James & Carrie Anderson Fund for Epilepsy Research, a Philanthropic Source related to Dr. Fisher’s Endowed Maslah Saul Chair. The major goals of this project are development of techniques, such as focal drug application and local brain stimulation to inhibit seizures in animal model systems, and eventually in humans.

Transcranial Magnetic Stimulation for Epilepsy, Fisher (PI), 9/1/2015 – 12/31/2018, funded by Steve Chen, co-inventor of YouTube. This grant will provide funding for the core of the current proposed project, with purchase of equipment and technician time.

## Completed Research Support

Study of Seizure Clustering Fisher (PI) 4/1/2014 – 3/31/2016

Source: Epilepsy Foundation. This will study the tendency of seizures to cluster by using a de-identified database of over 20,000 patients using an on-line epilepsy diary which I helped to develop.

A concentric EEG electrode for low-noise EEG recording. Fisher (co-PI) 7/1/2014 – 9/30/2017

NINDS (grant type SBIR). Phase II.