

BIOGRAPHICAL SKETCH

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NAME: CLIFFORD, DAVID

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

POSITION TITLE: Professor of Neurology and Medicine

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
Southwestern University, Georgetown, Texas	BA	05/1971	Chemistry and History
Washington University School of Medicine, Saint Louis, Missouri	MD	05/1975	Medicine
Barnes Hospital, Saint Louis, Missouri	OTH	06/1977	Residency in Medicine
Barnes Hospital, Saint Louis, Missouri	OTH	06/1980	Residency in Neurology
Washington University School of Medicine, Saint Louis, Missouri	OTH	06/1981	Fellowship in Neuropharmacology

A. Personal Statement

I am the Melba and Forest Seay Professor of Clinical Neuropharmacology in Neurology at Washington University in St. Louis. I have had education as a significant role in my career having led the neurology residency training program for a decade starting in the early 1990s. I continue to mentor students at all levels and junior faculty members. My primary career goal has been to improve therapeutics for neurological disorders, with a particular focus on neurological complications of HIV. I designed and led the Neurologic AIDS Research Consortium, an NIH funded national research group designed to develop improved therapy for neuroAIDS complications with an emphasis on HIV associated neurocognitive disorder. I have been the Principal Investigator of the AIDS Clinical Trials Unit at Washington University which is the premier international NIH funded AIDS therapeutic network, as well as being active investigator in the CHARTER study, a multicenter epidemiologic group studying neuroAIDS. I am also the Principal Investigator for the Washington University NeuroNEXT trial unit, one of 25 centers designed to accelerate Phase 2 clinical trials for neurological disorders. This is a setting in which many young faculty members will receive their first NIH supported translational research experience. In recent years I have turned attention to the problem of Alzheimer disease and its treatment. I currently participate as an investigator at the Knight Alzheimer Disease Research projects at Washington University, and am committed to the Dominantly Inherited Alzheimer Disease Trials Unit (DIAN-TU) serving as Medical Director for the ongoing prevention trial. I am delighted to share my experience and support the T-32 Training Grant in the Department of Neurology at Washington University in St. Louis.

1. Ances BM, Benzinger TL, Christensen JJ, Thomas J, Venkat R, Teshome M, Aldea P, Fagan AM, Holtzman DM, Morris JC, Clifford DB. 11C-PiB imaging of human immunodeficiency virus-associated neurocognitive disorder. Arch Neurol. 2012 Jan;69(1):72-7. PubMed PMID: [22232345](#); PubMed Central PMCID: [PMC3536500](#).
2. Clifford DB, Ances BM. HIV-associated neurocognitive disorder. Lancet Infect Dis. 2013 Nov;13(11):976-86. PubMed PMID: [24156898](#); PubMed Central PMCID: [PMC4108270](#).

3. Clifford DB, Nath A, Cinque P, Brew BJ, Zivadinov R, Gorelik L, Zhao Z, Duda P. A study of mefloquine treatment for progressive multifocal leukoencephalopathy: results and exploration of predictors of PML outcomes. *J Neurovirol.* 2013 Aug;19(4):351-8. PubMed PMID: [23733308](#); PubMed Central PMCID: [PMC3758507](#).
4. Clifford DB, De Luca A, Simpson DM, Arendt G, Giovannoni G, Nath A. Natalizumab-associated progressive multifocal leukoencephalopathy in patients with multiple sclerosis: lessons from 28 cases. *Lancet Neurol.* 2010 Apr;9(4):438-46. PubMed PMID: [20298967](#).

B. Positions and Honors

Positions and Employment

1975 - 1977	Intern and Assistant Resident in Medicine, Barnes Hospital, St Louis, MO
1977 - 1980	Assistant Resident in Neurology, Barnes Hospital, St Louis, MO
1980 - 1981	Postdoctoral Fellow in Neurology, Washington University School of Medicine, St Louis, MO
1980 - 1981	Research Instructor in Neurology, Washington University, St Louis, MO
1981 - 1982	Instructor in Neurology, Washington University, St Louis, MO
1982 - 1989	Assistant Professor in Neurology, Washington University, St Louis, MO
1989 - 1994	Associate Professor of Neurology, Washington University, St Louis, MO
1994 - 1999	Professor of Neurology, Washington University, St Louis, MO
1999 -	Melba and Forest Seay Professor of Clinical Neuropharmacology in Neurology, Washington University, St Louis, MO
2001 - 2003	Professor and Chairman of Neurology, Washington University, St Louis, MO
2005 -	Professor of Neurology and Medicine, Washington University, St Louis, MO

Other Experience and Professional Memberships

- Fellow, American Academy of Neurology
- Member, American Neurological Association

Honors

1971	Carl F and Gerty T Cori Prize in Biochemistry, Washington University
1975	Jacques J Bronfenbrenner Award, Washington University
1975	Alpha Omega Alpha, Washington University
2002	Board of Scientific Counselors, NIH, NINDS
2005	Commencement Speaker, Southwestern University
2009	Neville Grant Award for Clinical Excellence, Barnes Jewish Hospital
2010	Office of AIDS Research Advisory Council (ORAC), NIH, Office of AIDS Research
2014	Arnold P Gold Foundation Humanism in Medicine Award - Washington University, AAMC
2015	Samuel R Goldstein Distinguished Faculty Award in Medical Student Education, Washington University in St Louis

C. Contribution to Science

1. NeuroAIDS As a clinical neuropharmacologist, the largest part of my career has been focused on describing diagnosis and therapy for the neurologic disorders associated with HIV infection. This area of neurology emerged with the HIV epidemic early in my career, and I became a national leader in this work through participation in the AIDS Clinical Trials Group, an NIH funded trial network. Using that network, I established a separate grant from NINDS supporting neurological trials, most of them co-sponsored by the ACTG network. In that setting I organized a network of up to 20 sites participating in trials for diagnosis and management of HIV associated cognitive disorder, HIV associated painful peripheral neuropathy, HIV associated CNS lymphoma, cryptococcal meningitis, progressive multifocal leukoencephalopathy, toxoplasma encephalitis, neurosyphilis, and cytomegalovirus encephalitis. I would consider the

organization and refinement of therapies for these disorders to be one of the major career contributions I have had the opportunity to make.

- a. Clifford DB, Evans S, Yang Y, Acosta EP, Goodkin K, Tashima K, Simpson D, Dorfman D, Ribaud H, Gulick RM. Impact of efavirenz on neuropsychological performance and symptoms in HIV-infected individuals. *Ann Intern Med.* 2005 Nov 15;143(10):714-21. PubMed PMID: [16287792](#).
 - b. Heaton RK, Franklin DR, Ellis RJ, McCutchan JA, Letendre SL, Leblanc S, Corkran SH, Duarte NA, Clifford DB, Woods SP, Collier AC, Marra CM, Morgello S, Mindt MR, Taylor MJ, Marcotte TD, Atkinson JH, Wolfson T, Gelman BB, McArthur JC, Simpson DM, Abramson I, Gamst A, Fennema-Notestine C, Jernigan TL, Wong J, Grant I. HIV-associated neurocognitive disorders before and during the era of combination antiretroviral therapy: differences in rates, nature, and predictors. *J Neurovirol.* 2011 Feb;17(1):3-16. PubMed PMID: [21174240](#); PubMed Central PMCID: [PMC3032197](#).
 - c. Clifford DB, Ances BM. HIV-associated neurocognitive disorder. *Lancet Infect Dis.* 2013 Nov;13(11):976-86. PubMed PMID: [24156898](#); PubMed Central PMCID: [PMC4108270](#).
 - d. Clifford DB. Progressive multifocal leukoencephalopathy therapy. *J Neurovirol.* 2015 Dec;21(6):632-6. PubMed PMID: [25227934](#); PubMed Central PMCID: [PMC4363307](#).
2. Progressive Multifocal Leukoencephalopathy (PML) A rare polyoma viral disease became a prominent complication of AIDS patients resulting in the death of up to 5% of the untreated HIV patients in the early years of the HIV epidemic. This outbreak of a DNA virus brain disease gave the opportunity to learn about its biology, refine diagnosis, and investigate therapeutic approaches. My leadership of the Neurologic AIDS Research Consortium (NARC), an NIH funded neuroAIDS collaborative group that I developed through leadership of an NIH grant, organized two significant clinical trials for PML testing cytosine arabinoside and cidofovir. This experience with PML and the effort to treat it resulted in my participation in description and management of a second outbreak of PML that occurred as a result of use of natalizumab for treatment of multiple sclerosis. After the initial cases, I was one of three scientists appointed to an Independent Adjudication Committee to review and report the risk of this complication. Subsequently I had the opportunity to describe the unique features of natalizumab associated PML, as well as to lead an international trial of treatment with mefloquine. Through these roles I have had the opportunity to contribute to more accurate and less invasive diagnosis of PML, to help investigators optimize its management resulting in a large decrease in the mortality of this disease, and participate in risk assessment to help clinicians navigate recommendations related to PML and therapies that might cause it.
- a. Marra CM, Rajcic N, Barker DE, Cohen BA, Clifford D, Donovan Post MJ, Ruiz A, Bowen BC, Huang ML, Queen-Baker J, Andersen J, Kelly S, Shriver S. A pilot study of cidofovir for progressive multifocal leukoencephalopathy in AIDS. *AIDS.* 2002 Sep 6;16(13):1791-7. PubMed PMID: [12218391](#).
 - b. Yousry TA, Major EO, Ryschewitsch C, Fahle G, Fischer S, Hou J, Curfman B, Miszkil K, Mueller-Lenke N, Sanchez E, Barkhof F, Radue EW, Jäger HR, Clifford DB. Evaluation of patients treated with natalizumab for progressive multifocal leukoencephalopathy. *N Engl J Med.* 2006 Mar 2;354(9):924-33. PubMed PMID: [16510746](#); PubMed Central PMCID: [PMC1934511](#).
 - c. Clifford DB, De Luca A, Simpson DM, Arendt G, Giovannoni G, Nath A. Natalizumab-associated progressive multifocal leukoencephalopathy in patients with multiple sclerosis: lessons from 28 cases. *Lancet Neurol.* 2010 Apr;9(4):438-46. PubMed PMID: [20298967](#).
 - d. Clifford DB, Nath A, Cinque P, Brew BJ, Zivadinov R, Gorelik L, Zhao Z, Duda P. A study of mefloquine treatment for progressive multifocal leukoencephalopathy: results and exploration of predictors of PML outcomes. *J Neurovirol.* 2013 Aug;19(4):351-8. PubMed PMID: [23733308](#); PubMed Central PMCID: [PMC3758507](#).
3. Education has been a significant focus of my academic career. I have actively participated in medical education of medical students and resident physicians in particular. For a decade I was Director of the Neurology Residency Program for Washington University/Barnes Hospital in St. Louis. In this role I helped select and train more than 50 neurologists. The residency program in neurology was recognized as one of the larger programs and attracted highly talented students for training. I have also mentored resident physicians in writing projects helping them report interesting cases and learning the skills of research and medical writing. (selections below) Teaching medical students has also been a focus and my efforts have

been rewarded by a Distinguished Teacher award. In 2014 all four medical student classes voted me as the university representative for Humanism in Medicine Award. In addition to training and teaching in my own institution, I have developed an international teaching/learning program linking Washington University in St Louis with Ayder Hospital/Mekelle Medical School in northern Ethiopia. I visit Ethiopia annually providing a series of lectures for the medical school. Additionally I have helped organize teaching/learning rotations for Washington University trainees including medical students, as well as residents training in neurology, medicine, obstetrics/gynecology, pathology, emergency medicine and pediatrics. In 2015 I was recognized by Washington University with the Samuel R Goldstein Distinguished Faculty Leadership Award in Medical Student Education.

- a. Choi JY, Hightower GK, Wong JK, Heaton R, Woods S, Grant I, Marcotte TD, Ellis RJ, Letendre SL, Collier AC, Marra CM, Clifford DB, Gelman BB, McArthur JC, Morgello S, Simpson DM, McCutchan JA, Richman DD, Smith DM. Genetic features of cerebrospinal fluid-derived subtype B HIV-1 tat. *J Neurovirol.* 2012 Apr;18(2):81-90. PubMed PMID: [22528397](#); PubMed Central PMCID: [PMC3572198](#).
 - b. Solomon IH, Perrin RJ, Clifford DB, Ances BM. Tumefactive demyelination in a patient with human immunodeficiency virus. *J Neurovirol.* 2013 Jun;19(3):265-9. PubMed PMID: [23645348](#); PubMed Central PMCID: [PMC3700605](#).
 - c. Longbrake EE, Ances BM, Viets RB, Clifford DB. Susac syndrome in a patient with human immunodeficiency virus infection. *J Neurovirol.* 2013 Jun;19(3):270-3. PubMed PMID: [23690260](#); PubMed Central PMCID: [PMC4582780](#).
 - d. Hurth K, Tarawneh R, Ghoshal N, Benzinger TL, Clifford DB, Geschwind M, Morris JC, Galvin JE, Schmidt RE, Cairns NJ. Whipple's disease masquerades as dementia with Lewy bodies. *Alzheimer Dis Assoc Disord.* 2015 Jan-Mar;29(1):85-9. PubMed PMID: [23995819](#); PubMed Central PMCID: [PMC3938990](#).
4. Neurosarcoidosis has become a focus for translational research and practice. This inflammatory brain disease is one of the most common brain inflammatory conditions, but has received little systematic attention. No randomized clinical trial has ever been performed to identify optimal treatment(s) and understanding of its pathophysiology, biomarkers, and most reliable mode of diagnosing and treating remain to be clarified. I have begun to follow an increasing number of patients with this condition, and am leading an effort to establish a collaborative program to investigate neurosarcoidosis.
- a. Clifford DB. Nemesis of neglected neurosarcoidosis. *Ann Clin Transl Neurol.* 2015 Oct;2(10):947-8. PubMed PMID: [26478894](#); PubMed Central PMCID: [PMC4603377](#).
 - b. Stern BJ, Aksamit A, Clifford D, Scott TF. Neurologic presentations of sarcoidosis. *Neurol Clin.* 2010 Feb;28(1):185-98. PubMed PMID: [19932381](#).

Complete List of Published Work in MyBibliography:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/david.clifford.1/bibliography/43349733/public/?sort=date&direction=descending>

D. Research Support

Ongoing Research Support

UM1 AI069439-11

CLIFFORD, DAVID B (PI)

02/01/06-11/30/20

Vanderbilt HIV Clinical Trials Unit

Serve as Co-PI of this multi-institutional research center, and leader for the Washington University AIDS Clinical Research Site.

Role: PI

U10 NS077384-02

CLIFFORD, DAVID B (PI)

09/30/11-06/30/18

Washington University Network of Excellence in Neuroscience Clinical Trials Site

Lead this Phase II clinical trial unit currently performing studies related to stroke, myasthenia, and progressive multiple sclerosis. Additional studies for rarer neurological disorders are anticipated.

Role: PI

NR014449, NINR

Ances, Beau (PI)

05/03/13-02/28/18

Frailty and Brain Integrity in Older HIV-infected Individuals

The major goal of this project is to understand the effects of frailty on brain integrity (using functional neuroimaging and amyloid imaging) in older HIV+ individuals

Role: Co-Investigator

Dominantly Inherited Alzheimer Network Treatment Unit (DIAN-TU), Alzheimer Association/Lilly/Roche/NIH

Bateman, Randall (PI)

01/01/13-06/30/17

Dominantly Inherited Alzheimer Network (DIAN-TU)

The purpose of the DIAN Trial Unit is to run a clinical trial including multiple therapies for Alzheimer's disease in families of patients with dominant mutations causing Alzheimer disease. Appropriate biomarkers will be the initial primary outcome with ultimate adaptive design seeking cognitive protection as an ultimate primary endpoint.

Role: OP

NIMH-22005, NIH/NIMH/NINDS

Heaton, Robert (PI)

09/01/2007 – 06/30/2020

CHARTER Aging Project

Age related determinants of HAND: A 12 year follow-up of CHARTER participants

Role: Site PI

UL1 TR000448, NIH/NCATS

Evanoff, Brad (PI)

09/17/07 – 05/31/17

Washington University Institute of Clinical and Translational Sciences

The Clinical and Translational Science Award (CTSA) is the main funding source for the Washington University Institute of Clinical and Translational Science (ICTS).

Role: Co-investigator