

**BIOGRAPHICAL SKETCH**

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NAME: Fitting, Sylvia

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

POSITION TITLE: Assistant Professor of Psychology and Neuroscience

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
Free University of Berlin, Germany	Vordiplom	2000	Psychology
Free University of Berlin, Germany	Diplom	2003	Psychology
University of South Carolina, Columbia, SC	M.A.	2005	Behavioral Neuroscience
University of South Carolina, Columbia, SC	Ph.D.	2008	Behavioral Neuroscience
Virginia Commonwealth University, Richmond, VA	Postdoc	2008-2014	Pharmacology & Toxicology

**A. Personal Statement**

I am a neuroscientist with more than 15 years of experience in the fields of drug abuse and HIV neuropathogenesis. Specifically my goal is to develop a better understanding of how the underlying structural and functional substrates of behavior and neurocognition are affected by drug-related substances  $\pm$  HIV/HIV-1 protein infection. I have had extensive training in behavioral neuroscience during my Ph.D. career and extended my skill sets into more cellular and molecular neuroscience during my postdoctoral career. As an independent researcher at the University of North Carolina, Chapel Hill (UNC-CH), holding the position of an Assistant Professor in the Department of Psychology and Neuroscience since January 2015, I am taking my expertise acquired during my career and study specific pathways using wild-type, knockout, and transgenic mice to analyze gene function *in vitro* and *in vivo*, specifically focusing on the cellular, functional, and behavioral mechanisms of drugs of abuse, including opioids and cannabinoids, and HIV-1 protein interactions on the CNS. My lab has published multiple peer-reviewed papers (h-index: 23, see [Google Scholar](#)) with my research currently being supported by a R21 and a R01 award. My long-term goal is sorting the underlying structural and functional substrates of behavior/neurocognition in disease.

- a. Jacobs, I.R., Xu, C., Hermes, D.J., League, A.F., Xu, C., Nath, B., Niphakis, M.J., Cravatt, B.F., Mackie, K., Mukhopadhyay, S., Lichtman, A.H., Ignatowska-Jankowska, B.M. & **Fitting, S.** (2019). Inhibitory control deficits associated with upregulation of CB<sub>1</sub>R in the HIV-1 Tat transgenic mouse model of HAND. *Journal of Neuroimmune Pharmacology*. 14:661-678. PMID: 31372820
- b. Hermes, D.J., Xu, C., Poklis, J.L., Niphakis, M.J., Cravatt, B.F., Mackie, K., Lichtman, A.H., Ignatowska-Jankowska, B.M. & **Fitting, S.** (2018). Neuroprotective effects of fatty acid amide hydrolase catabolic enzyme inhibition in a HIV-1 Tat model of neuroAIDS. *Neuropharmacology*. 141:55-65. PMID: 30114402.
- c. Xu, C., Hermes, D.J., Nwanguma, B., Jacobs, I.R., Mackie, K., Mukhopadhyay, S., Lichtman, A.H., Ignatowska-Jankowska, B.M. & **Fitting, S.** (2017). Endocannabinoids exert CB<sub>1</sub> receptor-mediated neuroprotective effects in models of neuronal damage induced by HIV-1 Tat protein. *Molecular and Cellular Neuroscience*. 83:92-102. PMID: 28733129.
- d. Xu, C., Hermes, D.J., Mackie, K., Lichtman, A.H., Ignatowska-Jankowska, B.M. & **Fitting, S.** (2016). Cannabinoids occlude the HIV-1 Tat-induced decrease in GABAergic neurotransmission in prefrontal cortex slices. *Journal of Neuroimmune Pharmacology*. 11(2), 316-331. PMID: 26993829.

## **B. Positions and Honors**

### **Research**

- 2000 – 2001 Research Assistant, Experimental Psychology, Max-Planck-Institut for Human Development, Berlin, Germany, Laboratory of Judith Glueck, Ph.D., Berlin, Germany
- 2001 – 2002 Research Assistant, Experimental Psychology, University of Cardiff, Laboratory of Ulrich von Hecker, Ph.D., Cardiff, Great Britain
- 2004 – 2008 Graduate Research Assistant, Experimental Psychology, University of South Carolina, Laboratory of Gary L. Allen, Ph.D., & Douglas H. Wedell, Ph.D., Columbia, SC
- 2004 – 2008 Graduate Research Assistant, Experimental Psychology, University of South Carolina, Laboratories of Charles F. Mactutus, Ph.D., & Rosemarie M. Booze, Ph.D., Columbia, SC
- 2008 – 2014 Postdoctoral Student, Department of Pharmacology & Toxicology, Virginia Commonwealth University, Laboratories of Kurt F. Hauser, Ph.D. & Hamid I. Akbarali, Richmond, VA
- 2015 – Assistant Professor, Department of Psychology, University of North Carolina at Chapel Hill, Chapel Hill, NC

### **Teaching**

- 2003/04 Teaching Assistant, Survey of Learning and Memory (PSYC 400) and Survey of Developmental Psychology (PSYC 420), Psychological Statistics (PSYC 227), University of South Carolina, Columbia, SC
- 2013 Co-Instructor, Basic Concepts for Graduate Students, Virginia Commonwealth University, Richmond, VA
- Spring 2016 Assistant Professor, Research Seminar and Experimental Psychology (PSYC 721), Graduate Seminar, University of North Carolina at Chapel Hill, NC
- Fall 2016/17 Assistant Professor, Biological Psychology (PSYC 220), Undergraduate Class, University of North Carolina at Chapel Hill, NC
- Fall 2017/18 Assistant Professor, Brain and Behavior I (PSYC 701), Graduate Class, University of North Carolina at Chapel Hill, NC

### **Honors and Awards**

- 2001 – 2002 Fellowship to study a year abroad: DAAD-German Academic Exchange Service, Germany
- 2005 – 2006 Fellowship by the Graduate School Research Assistantships Program, University of South Carolina Graduate School
- 2006 CPDD Early Career Investigator Award for the 2006 meeting of the College on Problems of Drug Dependence (CPDD)
- 2006 Centennial Rhude M. Patterson Fellow (pre-doctoral) for Excellence in Research and Scholarship, University of South Carolina Graduate School
- 2007 USC Graduate School Centennial Fellowship (pre-doctoral) for Excellence in Research and Scholarship, University of South Carolina Graduate School
- 2007 Dean's Award of Excellence for Graduate Study, University of South Carolina Graduate School
- 2008 Outstanding Thesis Award 2008, University of South Carolina Graduate School
- 2012 Presentation in the Young Investigator Symposium at the 2012 International Narcotics Research Conference (INRC)
- 2012 Postdoctoral Award 2012 (selected by Faculty), Virginia Commonwealth University, Department of Pharmacology & Toxicology
- 2015 Stephenson and Lindquist Award Fund (\$2,500), University of North Carolina at Chapel Hill, Department of Psychology and Neuroscience
- 2016 Junior Faculty Development Award (\$7,500), University of North Carolina at Chapel Hill, Office of the Executive Vice Chancellor and Provost
- 2016 Stephenson and Lindquist Award Fund (\$3,760), University of North Carolina at Chapel Hill, Department of Psychology and Neuroscience
- 2017 Stephenson and Lindquist Award Fund (\$4,000), University of North Carolina at Chapel Hill, Department of Psychology and Neuroscience

### **Professional Societies and Public Advisory Committees**

- 2004 – Society for Neuroscience

- 2007 – International Society on for NeuroVirology (ISNV)
- 2009 – Society on NeuroImmune Pharmacology (SNIP)
- 2016 – International Cannabinoid Research Society (ICRS)

### **Service**

- 2013 – 2014 International Chair of the Postdoctoral Association, Virginia Commonwealth University
- 2013 – 2014 Postdoctoral Councilor in the Central Virginia Chapter of the Society for Neuroscience
- 2013 – 2014 Coordinator of the Departmental Postdoctoral Association, Pharmacology & Toxicology, Virginia Commonwealth University
- 2015 – Diversity Committee, University of North Carolina, Chapel Hill, Department of Psychology and Neuroscience
- 2018 – Ad hoc Grant Reviewer: National Institute on Drug Abuse: Special Emphasis Panel; HIV Comorbidities and Clinical Studies Study Section
- 2018 – BMC Neuroscience, Associate Editor for the *Neurobiology and Disease* Section

### **C. Contribution to Science**

1. For the past 12 years I have worked in the field of neuroscience, with a focus on exploring the effects of human immunodeficiency virus type 1 (HIV-1) proteins on the central nervous system. My primary Ph.D. training was in Professor Charles Mactutus's laboratory at the University of South Carolina (USC), Experimental Psychology, and centered on behavioral neuroscience. My research has made significant contributions in furthering our understanding of neurocognitive disorders characteristic of HIV-1/AIDS in development (HAND). Using a preclinical model we demonstrated direct synergistic effects of HIV-1 proteins, gp120 and Tat, on brain and behavioral development. These publications demonstrate that exposure of HIV-1 protein early in development induces deficits (1) on behavioral development (eye opening, early reflex development, and locomotor activity) and cognitive dysfunction in adulthood (preattentive processes and spatial memory), similar to what is seen in HAND, and (2) on the neuroanatomical level with significant neuronal loss and increased inflammatory response on number of glial cells using design-based stereology. In my Ph.D. career I have published a total of 16 papers (1<sup>st</sup> author: 10 publications), out of which 8 papers (all 1<sup>st</sup> author papers) are related to my dissertation work.
  - a. **Fitting, S.**, Booze, R.M., Hasselrot, U., & Mactutus, C.F. (2006). Intrahippocampal injections of Tat: Effects on prepulse inhibition of the auditory startle response in adult male rats. *Pharmacology, Biochemistry & Behavior*, 84:189-196. PMID: 16790267.
  - b. **Fitting, S.**, Booze, R.M., Hasselrot, U., & Mactutus, C.F. (2008). Differential long-term neurotoxicity of HIV-1 proteins in the rat hippocampal formation: A design-based stereological study. *Hippocampus*, 18(2), 135-147. PMID: 17924522.
  - c. **Fitting, S.**, Booze, R.M., Hasselrot, U., & Mactutus, C.F. (2010). Dose-dependent long-term effects of Tat in the rat hippocampal formation: A design-based stereological study. *Hippocampus*, 20(4), 469-480. PMID: 19489004.
  - d. **Fitting, S.**, Booze, R.M., & Mactutus, C.F. (2015). HIV-1 proteins Tat and gp120 target the developing dopaminergic system. *Current HIV Research*, 13(1), 21-42. PMID: 25613135.
  
2. During my postdoctoral career I joined the laboratory of Professor Kurt Hauser at the Virginia Commonwealth University (VCU), School of Medicine, whose research group is one of the leading teams in investigating the dual effects of substance abuse and HIV disease. Using a preclinical animal model my research has identified the substrate and mechanisms underlying the accelerated neurocognitive impairment seen in HIV-1-infected individuals who abuse opiates. More frequently than non-abusers, HIV-infected drug abusers demonstrate accelerated neuropathology and increased deficits in neurocognition, including memory loss, severe depression, difficulties in information processing, and movement disorders, making it less possible for these individuals to function normally. The publications have demonstrated that the exacerbated behavioral deficits seen with chronic opiate exposure are accompanied by a severe loss of synaptic connectivity rather than neuron death. While a loss of synaptic connectivity has been historically proposed as a substrate for behavioral/cognitive deficits in neuroAIDS, opiate abuse had not been previously shown to worsen synaptodendritic injury/culling. The knowledge gained from these studies will undoubtedly permit the development of novel therapeutic interventions to target immune-mediated neurological diseases including neuroAIDS more precisely.

- a. **Fitting, S.**, Xu, R., Bull, C., Buch, S.K., El-Hage, N., Knapp, P.E., & Hauser, K.F. (2010). Interactive comorbidity between opioid drug abuse and HIV-1 Tat. Chronic exposure augments spine loss and sublethal dendritic pathology in striatal neurons. *American Journal of Pathology*, 177(3), 1397-410. PMID: 20651230.
  - b. **Fitting, S.**, Scoggins, K.L., Ruqiang, X., Dever, S.M., Knapp, P.E., Dewey, W.L., & Hauser, K.F. (2012). Morphine efficacy is altered in conditional HIV-1 Tat transgenic mice. *European Journal of Pharmacology*. 689(1-3), 96-103. PMID: 22659585.
  - c. **Fitting, S.**, Ignatowska-Jankowska, B.M., Bull, C., Skoff, R.P., Lichtman, A.H., Wise, L.E., Fox, M.A., Su, J., Medina, A.E., Krahe, T.E., Knapp, P.E., Guido, W., Hauser, K.F. (2013). Synaptic dysfunction in the hippocampus accompanies learning and memory deficits in human immunodeficiency virus type-1 Tat transgenic mice. *Biological Psychiatry*, 73(5), 443-53. PMID: 23218253.
  - d. **Fitting, S.**, Zou, S., El-Hage, N., Suzuki, M., Paris, J.J., Schier, C.J., Rodriguez, J.W., Rodriguez, M., Knapp, P.E., & Hauser, K.F. (2014). Opiate addiction therapies and HIV-1 Tat: interactive effects on glial  $[Ca^{2+}]_i$ , oxyradical and neuroinflammatory chemokine production and correlative neurotoxicity. *Current HIV Research*, 12(6), 424-434. PMID: 25760046.
3. With the K99/R00 award in 2012 my research in the mentored K99 phase continued to elucidate the detailed sequence of events by which HIV-1-induced disruptions in glutamate signaling and ion ( $[Na^+]_i$  and  $[Ca^{2+}]_i$ ) homeostasis converge with the effects of opiate exposure to injured striatal synapses. These publications have made the unique observation that opioid drugs intrinsically exacerbate HIV-1 induced CNS inflammation and neuronal injury through  $\mu$ -opioid receptors on different cell types. Pursuing complementary studies I have examined how opiates and HIV-1 proteins alter neuronal membrane properties using whole-cell electrophysiological and physiological approaches in collaboration with my second mentor Professor Hamid I. Akbarali. These publications have shown that Tat enhances the excitability of enteric neurons and sensitizes the enteric neurons to the inhibitory effects of morphine. We specifically focused on defining the mechanisms of morphine sensitization with HIV-1 Tat in isolated striatal neurons using electrophysiological techniques. With these findings we have gained new insight into understanding how opiate drugs exacerbates functional consequences of HIV/AIDS in the nervous system.
- a. Zou, S., **Fitting, S.**, Hahn, Y.K., Welch, S.P., El-Hage, N., Hauser, K.F., & Knapp, P.E. (2011). Morphine potentiates neurodegenerative effects of HIV-1 Tat through actions at  $\mu$ -opioid receptor-expressing glia. *Brain*, 134(12), 3613-3628. PMID: 22102648.
  - b. **Fitting, S.**, Knapp, P.E., Zou, S., Marks, W.D., Bowers, M.S., Akbarali, H.I., & Hauser, K.F. (2014). Interactive HIV-1 Tat and morphine-induced synaptodendritic injury is triggered through focal disruptions in  $Na^+$  influx, mitochondrial instability, and  $Ca^{2+}$  overload. *Journal of Neuroscience*, 34(38), 12850-64. PMID: 25232120.
  - c. Ngwainmbi, J., De, D.D., Smith, T.H., El-Hage, N., **Fitting, S.**, Kang, M., Dewey, W.L., Hauser, K.F., & Akbarali, H.I. (2014). Effects of HIV-1 Tat on enteric neuropathogenesis. *Journal of Neuroscience*, 34(43), 14243-51. PMID: 25339738.
  - d. **Fitting, S.**, Ngwainmbi, J., Kang, M., Khan, F.A., Steven, D.L., Dewey, W.L., Knapp, P.E., Hauser, K.F., & Akbarali, H.I. (2015). Sensitization of enteric neurons to morphine by HIV-1 Tat protein. *Neurogastroenterology & Motility*, 27(4), 468-480. PMID: 25703354.
4. In addition to the contributions described above, I have been working together with different teams of Dr. Hauser's collaborators during my postdoctoral degree, nationally and internationally. For example, my background in biomedical statistics and genuine enjoyment of the discipline has made me a valuable biostatistical resource both within and outside of the Department of Pharmacology and Toxicology at VCU. Now as an independent research at UNC-CH I have started collaborations with Dr. Rick Meeker at the UNC Medical School Department of Neurology, conducting behavioral as well as PET imaging experiments on gp120 transgenic mice. I am collaborating with Dr. Somnath Mukhopadhyay at the North Carolina Central University, Department of Chemistry and Biochemistry, who is an expert in the cannabinoid field. Additionally I have continued collaborations with Dr. Aron Lichtman and Dr. Kurt Hauser at VCU, Department of Pharmacology and Toxicology, who are experts in the cannabinoid and HIV field, respectively.
- a. Hussain, Z.M.\*, **Fitting, S.\***, Watanabe, H., Usynin, I, Yakovleva, T., Knapp, P.E., Scheff, S.W., Hauser, K.F., & Bakalkin, G. (2012). Lateralized response in dynorphin A peptide levels after

traumatic brain injury. *Journal of Neurotrauma*, 29(9), 1785-1793. (Note: \* Authors contributed equally to this work). PMID: 22468884.

- b. Costin, B.N., Wolen, A.R., **Fitting, S.**, Shelton, K.L., & Miles, M.F. (2013). Role of adrenal glucocorticoid signaling in prefrontal cortex gene expression and acute behavioral responses to ethanol. *Alcoholism: Clinical and Experimental Research*, 37(1), 57-66. PMID: 22671426.
- c. Watanabe, H.\*, **Fitting, S.\***, Hussain, Z.M.\*, Kononenko, O., Iatsyshyna, A., Yoshitake, T., Kehr, J., Alkass, K., Druid, H., Wadensten, H., Andren, P.E., Nylander, I., Wedell, D.H., Krishtal, O., Hauser, K.F., Nyberg, F., Karpyak, V.M., Yakovleva, T., & Bakalkin, G. (2013). Asymmetry of the Endogenous Opioid System in the Human Anterior Cingulate: a Putative Molecular Basis for Lateralization of Emotions and Pain. *Cerebral Cortex*, 25(1): 97-108 (Note: \* Authors contributed equally to this work). PMID: 23960211.
- d. Ellis, K., Marlin, J.W., Taylor, T.A., **Fitting, S.**, Hauser, K.F., Rice, G., & McRae, M. (2015). The effects of human immunodeficiency virus infection on the expression of the drug efflux proteins P-glycoprotein and breast cancer resistance protein in a human intestine model. *Journal of Pharmacy & Pharmacology*, 67(2): 178-188. PMID: 25557407.

A complete list of my published work is available at PubMed: [Fitting S](#) For h-index (23): see [Google Scholar](#).

## D. Research Support

### Ongoing Research Support

R01 DA051890 (MPIs: Joseph, SB; Swanstrom, RI) 07/01/2020 – 03/31/2025  
NIH, National Institute on Drug Abuse (NIDA)  
Intersection of HIV, opioids, and amyloid fibrils in a CNS organoid model

R01 DA045596 (PI: Fitting, S) 06/01/2018 – 04/30/2023  
NIH, National Institute on Drug Abuse (NIDA)  
Endocannabinoid-mediated neuroprotection in models of neuroAIDS *in vivo*.

### Completed Research Support

R01S1 DA045596-S1 (PI: Fitting, S; Trainee: Key, M) 06/01/2019 – 05/30/2020  
NIH, National Institute on Drug Abuse (NIDA)  
Endocannabinoid-mediated neuroprotection in models of neuroAIDS *in vivo*.

R21 DA045597 (MPIs: Fitting, S; Kourkoutis, LF) 07/01/2018 – 06/30/2020  
NIH, National Institute on Drug Abuse (NIDA)  
Mapping HIV-Tat ± endocannabinoid induced synaptic changes at the macromolecular level via cryo-electron tomography

R21 DA041903 (PI: Fitting, S) 07/15/2016 – 05/31/2018  
NIH, National Institute on Drug Abuse (NIDA)  
Investigation of endocannabinoid-mediated neuroprotection in models of neuroAIDS

UNC CFAR P30 AI50410 (PI: Fitting, S) 08/01/2016 – 07/31/2017  
UNC Center of AIDS Research (CFAR) Developmental Award  
Neuroprotective potential of endocannabinoids in a model of neuroAIDS

R00 DA033878 (PI: Fitting, S) 01/01/2015 – 04/30/2018  
NIH, National Institute on Drug Abuse (NIDA)  
Opiate drug abuse & HIV-induced excitotoxicity in striatal neurons

K99 DA033878 (PI: Fitting, S) 06/01/2012 – 04/30/2014  
NIH, National Institute on Drug Abuse (NIDA)  
Opiate drug abuse & HIV-induced excitotoxicity in striatal neurons