## **BIOGRAPHICAL SKETCH**

# NAME POSITION TITLE Eric Edward Smith, MD, MPH, FRCPC Associate Professor of Neurology

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)

INSTITUTION AND LOCATION	DEGREE <i>(if</i>	YEAR(s)	FIELD OF STUDY
	applicable)		
McGill University	BSc	1989-1993	Biochemistry
McGill University	MD	1994-1998	Medicine
Massachusetts General Hospital	Internship	1998-1999	Internal Medicine
Mass General/Brigham and Women's Hospital	Residency	1999-2002	Neurology
Massachusetts General Hospital	Fellowship	2002-2003	Vascular Neurology
Harvard School of Public Health	MPH	2003-2005	Clinical Effectiveness

### A. Personal Statement

My independently funded research program investigates the relationships between cerebral small vessel diseases and Alzheimer's disease, and how they cause cognitive impairment. In prospective cohort studies we use neuroimaging such as MRI and PET to measure brain blood flow, brain ischemic lesions, brain microbleeds and brain amyloid deposits, with the objective of developing and validating better markers of the risk of cerebral small vessel diseases and their consequences. These studies are carried out in human populations, including stroke- and dementia-free community-dwelling middle-aged and elderly persons, and patients with mild cognitive impairment, ischemic stroke, hemorrhagic stroke, cerebral amyloid angiopathy and Alzheimer's disease. I lead the Vascular Illness Team of the Canadian Consortium for Neurodegeneration and Aging, Canada's national dementia research strategy. I have participated in several international collaborative initiatives, including as the CIHR-nominated co-PI of the Standards for Reporting Vascular Changes on Neuroimaging (funded by the multinational Centers Of Excellence in Neurodegeneration) and the Vascular Meta-Cohorts initiative (funded by the Joint Program on Neurodegenerative Diseases).

#### **B.** Positions and Honors

#### Positions and Employment

1993-1994	Research Assistant, Biochemistry Laboratory of Dr. E. A. Meighen, McGill University
1998-1999	Internship in Internal Medicine, Massachusetts General Hospital
1999-2002	Residency in Neurology, Massachusetts General Hospital/Brigham and Women's
	Hospital
2001-2002	Chief Resident in Neurology
2002-2003	Clinical Fellow in Vascular Neurology and Neurological Intensive Care, Massachusetts
	General Hospital
2003-2006	Instructor in Neurology, Harvard Medical School
2003-2008	Assistant in Neurology, Massachusetts General Hospital
2006-2008	Assistant Professor of Neurology, Harvard Medical School
2008-2012	Assistant Professor of Neurology, University of Calgary
2012-	Associate Professor of Neurology, University of Calgary

## <u>Honors</u>

1998	Holmes Gold Medal for highest standing in Medical School Class
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- 2001 Harvard Medical School Excellence in Teaching Award
- 2003 American Academy of Neurology Clinical Research Fellowship Award
- 2009 Fellow of the American Heart Association (FAHA)
- 2009-2014 New Investigator Award, Canadian Institutes for Health Research
- 2009-2014 New Investigator Award, Heart and Stroke Foundation of Canada
- 2010 Robert G. Siekert New Investigator Award in Stroke (from the American Heart Association)
- 2010-2017 Clinical Investigator Award, Alberta Innovates Health Solutions
- 2012-2017 Katthy Taylor Chair in Vascular Dementia, University of Calgary

# C. Selected Peer-Reviewed Publications (selected from 176 published or in press)

H index: 47 (Web of Science; http://www.researcherid.com/rid/C-5443-2012), 55 (Google Scholar).

- 1. Greenberg SM, Eng JA, Ning M, **Smith EE**, Rosand J. Hemorrhage burden predicts recurrent intracerebral hemorrhage after lobar hemorrhage. Stroke. 2004;35(6):1415-1420.
- 2. **Smith EE**, Gurol ME, Eng JA, Engel CR, Nguyen TN, Rosand J, Greenberg SM. White matter lesions, cognition, and recurrent hemorrhage in lobar intracerebral hemorrhage. Neurology. 2004;63(9):1606-1612.
- 3. Rosand J, Muzikansky A, Kumar A, Wisco JJ, **Smith EE**, Betensky RA, Greenberg SM. Spatial clustering of hemorrhages in probable cerebral amyloid angiopathy. Ann Neurol. 2005;58(3):459-462.
- Chen Y-W, Gurol ME, Rosand J, Viswanathan A, Rakich SM, Groover TR, Greenberg SM, Smith EE. Progression of white matter lesions and hemorrhages in cerebral amyloid angiopathy. Neurology. 2006;67(1):83-87.
- 5. **Smith EE**, Eichler F. Cerebral amyloid angiopathy and lobar intracerebral hemorrhage. Arch Neurol. 2006;63(1):148-151.
- 6. **Smith EE**, Vijayappa M, Lima F, Delgado P, Wendell L, Rosand J, Greenberg SM. Impaired visual evoked flow velocity response in cerebral amyloid angiopathy. Neurology. 2008;71(18):1424-1430.
- 7. Viswanathan A, Patel P, Rahman R, Nandigam RN, Kinnecom C, Bracoud L, Rosand J, Chabriat H, Greenberg SM, **Smith EE**. Tissue microstructural changes are independently associated with cognitive impairment in cerebral amyloid angiopathy. Stroke. 2008;39(7):1988-1992.
- 8. Greenberg SM, Nandigam RN, Delgado P, Betensky RA, Rosand J, Viswanathan A, Frosch MP, **Smith EE**. Microbleeds versus macrobleeds: evidence for distinct entities. Stroke. 2009;40(7):2382-2386.
- Kimberly WT, Gilson A, Rost NS, Rosand J, Viswanathan A, Smith EE, Greenberg SM. Silent ischemic infarcts are associated with hemorrhage burden in cerebral amyloid angiopathy. Neurology. 2009;72(14):1230-1235.
- Nandigam RN, Viswanathan A, Delgado P, Skehan ME, Smith EE, Rosand J, Greenberg SM, Dickerson BC. MR imaging detection of cerebral microbleeds: effect of susceptibility-weighted imaging, section thickness, and field strength. AJNR Am J Neuroradiol. 2009;30(2):338-343.
- 11. Patel PV, FitzMaurice E, Nandigam RN, Auluck P, Viswanathan A, Goldstein JN, Rosand J, Greenberg SM, **Smith EE**. Association of subdural hematoma with increased mortality in lobar intracerebral hemorrhage. Arch Neurol. 2009;66(1):79-84.
- 12. Smith EE, Greenberg SM. Beta-amyloid, blood vessels, and brain function. Stroke. 2009;40(7):2601-2606.
- Biffi A, Halpin A, Towfighi A, Gilson A, Busl K, Rost NS, Smith EE, Greenberg SM, Rosand J, Viswanathan A. Antiplatelet agents and recurrent intracerebral hemorrhage in cerebral amyloid angiopathy. Neurology. 2010;75(8):693-698.
- 14. Chen YW, Lee MJ, **Smith EE**. Cerebral amyloid angiopathy in East and West. Int J Stroke. 2010;5(5):403-411.
- 15. **Smith EE**, Nandigam KR, Chen YW, Jeng J, Salat D, Halpin A, Frosch M, Wendell L, Fazen L, Rosand J, Viswanathan A, Greenberg SM. MRI markers of small vessel disease in lobar and deep hemispheric intracerebral hemorrhage. Stroke. 2010;41(9):1933-1938.
- Smith EE, Auer RN. Cerebral Microbleeds in Relation to Hypertensive Arteriopathy. In: Werring DJ, ed. Microbleeds: From Pathophysiology to Clinical Practice. Cambridge: Cambridge University Press, 2011:99-108.

- Smith EE, Werring DJ, McCreary CR. Relationship of Cerebral Microbleeds to Other Imaging Findings. In: Werring DJ, ed. Microbleeds: From Pathophysiology to Clinical Practice. Cambridge: Cambridge University Press, 2011:71-78.
- 18. **Smith EE**, Schneider JL, Wardlaw J, Greenberg SM. Cerebral microinfarcts: the invisible lesions. Lancet Neurology. 2012;11(3):272-282.
- Fonarow GC, Pan W, Saver JL, Smith EE, Reeves MJ, Broderick JP, Kleindorfer DO, Sacco RL, Olson DM, Hernandez AF, Peterson ED, Schwamm LH. Comparison of 30-day mortality models for profiling hospital performance in acute ischemic stroke with vs without adjustment for stroke severity. JAMA. 2012;308(3):257-264.
- 20. Xian Y, Liang L, Smith EE, Schwamm LH, Reeves MJ, Olson DM, Hernandez AF, Fonarow GC, Peterson ED. Risks of intracranial hemorrhage among patients with acute ischemic stroke receiving warfarin and treated with intravenous tissue plasminogen activator. JAMA. 2012;307(24):2600-2608.
- 21. Moreau F, Patel S, Lauzon ML, McCreary CR, Goyal M, Frayne R, Demchuk AM, Coutts SB, **Smith EE**. Cavitation following acute symptomatic lacunar stroke depends on time, location and MRI sequence. Stroke. 2012;43(7):1837-1842.
- 22. Saver JL, Fonarow GC, **Smith EE**, Reeves MJ, Grau-Sepulveda MV, Pan W, Olson DM, Hernandez AF, Peterson ED, Schwamm LH. Time to treatment with intravenous tissue plasminogen activator and outcome from acute ischemic stroke. JAMA. 2013:309(23):2480-2488.
- 23. Tyndall AV, Davenport MH, Wilson BJ, Grazyna MB, Arsenault-Lapierre G, Haley E, Eskes GA, Friedenreich CM, Hill MD, Hogan DB, Longman RS, Anderson TJ, Richard Leigh R, Smith EE, Poulin MJ. The Brain-in-Motion Study: Effect of a 6-month aerobic exercise intervention on cerebrovascular regulation and cognitive function in older adults. BMC Geriatrics. 2013;13(2):21.
- 24. Wardlaw JM, Smith EE, Biessels GJ, Cordonnier C, Fazekas F, Frayne R, Lindley RI, O'Brien JT, Barkhof F, Benavente OR, Black SE, Brayne C, Breteler M, Chabriat H, Decarli C, de Leeuw FE, Doubal F, Duering M, Fox NC, Greenberg S, Hachinski V, Kilimann I, Mok V, Oostenbrugge R, Pantoni L, Speck O, Stephan BC, Teipel S, Viswanathan A, Werring D, Chen C, Smith C, van Buchem M, Norrving B, Gorelick PB, Dichgans M. Neuroimaging standards for research into small vessel disease and its contribution to ageing and neurodegeneration. Lancet Neurol. 2013;12(8):822-838.
- 25. Peca S, McCreary CR, Donaldson E, Kumarpillai G, Shobha N, Sanchez K, Charlton A, Steinback CD, Beaudin AE, Fluck D, Pillay N, Fick GH, Poulin MJ, Frayne R, Goodyear BG, Smith EE. Neurovascular decoupling is associated with severity of cerebral amyloid angiopathy. Neurology. 2013;81(19):1659-1665.
- 26. Fluck D, Beaudin AE, Steinback CD, Kumarpillai G, Shobha N, McCreary CR, Peca S, Smith EE, Poulin MJ. Effects of aging on the association between cerebrovascular responses to visual stimulation, hypercapnia and arterial stiffness. Frontiers in physiology. 2014;5:49.
- 27. Greenberg SM, Al-Shahi Salman R, Biessels GJ, van Buchem M, Cordonnier C, Lee JM, Montaner J, Schneider JA, **Smith EE**, Vernooij M, Werring DJ. Outcome markers for clinical trials in cerebral amyloid angiopathy. Lancet Neurol. 2014;13:419-428.
- 28. Smith EE, O'Donnell M, Dagenais G, Lear SA, Wielgosz A, Sharma M, Poirier P, Stotts G, Black SE, Strother S, Noseworthy MD, Benavente O, Modi J, Goyal M, Batool S, Sanchez K, Hill V, McCreary CR, Frayne R, Islam S, DeJesus J, Rangarajan S, Teo K, Yusuf S, Investigators P. Early cerebral small vessel disease and brain volume, cognition, and gait. Ann Neurol. 2015;77:251-261. PMID 25428654.
- 29. Ismail Z, **Smith EE**, Geda Y, Sultzer D, Brodaty H, Smith G, Aguera-Ortiz L, Sweet R, Miller D, Lyketsos CG, Area INSPI. Neuropsychiatric symptoms as early manifestations of emergent dementia: Provisional diagnostic criteria for mild behavioral impairment. Alzheimers Dement. 2015. Accessed online before publication

# D. Research Support

# <u>Ongoing</u>

 <u>Vascular Illness and its Impact on Neurodegeneration</u>. CIHR special initiative: Canadian Consortium on Neurodegeneration and Aging. Funded April 2014 to March 2019. Eric Smith, PI. Goal: Determine rates of decline in vascular MCI.  <u>PURE-MIND: A Population-based Study of Covert Cerebrovascular Disease and Its Contribution to Age-Related Cognitive Decline</u>. CIHR Operating Grant. Funded October 2013 to September 2018. Eric Smith, PI.

Goal: Risk factors for silent strokes.

- <u>NeuroVISION Study: Detection And Neurological Impact Of Cerebrovascular Events In Noncardiac Surgery</u> <u>Patients: A Cohort Evaluation Study</u>. CIHR Operating Grant. Funded July 2014 to June 2018. Philip Devereaux and Marko Mrkobrada, PIs; Eric Smith, co-I. Goal: Determine prevalence and consequences of peri-operative brain infarcts on MRI.
- <u>Canadian Alliance for Healthy Hearts and Minds</u>. Canadian Partnership Against Cancer. Funded January 2013 to December 2016. Sonia Anand, PI; Eric Smith, co-I. Goal: Subclinical predictors of stroke using brain MRI.
- <u>Relationship Between "Covert" Brain Ischemia and Cognitive and Physical Decline in Middle-Aged</u> <u>Canadians</u>. Heart and Stroke Foundation of Alberta Grant-in-Aid. Funded July 2013 to June 201. Eric Smith, PI.
  - Goal: Determine relationship between silent stroke and cognitive decline in middle-aged persons.
- <u>Realising the potential of cohort studies to determine the vascular contribution to neurodegeneration</u>. CIHR Working Groups on Longitudinal Cohorts. Funded September 2014 to August 2015. Joanna Wardlaw, PI; Eric Smith, co-PI.
- <u>Cognition and Vascular Dysfunction in Patients with Cerebral Amyloid Angiopathy.</u> Heart and Stroke Foundation of Alberta Grant-in-Aid. Funded July 2012 to June 2015. Eric Smith, PI. Goal: Determine cognitive and blood flow profiles in cerebal amyloid angiopathy.

# Completed within last 3 years

 <u>Cerebral Small Vessel Disease and Beta-Amyloid Deposition in Subjects with Mildly Impaired Cognition</u>. Establishment Award, Alberta Innovates – Health Solutions. Funded July 2012 to June 2014. Eric Smith, PI.

Goal: determined how beta-amyloid and white matter disease interact to cause cognitive impairment.

- <u>Cognitive and Blood Flow Profile of Cerebral Amyloid Angiopathy</u>. Alzheimer Society of Canada Biomedical Grant. Funded August 2012-July 2014. Eric Smith, PI. Goal: Determined cognitive and blood flow profiles in cerebal amyloid angiopathy.
- Standards for Determining the Vascular Contribution to Neurodegeneration. Catalyst Grant: International Network of Centres of Excellence in Neurodegeneration (CIHR). Funded October 2011 to September 2013, Eric Smith, PI.

Goal: established consensus standards for measurement of cerebral small vessel disease.

- 4. <u>Small vessel disease and beta-amyloid deposition in mildly impaired cognition.</u> NINDS R01 NS062028. Funded August 2008 to March 2013. Deborah Blacker, PI; Eric Smith, co-PI. Goal: determined how beta-amyloid and white matter disease interact to cause cognitive impairment.
- <u>PURE-MIND: An MRI and Outcome Assessment Study</u>. Canadian Stroke Network and Heart and Stroke Foundation of Canada. Funded March 2010 to March 2012. Eric Smith, PI (Martin O'Donnell, co-PI). Goal: provided pilot data on prevalence of silent stroke in 40s and 50s.
- Multi-modality study of vascular function in cerebral small vessel disease. Canadian Stroke Network/Heart and Stroke Foundation Canada. Funded April 2009 to March 2012. Eric Smith, PI. Goal: idenfied impaired neurovascular coupling in cerebral amyloid angiopathy.