

BIOGRAPHICAL SKETCH

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NAME Charles D. Smith	POSITION TITLE Robert P. and Mildred Moores Professor in Alzheimer's Research		
eRA COMMONS USER NAME CHARLES.SMITH			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Cornell University, Ithaca, NY	B.S.E.E	1974	Electrical Engineering
Cornell University, Ithaca, NY	M.S.E.E	1975	Electrical Engineering
Tulane University, New Orleans, LA	M.D.	1979	Medicine
University of Kentucky, Lexington, KY	Postdoc	1988	Magnetic Resonance

A. Positions and Honors**Professional Experience**

1979-1980 Intern, Department of Internal Medicine, Dartmouth Medical School, Hanover, New Hampshire
 1980-1981 Resident, Department of Internal Medicine, Dartmouth Medical School
 1981-1984 Resident, Department of Neurology, Dartmouth Medical School
 1983-1984 Instructor, Department of Neurology, Dartmouth Medical School
 1986 Board Certification, American Board of Psychiatry & Neurology
 1984-1987 Assistant Professor, Department of Neurology, University of Wisconsin Medical School
 1985-1987 Assistant Clinical Professor, Department of Neurology, Medical College of Wisconsin
 Milwaukee, Wisconsin (Joint Appt.)
 1989-1994 Recipient, Clinical Investigator Development Award (CIDA), NIH/NINCDS
 1989-1994 Assistant Professor, Department of Neurology, University of Kentucky, Lexington, Kentucky
 1994 Certification in Magnetic Resonance Imaging, American Society of Neuroimaging
 1993- Present Graduate Faculty, Center for Biomedical Engineering, University of Kentucky
 1994 Certification in Computed Axial Tomography, American Society of Neuroimaging
 1994-2001 Associate Professor, Department of Neurology, University of Kentucky
 1995- Present Director, Memory Disorders Clinic & Clinical Core B, Alzheimer's Disease Research Center
 (ADRC) & Sanders-Brown Center on Aging, University of Kentucky
 1998-2001 Associate Professor of Anatomy & Neurobiology, University of Kentucky (Joint Appt.)
 2001-Present Professor of Neurology, University of Kentucky
 2001-Present Professor of Anatomy & Neurobiology, University of Kentucky (Joint Appt.)
 2001-Present Professor of Biomedical Engineering, University of Kentucky (Joint Appt.)
 2007-Present Director, Magnetic Resonance Imaging and Spectroscopy Center (MRISC), University of
 Kentucky, Lexington, Kentucky
 2008- Subspecialty Certification, Neuroimaging, UCNS

Honors; Affiliations

1972-1974 McMullen Scholar, Cornell University
 1978 Tulane Medical School, AOA
 1985- Present International Society of Magnetic Resonance in Medicine
 1985- Present American Academy of Neurology
 1985- Present Cornell Society of Engineers
 1989- Present American Society of Neuroimaging
 1989- Present Faculty, Magnetic Resonance Imaging and Spectroscopy Center
 1990- 2001 Fellow, Stroke Council, American Heart Association
 1998- Present American Neurological Association

B. Selected peer-reviewed publications (in chronological order)(Selected from 96)

1. Smith CD, Carney JM, Starke-Reed PE, Oliver CN, Stadtmann ER, Floyd RA, Markesbery WR. Excess brain protein oxidation and enzyme dysfunction in normal aging and in Alzheimer's disease. PNAS 1991;

88:10540-10543.

2. Smith CD, Carney JM, Tatsumo T, Stadtmann ER, Floyd RA, Markesbery WR. Protein oxidation in aging brain. *Ann NY Acad Sci* 1992; 663:110-119.
3. Smith CD, Gallenstein LG, Layton WJ, Kryscio RJ, Markesbery WR. 31P Magnetic resonance spectroscopy in Alzheimer's and Pick's Disease. *Neurobiol Aging* 1993; 14:85-92.
4. Smith CD, Ain K.A. Human brain metabolism in hypothyroidism studied with 31P magnetic resonance spectroscopy. *Lancet* 1995; 345: 619-620.
5. Smith CD, Pettigrew LC, Avison MJ, Kirsch JE, Tinkhtman AJ, Schmitt FA, Wermeling DP, Wekstein DR, Markesbery WR. Frontal lobe phosphorus metabolism and neuropsychologic function in aging and Alzheimer's disease. *Ann Neurol* 1995; 38:584-591.
6. Smith CD, Landrum W, Carney JM, Landfield PW, Avison MJ. brain creatine kinase forward flux by magnetization transfer: effect of age in Fisher 344 rats. *Neurobiol Aging* 1997; 18(6):617-622.
7. Smith CD, Malcein M, Meurer K, Schmitt FA, Markesbery WA, Pettigrew LC. MRI Temporal Lobe Volumetric Measures and Neuropsychologic Function in Alzheimer's Disease: *J Neuroimaging* 1999; 9:2-9.
8. Smith CD, Trevathan ER, Zhang M, Andersen AH, Avison MJ. Functional MRI evidence for task-specific activation of developmentally abnormal visual association cortex. *Ann Neurol* 1999; 45:515-518.
9. Smith CD, Andersen AH, Kryscio RJ, Schmitt FA, Blonder LX, Kindy MS, Avison MJ. Altered brain activation in normal subjects at risk for Alzheimer's disease. *Neurology* 1999; 53:1391-1396.
10. Smith CD, Snowdon DA, Markesbery WR. Periventricular white matter hyperintensities on MRI: correlation with neuropathologic findings. *J Neuroimaging* 2000; 10:13-16.
11. Smith CD, Snowdon DA, Wang H, Markesbery WR. White matter volumes and periventricular white matter hyperintensities in aging and dementia. *Neurology* 2000; 54:838-842.
12. Snowdon DA, Tully CL, Smith CD, Riley KP, Markesbery WR. Serum folate and the severity of atrophy of the neocortex in Alzheimer's disease: Findings from the Nun study. *J Clin Nutrition* 2000; 71:993-998.
13. Schmitt FA, Davis DG, Wekstein DR, Smith CD, Ashford JW, Markesbery WR. "Preclinical" AD revisited: neuropathology of cognitively normal older adults. *Neurology* 2000; 55:370-376.
14. Wackerbarth SB, Johnson MMS, Markesbery WR, Smith CD. Urban-rural differences in a memory disorders clinical population. *J. Amer. Geriatr Soc* 2001; 49:647-650.
15. Smith CD. Serial MRI findings in a case of primary lateral sclerosis. *Neurology* 2002; 57:647-649.
16. Smith CD, Andersen AH, Kryscio RJ, Schmitt FA, Kindy MS, Blonder LX, Avison MJ. Women at high risk for Alzheimer's disease show increased parietal activation in a letter fluency task. *Neurology* 2002; 58:1197-02.
17. Gosche KM, Mortimer JA, Smith CD, Markesbery WR, Snowdon DA. Hippocampal volume as an index of Alzheimer neuropathology: Findings from the Nun study. *Neurology* 2002; 58: 1476-1482.
18. Gaugler JE, Mendiondo M, Smith CD, Schmitt FA. Secondary dementia caregiving and its consequences. *Am J Alzheimer's Disease* 2003; 18: 300-308.
19. Nath A, Hall E, Tuzova M, Dobbs M, Jons M, Anderson C, Woodward J, Guo Z, Fu W, Kryscio R, Wekstein D, Smith CD, Markesbery WR, Mattson MP. Autoantibodies to amyloid beta-peptide (A β) are increased in Alzheimer's disease patients and A β antibodies can enhance A β neurotoxicity: implications for disease pathogenesis and vaccine development. *Neuromolecular Med* 2003; 3:29-39.
20. Gaugler JE, Anderson KA, Leach, CR, Smith, CD, Schmitt, FA., Mendiondo, M. The emotional ramifications of unmet need in dementia caregiving. *Am JAD* 2004; 19:369-379.
21. Smith CD, Walton A, Loveland AD, Umberger GH, Kryscio RJ, Gash DM. Memories that last in old age: motor skill learning and memory preservation. *Neurobiol Aging*. 2005;26:883-890.
22. Slevin JT, Gerhardt GA, Smith CD, Gash DM, Kryscio R, Young B. Improvement of bilateral motor functions in patients with Parkinson disease through the unilateral intraputaminial infusion of glial cell line-derived neurotrophic factor. *J Neurosurg* 2005; 102:216-22.
23. Smith CD, Kryscio RJ, Schmitt FA, Lovell MA, Blonder LX, Rayens WS, Andersen AH. Longitudinal functional alterations in asymptomatic women at risk for Alzheimer's disease. *J Neuroimaging* 2005;15: 271-7.
24. Chebrolu H, Slevin JT, Gash DA, Gerhardt GA, Young B, Given CA, Smith CD. MRI volumetric and intensity analysis of the cerebellum in Parkinson's disease patients infused with glial-derived neurotrophic factor (GDNF). *Exp Neurol* 2006; 198: 450-456.
25. Gold BT, Balota DA, Jones SJ, Powell DK, Smith CD, Andersen AH. Dissociation of automatic and strategic lexical-semantics: functional magnetic resonance imaging evidence for differing roles of multiple frontotemporal regions. *J Neurosci* 2006; 26: 6523-6532.

26. Markesbery WR, Schmitt FA, Kryscio RJ, Davis DG, Smith CD, Wekstein DR. Neuropathologic substrate of mild cognitive impairment. *Arch Neurol* 2006; 63: 38-46.
27. Smith CD, Chebrolu H, Wekstein DR, Schmitt FA, Markesbery WR. Age and gender effects on human brain anatomy: a voxel based morphometric study in healthy elderly. *Neurobiol Aging* 2007; 28:1075-1087.
28. Slevin, JT, Gash DM, Smith CD, Gerhardt GA, Kryscio R, Chebrolu H, Walton A, Wagner R, Young BA. Unilateral intraputamin glial cell line-derived neurotrophic factor in patients with Parkinson disease: response to one year each of treatment and withdrawal. *J Neurosurg* 2007;106:1-7.
29. Mehta SG, Watts CDJ, Adamson J, Hutton M, G. Umberger G, Xiong S, Ramdeen S, Lovell M, Kimonis VE, Smith CD. *APOE* is a Potential Modifier Gene in an Autosomal Dominant Form of Frontotemporal Dementia (IBMPFD). *Genet Med* 2007; 9:9-13.
30. Neumann M, Mackenzie IR, Cairns NJ, Boyer PJ, Markesbery WR, Smith CD, Taylor JP, Kretschmar KZ, Kimonis VE, Forman F. TDP-43 in the ubiquitin pathology of frontotemporal dementia with VCP gene mutations. *J Neuropathol Exp Neurol*. 2007; 66:152-57.
31. Smith CD, Chebrolu H, Wekstein DR, Schmitt FA, Jicha GA, Cooper G, Markesbery WR. Brain Structural Alterations Before Mild Cognitive Impairment. *Neurology* 2007; 68:1268-1273.
32. Martin S, Covell J, Joseph J, Chebrolu H, Smith CD; Kelly T, Jiang Y, Gold BT. Human experience-seeking correlates with hippocampus volume: Convergent evidence from manual tracing and Voxel-Based Morphometry. *Neuropsychologia* 2007; 45:2874-2881.
33. Smith CD, Walton A, Slevin JT, Gerhardt GA, Umberger G, Smoot K, Schulze E, Gash DM. Validation Studies of the Human Movement Analysis Panel for Hand/Arm Performance *J Neurosci Meth* 2007;165:287-96.
34. Smith CD. Mild cognitive impairment is too late: The case for presymptomatic detection and treatment for Alzheimer's disease. *Cognitive Sciences* 2007; 3:127-177.
35. Gash DM, Rutland K, Carter N, Sullivan PG, Bing G, Cass W, Pandya JD, Liu M, Choi D-Y, Hunter RL, Gerhardt GA, Smith CD, Slevin JT, Prince S. Trichloroethylene: Parkinsonism and Complex 1 Mitochondrial Neurotoxicity. *Ann Neurol* 2008 63:193-203.
36. Liu X, Steinmetz NA, Farley AB, Smith CD, Joseph JE. Mid-fusiform activation during object discrimination reflects the process of differentiating structural descriptions. *J Cog Neurosci* 2008 (In Press)
37. Wehl CC, Temiz P, Miller, Watts G, Smith CD, Forman M, Hanson PI, Kimonis V, Pestronk A. TDP-43 accumulation in IBM muscle suggests a common pathogenic mechanism with Frontotemporal dementia. *JNPN* 2008 (In Press).
38. Kimonis VE, Mehta SG, Fulchiero EC, Thomasova D, Pasquali M, Boycott K, Neilan EG, Kartashov A, Forman MS, A. Brownell KW, Tucker S, Kimonis K, Mumm S, Whyte M, Smith CD, Watts GDJ. Clinical studies in familial VCP myopathy associated with Paget disease of bone and frontotemporal dementia. *Am J Med Genet* 2008 (In Press).
39. Smith CD, Chebrolu H, Markesbery WR, Liu, J. Improved Predictive Model for Presymptomatic Mild Cognitive Impairment and Alzheimer's Disease. *Neurological Research* 2008 (In Press).
40. Gold BT, Powell DK, Xuan L, Jicha GA, Smith CD. Age-related slowing of task switching is associated with decreased integrity of frontoparietal white matter. *Neurobiol Aging* 2008 (In Press).
41. Smith CD, Chebrolu H, Andersen AH, Powell DA, Lovell MA, Xiong S, Gold BT. White Matter Diffusion Alterations in Normal Women at Risk of Alzheimer's Disease. *Neurobiol Aging* 2008 (In Press)

C. Research Support

Ongoing Research Support

NIH/NINDS R01 036660 (PI Smith)

9/30/97-12/31/07 (No cost to 08)

Detection of Presymptomatic Alzheimer's Disease by fMRI

This study seeks to detect functional brain alterations in asymptomatic people with high risk of later developing AD.

NIH/NIA R01 AG025159 (PI Smith)

9/15/06-6/30/09

Imaging brain function/structure in presymptomatic FTD

Studies families harboring a known autosomal dominant mutation causing muscular dystrophy, Paget's disease of bone and frontotemporal dementia to determine imaging and psychometric biomarkers for dementia in asymptomatic carriers.

NIH/NIA P50 AG005144 (P50 PI Markesbery/ PI Core B/Clinic Smith) 9/30/85-6/30/11

Alzheimer's Disease Center (ADC)

The clinical core provides diagnostic services, performs clinical trials, and recruits and follows persons with dementia from diagnosis to autopsy.

NIH/NIA P50 AG005144 (PI Markesbery/ Co-PI Smith) 9/30/85-6/39/11

Alzheimer's Disease Center (ADC) Minority Emphasis Satellite Memory Disorders Clinic

This satellite clinic provides diagnostic services and research subjects from an underserved minority population in Lexington, Kentucky.

NIH/NIA U01 AG024904 (Weiner/ Site PI Smith) 9/30/04-9/29/09

Alzheimer's Disease Neuroimaging Initiative (ADNI)

Longitudinal multicenter study of neuroimaging and related biomarkers in normal subjects and those with mild cognitive impairment and early Alzheimer's Disease.

NIH/NIMH R01MH078228 (Blonder, L., PI, Co-PI Smith) 10/1/06-9/29/11

Neuroimaging Studies of Depression in Parkinson's Disease

This study uses fMRI methods to elucidate substrates of depression in Parkinson's disease.