BIOGRAPHICAL SKETCH

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NAME: Rosalind C. Roberts

POSITION TITLE: Kathy Ireland Professor of Psychiatry

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

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
University of California, Irvine, California	B.S.	1979	Biological Sciences
University of California, Irvine, California	Ph.D.	1986	Biological Sciences
Harvard Medical School & Mass. General	Postdoc	1989	Neuroscience

A. Personal Statement

My entire scientific career has been devoted to studying human and animal neuroanatomy and neuropathology. In my many years of experience I have dedicated my main efforts to the ultrastructural analyses of human postmortem brain in health and disease as well as to light and electron microscopy studies in animal models. Many of these studies have looked at combined EM immunohistochemistry in control and schizophrenia tissue with a track record of publication in the field of 130 papers.

One of my accomplishments has been directing two postmortem brain collections. I was the Director of the Maryland Brain Collection (which was devoted to the study of schizophrenia, and collected over 900 brains from schizophrenia, control and other neuropsychiatric disorders). Currently I am the Director of the Alabama Brain Collection (which is devoted to the study of neuropsychiatric and neurological disorders) and under my direction it has collected 117 cases. The study of human brain is crucial in order to understand brain diseases that are unique to humans. We have been able to collect and diagnose tissue that other banks have not, offering to the scientific community unique resources. Not only was I involved in collecting the brains, but I also did the matching, dissections and helped plan the appropriate experimental groups. Both collections include very well characterized cases from a diagnostic perspective, very high quality brains suitable for electron microscopy, and unique collections in numbers high enough for statistical significance. These unique cohorts include teen suicide victims and controls, subjects with schizophrenia off medication, and cases with short enough postmortem intervals to be useful for ultrastructural analyses. In fact, my lab is one of only two in the world that has the tissue and expertise to quantitatively analyze schizophrenia brain at the electron microscopic level.

My latest research interest is pathology in the white matter in schizophrenia. I want to pursue this with the goal of identifying molecular mechanisms and pharmacological targets for therapy in schizophrenia. I am perfectly suited to execute these specific aims as they address schizophrenia pathology, which I have been studying for 25 years.

1) Roberts RC (2003) The immunocytochemical localization of tyrosine hydroxylase in the human striatum and substantia nigra: a postmortem ultrastructural study. In: The Basal Ganglia VI, A.M. Graybiel, M.R. DeLong, and S.T. Kitai (eds.), Kluwer Academic/Plenum Publishers, 54:369-378.

2) Perez-Costas E, Melendez-Ferro M, Roberts, RC (2010) Basal ganglia pathology in schizophrenia: dopamine connections and anomalies. J Neurochemistry, 113:287-302. PMID 20089137.

3) Rice, MW, Roberts RC, Perez-Costas E, Melendez-Ferro M. Mapping dopaminergic deficiencies in the substantia nigra/ventral tegmental area in schizophrenia. Brain Structure and Function, 2014 Oct 1. [Epub ahead of print]

4) McCollum LA, Walker CK, Roche JK, Roberts RC (2015) Elevated excitatory input to the nucleus accumbens in schizophrenia: a postmortem ultrastructural study. Accepted Schizophrenia Bulletin.

B. Positions and Honors

1979-1982 Staff Research Associate, University of California, Irvine, California.
1989-1990 Instructor, Department of Neurology, Harvard Medical School and Massachusetts General Hospital-East, Charlestown, MA
1990-1995 Assistant Professor, Co-Director of the Maryland Brain Collection, University of Maryland School Medicine, Maryland Psychiatric Research Center, Baltimore, Maryland
1995-2000 Adjunct Assistant Professor, Anatomy & Neurobiology, University of Maryland School of Medicine, Baltimore, Maryland
1996-2000 Associate Professor, Director of Maryland Brain Collection, University of Maryland School of Medicine, Maryland Psychiatric Research Center, Baltimore, Maryland
2000-2007 Professor of Psychiatry and Neurobiology and Anatomy, University of Maryland School of Medicine, Maryland Psychiatric Research Center, Baltimore, Maryland.
2007- Primary Appointment: Professor of Psychiatry and Behavioral Neurobiology, University of Alabama at Birmingham, Birmingham Alabama
Secondary Appointments at UAB: Professor, Department of Neurobiology, Department of Cell, Developmental and Integrative Biology; Senior Scientist, Civitan International Research Center.
2008-present Director of The Alabama Brain Collection
2011-present Brain Tissue Coordinator for the Tourette's Syndrome Association
2014-present Member, Scientific Advisory Board for the Tourette's Syndrome Association

HONORS

1979 Excellence in Research Award
1985 American Epilepsy Society Award
2007- present Kathy Ireland Endowed Chair in Psychiatry
2009- present Member of the American College of Neuropsychopharmacology (ACNP)
2012 UAB Graduate Dean's Excellence in Mentorship Award

C. Contributions to Science

1. **Normal human brain electron microscopy**
When I started my own lab at the MPRC (Univ. of Maryland) in 1990, the scientific community was of the opinion that electron microscopy (EM) could not be done on postmortem human brain. The only EM studies in human brain were from tissue obtained from surgical resections of cortex or hippocampus that were adjacent to tumors or epileptic foci, respectively. Outside my lab and the one in Moscow, this still remains true. I went on to examine tissue with short postmortem intervals anyway and found decent preservation at least up to 8 hours after death. Using this tissue, I have published 14 papers on normal human brain ultrastructure and 10 on quantitative comparisons between schizophrenia and controls. Thus my contribution here is to fill a gap in the knowledge of human brain ultrastructure, and make it known that is type of work is possible if you have access to such tissue. Below are listed a sample of the work on control subjects.

1) Roberts RC, Knickman JK (2002) The ultrastructural organization of the patch matrix compartments in the human striatum. J Comp Neurol, 452(2):128-138.

2) Kirkpatrick B, Xu L, Cascella N, Ozeki Y, Sawa A, Roberts RC (2006) DISC1 immunoreactivity at the light and ultrastructural level in the human neocortex. J Comp Neurol, 497(3):436-450. PMID: 16736468

3) McCollum L, Roche J, Roberts RC (2012) Immunohistochemical localization of enkephalin in the human striatum: a postmortem ultrastructural study. Synapse, 66(3):204-219. PMID 22034050.

4) Roberts RC, Roche JK, McCullumsmith RE (2014) Localization of excitatory amino acid transporters EAAT1 and EAAT2 in human postmortem cortex: a light and electron microscopic study. Neuroscience, 277:522-40. PMID: 25064059

2. Antipsychotic effects in animal models

An important part of interpreting pathology in schizophrenic brain is ascertaining what could be caused or masked by antipsychotic treatment. One way to address this problem is to treat animals with antipsychotics and examine their brains. My early work involved anatomical (mostly EM) correlates of medication induced oral dyskinesias in rats, as a model of tardive dyskinesia.

1) Roberts RC, Gaither LA, Gao XM, Kashyap SM, Tamminga CA (1995) Ultrastructural correlates of haloperidol-induced oral dyskinesias in rat striatum. Synapse, 20(3):234-243.

2) Kelley JJ, Gao XM, Tamminga CA, Roberts RC (1997) The effect of chronic haloperidol treatment on dendritic spines in the rat striatum. Exp Neurol, 146(2):471-478.

3) Roberts RC, Force M, Kung L (2002) Dopaminergic synapses in the matrix of the ventrolateral striatum after chronic haloperidol treatment. Synapse, 45(2):78-85.

4) Perez-Costas E, Guidetti P, Melendez-Ferro M, Kelley JJ**,** Roberts RC (2008) Neuroleptics and animal models: feasibility of oral treatments monitored by plasma levels and receptor occupancy assays. Journal of Neural Transmission 115(5):745-53. PMID 18193153.

3. Mitochondria structure and function in normal and schizophrenic brain

Mitochondria are crucial to so many cellular functions, and are abnormal in many diseases. One of the most interesting contributions to the mitochondrial literature I have made was in collaboration with a colleague at UAB (see paper 1, below). In this work we found that mitochondria continue to respond to enzymatic challenges and make ATP as long as 10 hours postmortem in human brain. Moreover, they can be isolated and frozen, revived and tested in parallel with other samples such that comparisons could be made between mitochondrial function in particular diseases, in various brain regions. This holds a lot of promise for innovative research in human brain. Also, mitochondrial genes have been found to be abnormal in schizophrenia, and we find evidence of abnormalities at the ultrastructural and enzymatic levels.

1) Barksdale KA, Perez-Costas E, Gandy JC, Melendez-Ferro M, Roberts RC, Bijur GN (2010) Mitochondrial viability in mouse and human postmortem brain. FASEB J, 24(9):3590-3599. PMID 20466876

2) Somerville SM., Conley RR, Roberts RC (2011) Mitochondria in the Striatum of Subjects with Schizophrenia. World Journal of Biological Psychiatry, 12:48-56. PMID 20698738.

3) Somerville SM, Conley RR, Roberts RC (2012) Striatal mitochondria in subjects with chronic undifferentiated versus chronic paranoid schizophrenia. Synapse, 66 (1):29-41. PMID 21905126.

4) Rice, MW, Smith KL, Roberts RC, Perez-Costas E, Melendez-Ferro M (2014) Assessment of cytochrome C oxidase Dysfunction in the substantia nigra/ventral tegmental area in schizophrenia. PLoS One 9(6).

4. Synaptic organization and other pathology in schizophrenic brain

Quantitative electron microscopy of postmortem schizophrenia brain is only published regularly by my lab and Uranova and colleagues. The results obtained from EM studies have a much greater resolution than human imaging techniques. The results indicate more glutamate synapses in schizophrenia striatum, findings that are supported by imaging studies in larger cohorts.

1) Roberts RC, Conley R, Kung L, Peretti FJ, Chute DJ (1996) Reduced striatal spine size in schizophrenia: a postmortem ultrastructural study. Neuroreport, 7(6):1214-1218.

2) Roberts RC, Roche JK, Conley RR (2005) Synaptic differences in the patch matrix compartments of subjects with schizophrenia: a postmortem ultrastructural study of the striatum. Neurobiol Dis, 20(2):324-335.

3) Roberts RC, Roche JK, Conley RR (2008) Differential synaptic changes in the striatum of subjects with undifferentiated versus paranoid schizophrenia. Synapse, 62(8):616-27. PMID 18509852.

4) Perez-Costas E, Melendez-Ferro M, Rice MW, Conley RR, Roberts RC (2012) Dopamine pathology in schizophrenia: tyrosine hydroxylase expression in the substantia nigra/ventral tegmental area. Frontiers in Schizophrenia, 3:31 PMID 22509170.

5. Neuropathological correlates of treatment resistant/response in schizophrenic brain

Treatment resistance affects about 30% of patients with schizophrenia; they do not get better with current antipsychotic treatment. Imaging studies have supported biological correlates to treatment resistance and response, but no postmortem work has been published addressing this issue. We were able to rate postmortem subjects for treatment resistance and have published the only studies, to my knowledge, that examine this problem in postmortem brain. The results also indicate a biological basis to treatment response, and implicate both the dopamine and glutamate system in response and resistance, respectively.

1) Roberts RC, JK Roche, RR Conley, Lahti A. (2009) Dopaminergic synapses in the caudate nucleus of subjects with schizophrenia: relationship to treatment response. Synapse 63:520-530. PMID 19226604.

2) Somerville SM., Lahti AC, Conley RR, Roberts RC. (2011) Mitochondria in the Striatum of Subjects with Schizophrenia: relationship to treatment response. Synapse, 65:215-224. PMID 20665724.

3) Roberts, RC, Roche, JK, Somerville S, Conley RR (2011) Ultrastructural Distinctions Between Treatment Responders and Non-Responders in Schizophrenia: Postmortem Studies of the Striatum, in Mental Illnesses - Evaluation, Treatments and Implications, Prof. Luciano L'Abate (Ed.), pp. 261-286. ISBN: 978-953-307-645-4, InTech, Available from: http://www.intechopen.com/books/mental-illnesses-evaluation-treatments-and-implications/ultrastructural-distinctions-between-treatment-responders-and-non-responders-in-schizophrenia-postmo

4) Barksdale KA, Lahti AC, Roberts RC (2014) Synaptic proteins in the postmortem anterior cingulate cortex in schizophrenia: relationship to treatment and treatment response. Neuropsychopharmacology, 9:2095-103. PMID 24603856.

A complete list of my manuscripts and book chapters can be found at this website: http://www.ncbi.nlm.nih.gov/sites/myncbi/1JkHoDLYgjmAt/bibliography/47442416/public/?sort=date&direction=ascending.

D. Research Support

Kathy Ireland Endowed Chair
Endowment funds each year for unrestricted laboratory use.

Tourette's Syndrome Association
$10,000 per year for unrestricted laboratory funds.

Ongoing Research Grants

RO1MH066123 4/1/2003-11/30/2015
Role: PI; I have overseen the experiments and as senior scientist supervised the junior investigators conducting the science.
Title: Neuropathology of dopamine systems in schizophrenia
Goals: The overall goal of this proposal is to gain insight in the anomalies of dopaminergic neurotransmission in the substantia nigra-ventral tegmental area of schizophrenia that were observed in my previous grant cycle.

1F31MH098566-01A1 (NIH/NIMH) [PI, Lesley McCollum] 9/24/2013-09/23/2015
Role: mentor
Title: Dopamine levels in postmortem human nucleus accumbens in schizophrenia
Goals: The goals of this proposal are to study tyrosine hydroxylase levels in the NA using protein analysis, immunohistochemistry and electron microscopy.

Pending Grant Support

R01MH107730-01 [PI Akira Sawa, Johns Hopkins University]
Title: High throughput marker for cognitive deficit: cellular autofluorescence
Role: Site PI at UAB; My role will be to conduct the electron microscopic analyses and supervise personnel doing this in my lab.
Submitted: 10/2014

Completed Grant Funding

R01 MH081014-01A2 (NIH/NIMH) [PI, Adrienne Lahti] 12/08-11/13
Title: Treatment response in schizophrenia: bridging imaging and postmortem studies
Role: Co-Investigator: conducted an electron microscopic study and supervised a postdoc in my lab who conducted a protein analysis on various transmitters.

1R21 MH087752 (NIH/NIMH) 2/10-11/13
Title: Abnormalities of glutamate transporter localization in schizophrenia
Goals: Using electron microscopy in postmortem tissue from subjects with schizophrenia and rats treated with antipsychotics, we will study the perisynaptic localization of glutamate transporters.
Role: multiple PI with Robert McCullumsmith; I was responsible for all of the electron microscopy on this project.