BIOGRAPHICAL SKETCH

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NAME: Harrison, Fiona E

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

POSITION TITLE: Assistant Professor of 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
University of Wales, Cardiff, UK	B.Sc.	05/2000	Psychology
University of Wales, Cardiff, UK	Ph.D.	06/2005	Behavioral Neuroscience
Vanderbilt University Medical Center, Nashville, TN	Postdoctoral	10/2006	Behavioral Neuroscience
Vanderbilt University Medical Center, Nashville, TN	Postdoctoral	10/2008	Neuroscience/Molecular biology

A. Personal Statement

My core interest is in the investigation of factors directly involving Alzheimer's-related dementias that can impact cognition, but are not the in the main pathways that are traditionally associated with the disease. Work performed during the course of an earlier R01 project in a related area led to 13 publications from my lab and the laboratory of collaborators. Together those manuscripts provide firm support for the critical role of vitamin C as an antioxidant in the brain in neurodegenerative diseases such as Alzheimer's disease, during brain development, and for normal brain function. This success was achieved despite two brief periods of leave to attend to family situations. Most critically, arising from this project was the observation, confirming a finding in my earlier work, that low ascorbate significantly increases the likelihood and severity of seizures in an Alzheimer's disease model. This led me to develop the novel hypotheses that provide a more specific role for ascorbate in synaptic function and cognitive decline through its role in glutamate clearance. I am a knowledgeable and experienced behaviorist, as demonstrated by multiple publications and my role as Scientific Director of the Vanderbilt Neurobehavioral Core. I have previously successfully secured and administered all aspects of an NIA-funded R01 project, and was very productive despite two brief disruptions to my career due to family obligations during that period. As Scientific Director of the Vanderbilt Murine Behavioral Core, and Associate Core Directorship positions within the NICHD-funded U54 grant to the Vanderbilt Kennedy Center and NIMH-funded P30-Conte Center, I am extremely proficient at working with colleagues and trainees at all levels, managing complex data sets, and realizing research goals. I enjoy leading by example, and conducting experiments myself whenever possible. I am proud to participate in outreach programs teaching Neuroscience to children in elementary school through high school, and to non-scientist adults in the community.

B. Positions and Honors

Positions and Employment

2000-2004	Pre-doctoral student, Department of Psychology, Cardiff University, Cardiff, UK
2004-2007	Postdoctoral Fellow, Department of Pharmacology, Vanderbilt University Medical Center (VUMC), Nashville, TN
2007-2008	Postdoctoral Fellow, Diabetes & Endocrinology, VUMC, Nashville, TN
2008-2011	Research Assistant Professor, Diabetes & Endocrinology, VUMC, Nashville, TN
2011–	Assistant Professor, Department of Medicine, VUMC, Nashville, TN
2011-	Faculty member, Vanderbilt Kennedy Center
2012-	Faculty member, Vanderbilt Brain Institute
2015-	Director, Murine Neurobehavioral Core Facility, VUMC, Nashville, TN

Other Experience and professional organizations and services:

1998-2000	Member, British Society for Neuroscience (BNA)
1999-	Vanderbilt Postdoctoral Association: Secretary/treasurer; Committee member
2005-2008	Member, Society for Neuroscience
2005-	Ad hoc reviewer for > 20 peer-reviewed scientific journals: e.g. Free Radical and Molecular Biology, Journal Physiology, Journal Alzheimer's Disease, European Journal of Neuroscience, Behavioral Brain Research, Journal of the American Association for Aging, Nutrition & Metabolism, Cell Death & Disease, Journal of Neural Transmission, Neuroscience, Neurobiology of Aging, Pharmacology, Biochemistry & Behaviour, Neuropharmacology
2009	Ad hoc reviewer for grant applications; Alzheimer's Association
2010	Ad hoc reviewer grant applications; Medical Research Council
2012	Guest Editor, Antioxidants and Redox Signaling - Forum Issue on Vitamin C
2012-2013	Associate Editor J. Alzheimer's disease
2013	Ad hoc reviewer grant applications; Mouse Metabolic Phenotyping Center
2014	Member, Middle Tennessee Chapter of Society for Neuroscience

Honors

2013	Diet and Optimum Health Conference, Linus Pauling Institute, Oregon State University
2014	David Nichol Smith Seminar, University of Sydney, Australia
2014	Korean Society for Food Science and Technology International, 4th International Symposium on Vitamin C, Seoul, South Korea
2014	Hanyang University, Seoul, S. Korea
2016	Invited speaker; American Association for Laboratory Animal Science (AALAS) Appalachian Branch Winter Meeting.

C. Contribution to Science

1. Promoting the idea of critical roles of vitamin C in the brain and characterization of vitamin C synthesis and transport models, and their utilization in models of aging and Alzheimer's disease. Vitamin C is often thought of only as an anti-scorbutic but in addition to its unmatched antioxidant properties, ascorbic acid is a critical co-factor for a number of enzymatic functions in the brain including neurotransmitter synthesis and DNA methylation. Most rodents synthesize their own vitamin C in the liver and thus can never exist in a low or depleted state as humans can. The majority of neuroscience studies, including those that test mechanisms directly involving vitamin C, are therefore tested in non-clinically relevant conditions. Vitamin C deficiency is particularly relevant in age-related diseases. Critically, this point is often missed due to weaknesses inherent in many population studies. Failure to understand the complexities of vitamin C biochemistry and transport may explain why many studies fail to find expected results**.** Over the last 5 years I have worked with all of the known models of vitamin C synthesis and

transport, characterizing many of the brain changes that occur over the course of development, and in animal models of disease, such as Alzheimer's disease models.

a. **Harrison FE**, Yu SS, Van Den Bossche KL, Li L, May JM, McDonald MP (2008) Elevated oxidative stress and sensorimotor deficits but normal cognition in mice that cannot synthesize ascorbic acid. *J Neurochem* **106**, 1198-1208. PMCID: PMC2575028 **(60 citations)**
b. **Harrison FE**, May JM (2009) Vitamin C function in the brain: vital role of the ascorbate transporter SVCT2. *Free Radic Biol Med* **46**, 719-730. PMC2649700 **(287 citations)**
c. Dixit, S; Bernardo, A; Walker, JM; Kennard, JA; Kim, GY; Kessler, ES; **Harrison, FE** (2015) Vitamin C deficiency in the brain impairs cognition, increases amyloid accumulation and deposition, and oxidative stress in APP/PSEN1 and normally-aging mice. *ACS Chemical Neuroscience*, 6(4):570-81. PMC4476071.
d. Warner, TA.; Kang, JQ.; Kennard, JA.; **Harrison, FE**. Low brain ascorbic acid increases susceptibility to seizures in mouse models of decreased brain ascorbic acid transport and Alzheimer's disease. *Epilepsy Res,* **2015,** 110, 20-5. PMC4306812

2. More comprehensive analysis of Barnes maze behaviors, including new analysis techniques, and a direct comparison with water maze in terms of anxyiolytic response. My early publications directly addressed the idea that apparently small differences in testing methodologies for behavioral studies, and differences between labs, can have a huge impact on the quality of data produced. Furthermore, commonly-used analysis techniques are often not the most informative output measures. A number of methodological factors had been assumed, such as anxiety response in water maze, but not tested explicitly. I showed directly differing corticosterone response between the two highly exploited tasks of spatial learning (Water maze and Barnes maze), and showed the extent to which this impacts learning. The additional methods developed for interpretation of Barnes maze are interesting from a learning and memory point of view but are also critical for teasing out more subtle differences in disease models. I conducted and analyzed all of the maze-learning experiments for the below well-cited papers.

a. Harrison FE, Hosseini AH, McDonald MP (2009) Endogenous anxiety and stress responses in water maze and Barnes maze spatial memory tasks. *Behav Brain Res* **198**, 247-251. PMC2663577 **(155 citations)**
b. Harrison FE, Reiserer RS, Tomarken AJ, McDonald MP (2006) Spatial and nonspatial escape strategies in the Barnes maze. *Learn Mem* **13**, 809-819. PMC1783636 **(86 citations)**
c. Reiserer RS, **Harrison FE,** Syverud DC, McDonald MP (2007) Impaired spatial learning in the APPSwe + PSEN1DeltaE9 bigenic mouse model of Alzheimer's disease. *Genes Brain Behav* **6**, 54-65. PMID: 17233641 **(162 citations)**

3. First to report behavioral differences in a mouse model for Smith Lemli Opitz Syndrome. My focus on behavioral methodology and model development, particularly in diseases with a strong oxidative stress component, led me to a collaboration in which I characterized behavioral and neurochemical deficits in different mouse models for Smith Lemli Opitz Syndrome. Given the strong autism-like phenotype of these patients, it is vital that any useful model have valid and relevant, reproducible behavioral changes that can be studied and targeted with therapeutic strategies.

a. Korade Z, Folkes OM, **Harrison FE** (2013) Behavioral and serotonergic response changes in the Dhcr7-HET mouse model of Smith-Lemli-Opitz syndrome. *Pharmacol Biochem Behav* **106**, 101-108. 23541496
b. Korade, Z., Xu, L.**, Harrison, F.E**., Ahsen, R., Hart, S.E., Folkes, O.M., Mirnics, K., Porter, N.A., 2013. Antioxidant Supplementation Ameliorates Molecular Deficits in Smith-Lemli-Opitz Syndrome. Biol Psychiatry. 75(3): 215-22. PMC3874268

Complete List of Published Work from NCBI *My Bibliography* publications (from 30 published works): **http://www.ncbi.nlm.nih.gov/sites/myncbi/fiona.harrison.1/bibliography/40380925/public/?sort=date&direction=ascending.**

Scientific Metrics (on November 28, 2016) H-index: 18; I-10 Index: 23; Total Citations: 1,349

D. Research Support

Ongoing Research Support

1U54 HD083211-01A1 (Dykens) 09/01/2015 – 08/31/2020 1.2 CM
NIH $828,024
Eunice Kennedy Shriver Intellectual and Developmental Research Center at Vanderbilt University
In the current proposal we seek to provide a better view into the sensory and multisensory processing changes that accompany autism, and changes in the brain networks that subserve sensory and multisensory function. Although extraordinarily valuable in their own right, our goal is to map these sensory- and brain-based changes onto weaknesses in social communicative function, and to use this information in an effort to develop behavioral tools that could be used in remediation. The overarching conceptual framework is that alterations in sensory and multisensory function and the associated brain networks contribute to the social communication deficits that characterize ASD, and can be key targets in the development of novel remediation tools.

W81XWH-15-1-0096 (Rex) 09/30/2015-09/29/2016 1.2 CM
Department of Defense $139,838
Dietary approaches to protect against eye blast-induced oxidative stress and vision loss
The major goal of this project is to determine if vision can be preserved after eye trauma by treatment with antioxidants and/or a ketogenic diet. We hypothesize that delayed vision loss from trauma is due oxidative stress-induced neuronal damage that can be blocked by the proposed therapeutic interventions.

VUMC(4P50MH096972-05) (Blakely) 07/01/2016-06/30/2017 1.2 CM
NIMH $1,629,738
Enduring Effects of Early-Life Serotonin Signaling - Physiology & Behavior Core
Serotonin (5-HT) influences a wide variety of behaviors including anxiety, mood, appetite, sleep, and aggression. Disrupted 5-HT signaling is linked to anxiety, depression, suicide, schizophrenia, obsessive compulsive disorder (OCD) and autism. Increasingly, we recognize that 5-HT signaling initiates during embryonic development and involves a dynamic interaction between CNS and peripheral tissues. Our studies represent an integrated analysis, using novel transgenic mouse models, of how embryonic and early postnatal 5-HT signaling dictates enduring facets of physiology whether altered developmental 5-HT signaling leads to permanent or reversible alterations. Finally, we extend the impact of our work beyond the sphere of the academic community, enhancing the training mission and outreach efforts of the Vanderbilt Conte Center.

Completed Research Support

1R01AG038739-01
NIH/NIA 03/01/11-02/29/16 (NCE)
Vitamin C and cognition in Alzheimer's disease **(Harrison – PI)**
The project examines the role of vitamin C in the brain in prevention of Alzheimer's disease in genetically engineered mouse models. The mice carry two mutated genes known to cause Alzheimer's disease in humans, and also additional or fewer copies of the brain vitamin C transporter (SVCT2). It also examines the possibility of vitamin C as a therapeutic agent by administration directly into the CSF.
Role: **Principal Investigator**

R01 5R01CA163838
NIH/NCI
The role of GSK3 in radiation brain damage (Xia – PI) 07/01/12-06/30/17
This project examines the potential role of GSK3b in regulating NHEJ-mediated repair of double strand DNA breaks, and determining neuron cytotoxicity following cranial irradiation, via suppression of 53BP1 and 2-catenin function. A key experiment of this project is the behavioral testing of different mouse lines that have

undergone irradiation, with or without pre-treatment, to determine changes in learning and memory
Role: **Collaborator** (PI - Fen Xia, Ohio State University)

Serotonergic and behavioral changes in a mouse model of Smith Lemli Opitz Syndrome. 04/01/14-03/31/15
(Harrison – PI)
Conte Center Pilot Funding, Vanderbilt University $20'000
Role: **Principal Investigator**