BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: James Patterson (Pat) McAllister II, PhD

eRA COMMONS USER NAME (credential, e.g., agency login): AD9371

POSITION TITLE: Professor

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
Earlham College, Richmond, IN	BA	06/1970	Biology
Purdue University, West Lafayette, IN	PhD	12/1976	Neurobiology
University of Vermont College of Medicine, Dept. of Anatomy & Neurobiology, Burlington, VT	Postdoctoral Fellow	06/1978	Developmental Neuroanatomy

A. Personal Statement

The Limbrick/McAllister lab maintains a comprehensive interdisciplinary research program whose ultimate goal is to improve clinical treatments for hydrocephalus, a prevalent disorder caused by failure to absorb cerebrospinal fluid (CSF). This program continues to explore the cellular and physiological neuropathology associated with pediatric hydrocephalus and uses various animal models to focus on neuroinflammation, non-invasive neuroimaging (MRI, diffusion tensor imaging, and MR elastography), pharmacological strategies for neuroprotection and recovery of function, and the development and testing of novel surgical and bioengineering approaches for new treatment applications. Our recent initiation of infant/juvenile piglet models of post-inflammatory and post-hemorrhagic hydrocephalus sets the stage for a wide variety of experimental and surgical studies on these clinically-relevant models; these include (but are not limited to) systematic evaluations of novel neurosurgical treatments. We currently have ongoing bioengineering studies, including those with Dr. Harris as a key collaborator, on novel catheters designed to reduce shunt obstruction. Having spent 38 years investigating the pathophysiology of hydrocephalus and having received the Robert H. Pudenz Award for Excellence in Cerebrospinal Fluid Physiology and Hydrocephalus, as well as a Distinguished Service Award from the Hydrocephalus Association, I can attest to the importance elucidating the cell types that obstruct ventricular catheters and the mechanisms underlying cell adhesion and growth; this proposal will help to fill these gaps and identify critical targets for future pharmacological interventions. On a personal level, it is a great pleasure to continue my collaboration with Dr. Harris, who received her doctorate with me and has now become a leader in the field of shunt obstruction. The following most-recent publications support this project:

1. Hariharan P, Sondheimer J, Petroj A, Gluski J, Jea A, Whitehead WE, Sood S, Ham SD, Rocque BG, Marupudi NI, **McAllister JP 2nd**, Limbrick D, Del Bigio MR, Harris CA. A multicenter retrospective study of heterogeneous tissue aggregates obstructing ventricular catheters explanted from patients with hydrocephalus. *Fluids Barriers CNS*. 2021; 18(1):33.
2. Harris CA, Morales DM, Arshad R, **McAllister JP 2nd**, Limbrick DD, Jr. Cerebrospinal fluid biomarkers of neuroinflammation in children with hydrocephalus and shunt malfunction. *Fluids Barriers CNS.* 2021;18(1):4.
3. Al-Saloum S, Zaranek M, Horbatiuk J, Gpalalkrishhnan P, Dumitrescu A., **McAllister JP 2nd**, Harris CA. Analysis of N-acetyl cysteine modified polydimethylsiloxane shunt for improved treatment of hydrocephalus. *J Biomed Mater Res B Appl Biomater.* 2021; 109(8):1177-1187.
4. Gluski J, Zajciw P, Hariharan P, Morgan A, Morales DM, Jea A, Whitehead W, Marupudi N, Ham S, Sood S, **McAllister JP 2nd**, Limbrick DD Jr, Harris CA. Characterization of a multicenter pediatric-hydrocephalus shunt biobank. *Fluids Barriers CNS.* 2020. 17(1):45.

B. Positions and Honors

Employment

1978-1981	Assistant Research Anatomist, UCLA Mental Retardation Research Center, Los Angeles, CA
1981-1993	Assistant & Associate Professor with tenure, Temple University School of Medicine, Departments of Anatomy and Cell Biology and Neurosurgery, Philadelphia, PA
1993-1997	Associate Professor, Director of Neurosurgical Research, and co-director of the Cleveland Clinic Hydrocephalus Project, Cleveland Clinic Foundation, Dept. of Neurosurgery, Cleveland, OH
1997-2007	Professor, Director of Basic Science Research, and Director of the Cortical Implant Project, Wayne State Univ. Sch. Medicine, Depts of Neurological Surgery & Ophthalmology, Detroit, MI
2007-2014	Professor of Neurosurgery with tenure, University of Utah, Salt Lake City, UT
2014-	Professor Emeritus, University of Utah, Salt Lake City, UT
2014-	Research Professor of Neurosurgery, Washington University School of Medicine and St. Louis Children's Hospital, St. Louis, MO

Other Experience and Professional Memberships

Federal Government Public Advisory Committee(s) – last 5 years

2013-present	Grant Review Committee/Study Section, 2013/08 ZNS1 SRB-M (81) Loan Repayment Program
2011-present	Grant Review Committee/Study Sections (14 times), NIH Study Section ZRG1 ETTN-K 10, Neuroprosthetics and Neurological and Auditory Devices Small Business
2010-present	Special Emphasis Panel Small Business: Clinical Neurophysiology, Devices, Neuroprosthetics and Biosensors

Teaching and Professional Activities (last 8 years)

2013-present	Mentored 4 doctoral, 3 masters, 1 post-doctoral (resident), 1 medical, and 4 undergraduate students
2006-present	Hydrocephalus Association Medical Advisory Board
2014-2018	President and President-Elect, Society for Research into Hydrocephalus and Spina Bifida

Honors

2002	Faculty College Teaching Award – Wayne State University School of Medicine
2005	Robert H. Pudenz Award for Excellence in Cerebrospinal Fluid Physiology and Hydrocephalus, International Society for Pediatric Neurosurgery
2006	Matson Memorial Lecturer, American Association of Neurological Surgeons/Congress of Neurological Surgery Section on Pediatric Neurological Surgery
2014	Casey Holter Memorial Lecturer, Society for Research into Hydrocephalus and Spina Bifida
2015	Distinguished Service Award, Hydrocephalus Association

C. Contributions to Science

1. **Characterized the pathophysiology of neonatal and infantile hydrocephalus.** Hydrocephalus is a common and debilitating condition that primarily afflicts children and elderly adults. Prognosis is poor, especially because the only treatment available is surgical diversion (shunting) of cerebrospinal fluid (CSF), and 90% of these procedures fail, often repeatedly, within 10 years. Furthermore, both surgical and potentially medical treatments are hampered because the pathophysiology of hydrocephalus is extremely multifactorial. Nevertheless, 38 years ago a neurosurgical colleague raised my awareness of the need to characterize the pathophysiology of neonatal and infantile hydrocephalus, and that has been my mission since that time. As a basic developmental neuroanatomist, I have developed new experimental models (acquired and congenital in rodent, feline, ferret, canine and porcine species). I have also evaluated human species. I have used all of these approaches to describe the time course and magnitude of alterations in dendrite morphology and synapses, cell death, connectivity, neurotransmitters and neuromodulators, CSF physiology and hydrodynamics, and especially astrocytes, microglia and neural progenitor cells. The following most-recent publications support this contribution:

a. Wagshul ME, **McAllister JP II**, Limbrick DD, Jr., et al. MR Elastography Demonstrates Reduced White Matter Shear Stiffness in Early-Onset Hydrocephalus. *NeuroImage Clinical.* 2021;in press.
b. Isaacs AM, Shimony JS, Morales DM, Castaneyra-Ruiz L, Hartman A, Cook M, Smyser CD, Strahle J, Smyth MD, Yan Y, **McAllister JP**, McKinstry RC, Limbrick DD.. Feasibility of fast brain diffusion MRI to quantify white matter injury in pediatric hydrocephalus. *J Neurosurg Pediatr.* 2019:1-8.

c. Castaneyra-Ruiz L, Morales DM, **McAllister JP**, Brody SL, Isaacs AM, Strahle JM, Dahiya SM, Limbrick DD. Blood Exposure Causes Ventricular Zone Disruption and Glial Activation In Vitro. *J Neuropathol Exp Neurol.* 2018;77(9):803-813.
d. **McAllister JP II**, Guerra MM, Morales DM, Jimenez AJ, Castaneyra Ruiz L, Dominguez-Pinos, D, Sival D, den Dunnen W, Schmidt RE, Rodriguez EM, Limbrick DD, Jr. (2017). Ventricular zone disruption in human neonates with intraventricular hemorrhage. *J Neuropathol Exp Neurol* 76(5):358-375.

2. **Developed animal models amenable to CSF shunting and advanced understanding of recovery mechanisms in hydrocephalus**. When I first began my studies in hydrocephalus there were no animal models that replicated the standard treatment of CSF shunting. Since recovery and plasticity were a focus of my interests in developmental neurobiology, we began to develop infantile feline and rodent models with customized and/or commercial CSF diversion systems. We were the first to introduce these models and our contributions have continued to provide a better understanding of the timing, effectiveness, and cellular responses to shunting. Related to this work was the introduction for the first time of a reliable model of communicating hydrocephalus; practically all previous experimental work utilized models of non-communicating (obstructive) hydrocephalus, although communicating hydrocephalus was prevalent in many forms of hydrocephalus. Recently, we have perfected the juvenile porcine model of communicating hydrocephalus and successfully treated these animals with CSF shunt and endoscopic third ventriculostomy with and without choroid plexus cauterization.

a. **McAllister JP II**, Talcott M, Isaacs AM, Hartman A, Castaneyra Ruiz L, Zwick S, Limbrick DD Jr. Development of a clinically-relevant porcine model of juvenile hydrocephalus. *Fluids Barr CNS,* 2021; in press.
b. Eskandari R, **McAllister JP II**, Miller JM, Ding Y, Ham SD, Shearer DM, Way JS (2004). Effects of hydrocephalus and ventriculoperitoneal shunt therapy on afferent and efferent connections in the feline sensorimotor cortex. *J Neurosurg*, *101*(2 Suppl), 196-210.
c. Li J, **McAllister JP II**, Shen Y, Wagshul ME, Miller JM, Egnor MR, Johnston MG, Haacke EM, Walker ML (2008). Communicating hydrocephalus in adult rats with kaolin obstruction of the basal cisterns or the cortical subarachnoid space. *Exp Neurol*, *211*(2), 351-61.
d. **McAllister JP II**, Cohen, MI, O'Mara KA, Johnson MH (1991). Progression of experimental infantile hydrocephalus and effects of ventriculoperitoneal shunts: an analysis correlating magnetic resonance imaging with gross morphology. *Neurosurg, 29*(3), 329-340.

3. **Explored pharmacological interventions and compared shunt timing for improved treatments in hydrocephalus.** Although current surgical treatments for hydrocephalus are fraught with problems that seriously impact prognosis, very few attempts have been made to supplement shunting with pharmacological interventions. Therefore, we have shown that early shunting is more effective than late CSF diversion and explored the potential for anti-inflammation agents to promote recovery, with our initial results showing promise.

a. **McAllister JP II,** Miller JM (2010). Minocycline inhibits glial proliferation in the H-Tx rat model of congenital hydrocephalus. *Cerebrospinal Fluid Research*, *7*, 7.
b. Eskandari R, Packer M, Burdett EC, **McAllister JP II** (2012). Effect of delayed intermittent ventricular drainage on ventriculomegaly and neurological deficits in experimental neonatal hydrocephalus. *Childs Nerv Syst*, *28*(11), 1849-1861.
c. Botfield H, Gonzalez AM, Abdullah O, Skjolding AD, Berry M, **McAllister JP II**, Logan A (2013). Decorin prevents the development of juvenile communicating hydrocephalus. *Brain*, *136*(Pt 9), 2842-58.
d. Aojula A, Botfield H, **McAllister JP II**, Gonzalez AM, Abdullah O, Logan A, Sinclair A (2016). Diffusion tensor imaging with direct cytopathological validation: characterisation of decorin treatment in experimental juvenile communicating hydrocephalus. *Fluids and Barriers of the CNS 13*(1), 1-9.

4. **Developed bioengineering applications to improve treatment of hydrocephalus**. Because shunt catheters often become obstructed with tissue (30%, 40% and 90% in years 1, 2 and 10, respectively), we have been using bioengineering advancements to prevent cell adhesion on silicone catheters. Our findings using NAC are particularly promising.

a. Harris CA, Resau JH, Hudson EA, West RA, Moon C, Black AD, **McAllister JP II** (2011). Effects of surface wettability, flow, and protein concentration on macrophage and astrocyte adhesion in an in vitro model of central nervous system catheter obstruction. *J Biomed Mater Res A*, *97*(4), 433-40

b. Harris CA, Resau JH, Hudson EA, West RA, Moon C, Black AD, **McAllister JP II** (2011). Reduction of protein adsorption and macrophage and astrocyte adhesion on ventricular catheters by polyethylene glycol and N-acetyl-L-cysteine. *J Biomed Mater Res A*, *98*(3), 425-33.
c. Harris CA, **McAllister JP II** (2012). What we should know about the cellular and tissue response causing catheter obstruction in the treatment of hydrocephalus. *Neurosurgery*, *70*(6), 1589-601; discussion 1601-2.
d. Galarza M, Gimenez A, Amigo JM, Schuhmann MU, Gazzeri R, Thomale U, **McAllister JP II** (2017). Next generation of ventricular catheters for hydrocephalus based on parametric designs. *Childs Nerv Syst*: epub in press.

5. **Mentored basic and clinical scientists in hydrocephalus research and promoted constructive reviews of the field**. In order to expand research efforts and improve treatments for hydrocephalus, it is very important to motivate and train young investigators. In addition, it is critical to share information and critique ongoing research so that advancements can be clinically relevant. I have tried to contribute to these efforts by mentoring promising students and organizing international symposia to review progress in hydrocephalus research.

a. Bergsneider M, Egnor MR, Johnston M, Kranz D, Madsen JR, **McAllister JP II**, Stewart C, Walker ML, Williams MA (2006). What we don't (but should) know about hydrocephalus. *J Neurosurg*, *104*(3 Suppl), 157-9.
b. Williams MA, **McAllister JP II**, Walker ML, Kranz DA, Bergsneider M, Del Bigio MR, Fleming L, Frim DM, Gwinn K, Kestle JR, Luciano MG, Madsen JR, Oster-Granite ML, Spinella G (2007). Priorities for hydrocephalus research: report from a National Institutes of Health-sponsored workshop. *J Neurosurg*, *107*(5), 345-357
c. **McAllister JP II**, Williams MA, Walker ML, Kestle JR, Relkin NR, Anderson AM, Gross PH, Browd SR, Hydrocephalus Symposium Expert Panel. (2015). An update on research priorities in hydrocephalus: overview of the third National Institutes of Health-sponsored symposium "Opportunities for Hydrocephalus Research: Pathways to Better Outcomes". *J Neurosurg*, *123*(6), 1427-1438.
d. Koschnitzky JE, Keep RF, Limbrick DD, **McAllister JP**, Morris JA, Strahle J, Yung YC. Opportunities in posthemorrhagic hydrocephalus research: outcomes of the Hydrocephalus Association Posthemorrhagic Hydrocephalus Workshop. *Fluids Barriers CNS, 15*(1), 1-11.

Complete List of Published Work in MyBibliography (109 total publications)**:**
https://www.ncbi.nlm.nih.gov/myncbi/james.mcallister.1/bibliography/public/

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

NIH 5R21NS111249-02 McAllister JP (Contact PI); Limbrick DD (Co-PI) 01/01/2020 - 12/31/2021
Experimental endoscopic third ventriculostomy with choroid plexus cauterization and its effects on brain development
The major goal of this project is to evaluate the effects of endoscopic third ventriculostomy with or without choroid plexus cauterization in a porcine model of juvenile hydrocephalus, which we have developed.
Role: Contact PI. Overlap: none

NIH R42NS103704 Bandyopadhyay S (PI); McAllister JP (subaward PI) 09/30/2020-08/31/2023
NIH/NINDS
Omniphobic cerebral shunt to eliminate clogging and dysfunction
This is a collaborative effort with FreeFlow Medical, Inc. to improve the outcomes of patients with hydrocephalus by designing shunt catheters resistant to obstruction.
Role: Co-Investigator

NIH 1R01NS094570-01A1 Harris CA (PI); Limbrick DD (Co-PI) 06/15/2016-12/31/2021
Investigating the Cellular Mechanisms Leading to Repetitive Shunt Failure in the Treatment of Pediatric Hydrocephalus
The major goals of this project are to characterize in children with hydrocephalus the types of cells that obstruct CSF drainage catheters, to identify CSF biomarkers associated with catheter obstruction, and to begin to develop catheter coatings that prevent shunt obstruction.

Role: Subaward PI. Overlap: none

NIH 1U44NS121555 - 01 Somera AL (PI); Limbrick DD (Co-PI). 11/01/2021-10/31/2022
Noninvasive Wireless Thermal Sensors for the Quantitative Monitoring of Ventricular Shunt Function in Patients with Hydrocephalus
The major goal of this project are to provide proof-of-concept for a CSF-flow sensor. The Washington University subaward will test this cutaneous device on shunt catheters placed in a juvenile model of hydrocephalus.
Role: Co-Investigator. Overlap: none

Hydrocephalus Association Limbrick (PI) 10/01/2018-12/31/2021
Pharmacological Prevention of Post-hemorrhagic Hydrocephalus of Prematurity (PHH)
The major goal of this project is to develop and test several promising drugs and molecular mechanisms in order to prevent or reduce the pathogenesis and pathophysiology of PHH using cell culture and animal model experiments.
Role: Co-Investigator. Overlap: none

Completed Research Support (last 3 years)

Microbot Medical, Inc. McAllister & Limbrick (Co-PI) 02/15/2017-6/1/2021
In Vivo Tests of the Microbot Medical SCS Device
The major goal of this project is to determine the efficacy of the Microbot Medical SCS device to prevent or remove tissue obstructions from ventricular catheters by testing the device in a porcine model of hydrocephalus.
Role: Lead PI. Overlap: none

Rudi Schulte Research Institute McAllister (PI) 12/01/2018-11/30/20
Experimental Studies to Validate Magnetic Resonance Elastography in Hydrocephalus
The major goal of this clinical project is to measure brain tissue compliance using magnetic resonance elastography and diffusion tensor imaging in early and middle stages of experimental post-hemorrhagic hydrocephalus (infant ferrets), and to determine the role that compliance plays in the development and progression of the cytopathology associated with this disorder.
Role: Co-Investigator. Overlap: none

Rudi Schulte Research Institute Wagshul (PI) 03/10/14-06/01/20
MR Elastography: A Non-invasive Tool for Management of Shunted Pediatric Hydrocephalus
The major goal of this clinical project is to measure brain tissue compliance using magnetic resonance elastography in early and middle stages of human pediatric hydrocephalus, and to determine the role that compliance plays in the development and progression of slit ventricles.
Role: Co-Investigator, subaward PI. Overlap: none

Hydrocephalus Association Harris & McAllister (Co-PI) 12/1/2018-11/30/2019
Development of Shunt Catheters that Resist Occlusion
The major goal of this project is perform preliminary tests on ventricular catheters coated with a tissue-resistant polymer, N-acetyl cysteine, in vitro and in vivo using our piglet model of hydrocephalus.
Role: Subaward PI. Overlap: none.