BIOGRAPHICAL SKETCH

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NAME: Jeffrey J Neil

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

POSITION TITLE: Professor of Neurology

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
Washington University, St. Louis	B.A.	1977	Biology
Washington University, St. Louis	M.D.	1984	Medicine
Washington University, St. Louis	Ph.D.	1984	Neurobiology

A. Personal Statement

I am a practicing child neurologist with a research career that has spanned over three decades. My career has been focused on both technical development of magnetic resonance imaging (MRI) methods and the application of MRI to understanding brain development and injury. The model systems I have studied range from single frog oocytes through cultured neurons/glia through human infants. Thus, I am thoroughly familiar with both preclinical and clinical applications of MRI. While many of these studies have focused on brain development and its disruption, I have also performed a number of studies aimed at understanding the basic biophysics of water diffusion as measured by MR.

1. Sehy JV, Ackerman JJH, **Neil JJ**, The apparent diffusion coefficient of water, ions, and small molecules in *Xenopus* oocyte is consistent with Brownian displacement, Magn Reson Med 2002: 48: 42-51.
2. Yang DM, Huettner JE, Bretthorst GL, **Neil JJ**, Garbow JR, Ackerman JJH, Intracellular water preexchange lifetime in neurons and astrocytes, Magn Reson Med 2018: 79: 1616-1627 PMC5754269.
3. Duong TQ, Ackerman JJH, Ying HS, **Neil JJ**, Evaluation of extra- and intracellular apparent diffusion in normal and globally-ischemic rat brain *via* ^{19}F NMR, Magn Reson Med 1998: 40: 1-13.
4. McKinstry RC, MD, Mathur A, Miller JH, Ozcan A, Snyder AZ, Schefft GL, Almli CR, Shiran SI, Conturo TE, **Neil JJ**, Radial organization of developing human cerebral cortex revealed by non-invasive water diffusion anisotropy MRI, Cerebral Cortex 2002: 12: 1237-1243
5. Smyser CD, Snyder AZ, Shimony JS, Mitra A, Inder TE, **Neil JJ**, Resting-state network complexity and magnitude are reduced in prematurely born infants, Cerebral Cortex 2016: 26: 322-333 PMC4677980

B. Positions and Honors

Positions and Employment

1976-1977 Senior year at Washington University in St. Louis; graduated summa cum laude with a B.A. in Biology.
1977-1984 Attended Washington University School of Medicine in the Medical Scientist Training Program; graduated with Ph.D. in Neurobiology and M.D.
1984-1986 General Pediatric Residency, St. Louis Children's Hospital, St. Louis, MO.
1986-1990 Fellow in Pediatric Neurology at St. Louis Children's Hospital, St. Louis, MO.
1990-1992 Instructor in Pediatrics and Neurology, St. Louis Children's Hospital, St. Louis, MO.
1992-1999 Assistant Professor of Neurology and Pediatrics, St. Louis Children's Hospital, St. Louis, MO.
1999-2004 Associate Professor of Neurology, Pediatrics and Radiology, St. Louis Children's Hospital, Washington University School of Medicine, St. Louis, MO.
2004-2013 Professor of Neurology, Pediatrics and Radiology, St. Louis Children's Hospital, Washington

University School of Medicine, St. Louis, MO.
2014-2018 Visiting Professor of Neurology, Boston Children's Hospital, Boston, MA.
2018-present Professor of Neurology, Pediatrics and Radiology, St. Louis Children's Hospital, Washington University School of Medicine, St. Louis, MO.

Other Experience and Professional Memberships

1983 Society for Neuroscience
1989 Missouri medical license R7J33
1989 Board certification in General Pediatrics
1989 Society of Magnetic Resonance in Medicine
1991 Board certification in Neurology with special competence in Child Neurology
1992 Child Neurology Society
2003 Society for Pediatric Research

Honors

1978 The Antoinette Frances Dames Prize in Physiology and Biophysics
Phi Beta Kappa, Washington University
1984 The George F. Gill Prize in Pediatrics
1984 The James L. O'Leary Research Prize in Neurosciences
1993 Child Neurology Society Young Investigator Award
2004 Allen P. and Josephine B. Green Chair of Neurology and Pediatrics
2009 Fellow of the International Society for Magnetic Resonance in Medicine
2014 President, International Society for Magnetic Resonance in Medicine

C. Contribution to Science

C.1. The reduction of brain water apparent diffusion coefficient following injury forms the basis for the widespread use of this method in clinical practice for early detection of brain injury. We have been seeking to understand the biophysical basis of this phenomenon by measuring compartment-specific (intracellular/extracellular) changes in water displacements following brain injury. We have employed model systems ranging from single *Xenopus* oocytes to cultured HeLa cells to rodents. To obtain compartment-specific measures, we have employed a variety of reporter molecules and nuclei for MR detection (^{1}H, ^{19}F, ^{23}Na, ^{31}P and ^{133}Cs). In addition, we have measured intracellular water preexchange lifetimes to better model water diffusion in mammalian systems. We have refuted the once commonly held hypothesis that the reduction in diffusion is caused by shift of water from the extra- to the intracellular compartment, and identified the important role of changes in intracellular water displacements in this process.

1. Duong TQ, Ackerman JJH, Ying HS, **Neil JJ**, "Evaluation of extra- and intracellular apparent diffusion in normal and globally-ischemic rat brain *via* ^{19}F NMR," *Magn Reson Med* **40**, 1-13 (1998).
2. Sehy JV, Ackerman JJH, **Neil JJ**, "The apparent diffusion coefficient of water, ions, and small molecules in *Xenopus* oocyte is consistent with Brownian displacement," *Magn Reson Med* **48**, 42-51 (2002).
3. Kroenke CD, Ackerman JJH, **Neil J**, "Magnetic resonance measurement of tetramethylammonium diffusion in rat brain: Comparison if magnetic resonance and ionophoresis *in vivo* diffusion measurements." *Magn Reson Med* **50**, 717-726 (2003).
4. Goodman JA, Ackerman JJH, **Neil JJ**, "Intracellular cesium ion diffusion in the rat brain decreases markedly upon death," *Magn Reson Med* **59**, 65-72 (2008).

C.2. I have had a longstanding interest in cortical development and its disruption in association with preterm birth. One approach to evaluating cortical maturation is to employ water diffusion anisotropy. In immature cortex, water displacements are anisotropic because of the radial organization of radial glial cells and the apical dendrites of pyramidal cells. As cortex matures (prior to term-equivalent postmenstrual age), this anisotropy is lost due to the elaboration of basal dendrites on pyramidal cells, maturation of interneurons, and myelination of intracortical axons. We detected this phenomenon first in preterm human infants, and further clarified its mechanism in baboon studies. We have shown that the reduction in anisotropy varies regionally, in parallel with differential rates of regional cortical development, and provides a means by which to assess cortical development and its disruption in preterm infants.

1. McKinstry RC, MD, Mathur A, Miller JH, Ozcan A, Snyder AZ, Schefft GL, Almli CR, Shiran SI, Conturo TE,

Neil JJ, "Radial organization of developing human cerebral cortex revealed by non-invasive water diffusion anisotropy MRI," *Cerebral Cortex*, **12**, 1237-1243 (2002).
2. Kroenke CD, Bretthorst GL, Inder TE, **Neil JJ**, "Diffusion MR imaging characteristics of the developing primate brain," *NeuroImage* **25**, 1205-1219 (2005).
3. Kroenke CD, Bretthorst GL, Inder TE, **Neil JJ**, "Modeling water diffusion anisotropy within fixed prenatal primate brain using Bayesian probability theory," *Magn Reson Med* **55**, 187-197 (2006).
4. Kroenke CD, Van Essen DC, Inder TE, Rees S, Bretthorst GL, **Neil JJ**, "Microstructural changes of the baboon cerebral cortex during gestational development reflected in MRI diffusion anisotropy," *J Neurosci* **27**, 12506-12515 (2007).

C.3. A second means by which to evaluate cortical maturation is *via* resting state functional connectivity MRI (fcMRI). Unlike conventional, task-based functional MRI, fcMRI data are collected while the subject is resting quietly, making it suitable for studying infants. We have applied this method to both normal development and the effects of preterm birth. We have shown that networks develop at different rates for different systems, with physically longer connections developing more slowly than shorter ones, and also systems known to mature faster on the basis of histologic studies (*e.g.,* motor cortex) developing faster than those known to mature slower (*e.g.,* frontal cortex). We have also shown that cortical networks are altered by preterm birth.
1. Smyser CD, Inder TE, Shimony JS, Hill JE, Degnan AJ, Snyder AZ, **Neil JJ**, "Longitudinal analysis of neural network development in preterm infants," *Cerebral Cortex* **20**, 2852-2862 (2010). PMC2978240
2. Smyser C, Snyder AZ, **Neil JJ**, "Functional connectivity MRI in infants: Exploration of the functional organization of the developing brain," *Neuroimage* **56**, 1437-1452 (2011). PMC3089442
3. Smyser C, Snyder AZ, Shimony JS, Blazey TM, Inder TE, **Neil JJ**, "Effects of white matter injury on resting state fMRI measures in prematurely born infants," *PLoS ONE* **8**, e68098 (2013). PMC3706620
4. Smyser CD, Snyder AZ, Shimony JS, Mitra A, Inder TE, **Neil JJ**, "Resting-state network complexity and magnitude are reduced in prematurely born infants," *Cerebral Cortex* **26**, 322-333 (2016). PMC4677980

C.4. In collaboration with research groups in Boston, St. Lois and Melbourne, I have been studying the effects of preterm birth on brain development (*via* MRI) and neurodevelopmental outcome. This includes identifying the location and timing of alterations in brain structure that underly adverse neurodevelopmental outcomes. Among our more recent publications, we have evaluated the effect of NICU environment. In one of these studies, we found that premature infants who spent their NICU stay in single-patient rooms had worse neurodevelopmental outcomes, particularly for language, than those who stayed in an open ward. Further, the normal asymmetry of the superior temporal sulcus, a language area, was present at term-equivalent age in infants from open wards, but not those from single-patient rooms. Recordings from these environments suggest that infants in single-patient rooms have less language exposure than those in open wards. We hypothesize that this relative sensory deprivation during a critical period of development adversely affects development of language areas. These findings are leading to reconsideration of the American Board of Pediatrics recommendation that preterm infants be housed in a single-patient room environment.
1. Rogers CE, Anderson PJ, Thompson DK, Kidokoro H, Wallendorf M, Treyvaud K, Roberts G, Doyle LW, **Neil JJ**, Inder TE, "Regional cerebral development at term relates to school-age social-emotional development in very preterm children," *J Am Acad Child Adolesc Psychiatry* **51**, 181-191 (2012). PMC3411187
2. Pineda R, **Neil J**, Dierker D, Smyser C, Wallendorf M, Kodokoro H, Reynolds L, Walker S, Rogers C, Mathur A, Van Essen D, Inder T, "Alterations in brain structure and neurodevelopmental outcome in preterm infants hospitalized in different neonatal intensive care unit environments," *J Pediatr* **164**, 52-60 (2014). PMC3872171
3. Engelhardt E, Inder TE, Alexopoulos D, Dierker DL, Hill J, Van Essen DC and **Neil JJ**, "Regional impairments of cortical folding in premature infants," *Ann Neurol*. **77**, 154-162 (2015). PMC4324979
4. Steinhorn R, McPherson C, Anderson P, Zhang Y, Alexopoulous D, **Neil JJ**, Doyle LW, Inder T. Neonatal morphine exposure in very preterm infants – cerebral development and outcomes. *J Peds* **166**, 1200-1207 (2015).

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/jeffrey.neil.1/bibliograpahy/40816801/public/?sort=date&direction=ascending