**BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person.

| NAME<br>Warren David Lo | POSITION TITLE<br>Clinical Professor<br>Depts. Pediatrics and Neurology<br>The Ohio State University |
|---|---|
| eRA COMMONS USER NAME<br>LOWARR | |

EDUCATION/TRAINING

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | MM/YY | FIELD OF STUDY |
|---|---|---|---|
| Northwestern University, Illinois | BS | 06/1973 | Medical Education |
| Northwestern University, Illinois | MD | 06/1977 | Medical School |
| University of Minnesota, Minnesota | | 06/1980 | Pediatric Resident |
| University of California, California | | 06/1983 | Neurology Resident |
| University of Michigan, Michigan | | 06/1985 | Post-Doctoral Scholar |

**A. Personal Statement**

I am excited to be a part of this proposal to create a National Pediatric Rehabilitation Resource Center. This is an outstanding opportunity to gather experts from diverse specialties to pursue high quality, high impact research on pediatric rehabilitation. I will lead the Mentored Collaborative Opportunities as well as serve on the Steering Committee. I contribute to the Didactic Interactions, Promoting Center Expertise, and Techniques Development cores. My research focuses upon assessing the outcomes of pediatric stroke, with an emphasis upon measures that address quality of life and function. One of my contributions that has had broad impact in pediatric stroke research was the development of a telephone interview version of the Pediatric Stroke Outcome Measure, the Recurrence and Recovery Questionnaire. That questionnaire has been adopted as a key outcome measure in multiple studies of pediatric stroke. Beyond that work with the questionnaire, I have pursued studies that examined the social and cognitive sequelae of pediatric stroke. To illustrate my experience and productivity in this area, I list four related publications.


1. Lo W, Gordon AL, Hajek C, Gomes A, Greenham M, Anderson V, Yeates KO, Mackay M. Pediatric Stroke Outcome Measure: Predictor of Multiple Impairments in Childhood Stroke. J Child Neurol. 2014;29(11):1524-30.
2. Lo W, Ichord R, Dowling M.M. The Pediatric Stroke Recurrence and Recovery Questionnaire: Validation in a Prospective Cohort. For the International Pediatric Stroke Study (IPSS) Investigators. The Pediatric Stroke Recurrence and Recovery Questionnaire: Validation in a prospective cohort. Neurology. 2012 Aug 28;79(9):864-870.
3. Lo W, Gordon A, Hajek C, Gomes A, Greenham M, Perkins E, Zumberge N, Anderson V, Yeates KO, Mackay MT. Social Competence Following Neonatal and Childhood Stroke. Int J Stroke. 2014;9(8):1037-44.
4. Anderson V, Gomes A, Greenham M, Hearps S, Gordon A, Rinehart N, Gonzalez L, Yeates K, Hajek C, Lo W, Mackay M. Social competence following pediatric stroke: Contributions of brain insult and family environment. Social Neurosci, 2014;9:471-483.


Regarding my qualifications for this proposal, I have participated in a multi-center observational study that examined the role of infection as a cause of vasculopathy in pediatric stroke, and a multi-center registry for pediatric ischemic stroke. From that participation I have developed an appreciation for the collaboration and communication that is necessary for the success of multi-center studies. I have collaborated in pilot studies of kinematic analysis in very young infants with other team members of involved in this proposal. Most importantly, I am an active Co-PI or Co-I on three multi-center randomized clinical trials involving intensive rehabilitation therapies in infants. As a result of this involvement I am well-versed in the research designs and the robust outcome measures that are needed in studies of rehabilitation and neuroplasticity in children with disabilities. Because of my involvement with networks to study pediatric stroke, I can provide a conduit for pediatric stroke doctors who wish to learn rehabilitation research designs from this core. In turn I can inform the core what the pediatric stroke community needs in terms of rehabilitation research priorities. Beyond the realm of pediatric stroke, at Nationwide Children's Hospital I am part of a research group that examines cognitive and behavioral

outcomes of acquired brain injury with a strong emphasis on traumatic brain injury. In that position, I can reach out to groups of investigators working on TBI and childhood brain cancer to expand the scope of pediatric rehabilitation research to involve these conditions with major public health impact.

**B. Position and Honors**

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|---|---|---|
| 1985 | Attending Pediatric Neurologist, Nationwide Children's Hospital | |
| 1985 | Assistant Professor, Department of Pediatrics | Ohio State University |
| 1986 | Assistant Professor, Department of Neurology | Ohio State University |
| 1991 | Associate Professor, Department of Pediatrics | Ohio State University |
| 1992 | Associate Professor, Department of Neurology | Ohio State University |
| 2011 | Associate Clinical Professor, Dept. Pediatrics | Ohio State University |
| 2013 | Clinical Professor, Dept. Pediatrics and Neurology | Ohio State University |

**National Leadership**

Councilor, Child Neurology Section, American Academy of Neurology, 2008-2010
Member, Child Neurology Society Executive Committee, 2009-2011
Chair, Child Neurology Section, American Academy of Neurology 2015-2017

**National Honors**

Fellow, American Neurological Association 2012

**C. Contribution to Science**

**1. Neonatal stroke and motor outcomes**

I collaborated with Dr. Jill Heathcock (director of the Outcomes Assessment Core for this proposal) in two clinical studies that analyzed the movements of young infants who have suffered stroke. This work identified early indicators of infants who progress to significant neurological impairment. My role was to identify infants with neonatal stroke, recruit them to the study, review the brain imaging studies to assure they met inclusion/exclusion criteria, and perform an initial clinical neurological exam. These studies are important because the clinical exam of a young infant is limited in the ability to identify severe deficits, which leads to delays in referring an affected infant for intervention. This early detection has direct implications for intervention. These studies were important because they demonstrated feasibility and tolerance of this intervention in very young infants, which had not been previously demonstrated.

1. Chen CY, **Lo WD, Heathcock J**. Neonatal stroke causes poor midline motor behaviors and poor fine and gross motor skills during early infancy. *Research in Developmental Disabilities.* 2013 Jan 2;34(3):1011-1017.
2. Chen CY, Tafone S, **Lo W, Heathcock JC**. Perinatal stroke causes abnormal trajectory and lateral reaching during early infancy. *Res Dev Disabil*. 2015, 38:301–308.
3. Lowes LP, Mayhan M, Orr T, Batterson N, Tonneman JA, Meyer A, Alfano L, Wang W, Whalen CN, Nelin MA, **Lo WD**, Case-Smith J. Pilot study of the efficacy of constraint-induced movement therapy for infants and toddlers with cerebral palsy. *Phys Occup Ther Pediatr*. 2014 Feb;34(1):4-21

**2. Outcomes of childhood stroke**

I have pursued studies that examined the social and cognitive sequelae of stroke in older children. Social competence is important for many aspects of an individual's integration with the larger society and social cognition has been examined extensively in childhood autism, however, little work has examined this aspect of social behavior following stroke. With my colleagues, I have shown that social competence is impaired in children who have more severe neurological impairments after stroke while less impaired children have relative sparing of this function. In that study we showed that worse scores on the PSOM are associated with impairments in adaptive behavior and cognition, so that one can anticipate these areas of impairments in children based upon the PSOM scores.

When we compared typically developing children with those who had AIS, the AIS children had significantly more internalizing and social problems, and engaged in less social activities than typically developing children. Poorer parent mental health predicted more internalizing and social problems and lower social participation. Family dysfunction was associated with internalizing problems. Lower parent education contributed to children's social function. These results indicated that children with AIS are at elevated risk of poorer mental health and

social function. The home environment contributes to children's outcomes, suggesting that supporting parent and family function provides an opportunity to optimize child mental health and social outcomes.

Collectively, my work together with my colleagues demonstrates that social functioning is impaired in stroke patients, particularly those who have greater neurological impairment. This impairment spans a range of social skills (competence, participation, adjustment), but specific elements are influenced by family dysfunction and mental health. These elements suggest specific targets for intervention that can may be employed in the improvement of outcomes after childhood AIS. I am currently working on an outcome study of the subjects in the VIPS observational study covered in #**3** below.

1. **Lo W**, Gordon AL, Hajek C, Gomes A, Greenham M, Anderson V, Yeates KO, Mackay M. Pediatric Stroke Outcome Measure: Predictor of multiple impairments in childhood stroke. *J Child Neurol*. 2014;29:1524-30.
2. **Lo W**, Gordon A, Hajek C, Gomes A, Greenham M, Perkins E, Zumberge N, Anderson V, Yeates KO, Mackay MT. Social competence following neonatal and childhood stroke*. Int J Stroke*. 2014;9:1037-44.
3. Anderson V, Gomes A, Greenham M, Hearps S, Gordon A, Rinehart N, Gonzalez L, Yeates K, Hajek C, **Lo W**, Mackay M. Social competence following pediatric stroke: Contributions of brain insult and family environment. *Social Neurosci,* 2014;9:471-483.
4. Araujo GC, Antonini TN, Anderson V, Vannatta KA, Salley CG, Bigler ED, Taylor HG, Gerhardt C, Rubin K, Dennis M, **Lo W**, Mackay MT, Gordon A, Hajek Koterba C, Gomes A, Greenham M, Owen Yeates K. Profiles of executive function across children with distinct brain disorders: Traumatic brain injury, stroke, and brain tumor. *J Int Neuropsychol Soc*. 2017 May 15:1-10.

**3. Effects of infection upon vascular predisposition to ischemic stroke in children**

I have been part of the team that conducted the VIPS observational study of pediatric stroke. The aims of the study were: 1) to determine the association between infection and arteriopathy observed in children with arterial ischemic stroke; 2) to prospectively determine if arteriopathy and inflammatory markers predict stroke recurrence. The three most important findings from that study were: 1) children who had arteriopathy had a high risk of recurrence despite treatment with anti-thrombotic agents; 2) children with few or no routine vaccinations were at a higher risk of stroke than those children who received most or all vaccinations; and 3) evidence of acute herpesvirus infection was associated with a doubling of the odds of stroke, with HSV-1 found to be the most frequent virus. These studies are the first large-scale characterization of risk factors in childhood ischemic stroke, and for the first time identified the importance of herpesvirus infection and vaccination status as risk factors for stroke. I am currently working with colleagues to analyze additional features of this cohort as predictors of clinical outcome after ischemic stroke.

1. Fullerton HJ, Wintermark M, Hills NK, Dowling MM, Tan M, Rafay MF, Elkind MS, Barkovich AJ, deVeber GA; and the **VIPS Investigators**. Risk of recurrent arterial ischemic stroke in childhood: A prospective International study. *Stroke.* 2016 Jan;47(1):53-9.
2. Fullerton HJ, Hills NK, Elkind MS, et al. Infection, vaccination, and childhood arterial ischemic stroke: Results of the **VIPS Study**. *Neurology*. 2015; 85: 1459-66.
3. Elkind MS, Hills NK, Glaser CA, **Lo WD**, Amlie-Lefond C, Dlamini N, Kneen R, Hod EA, Wintermark M, deVeber GA, Fullerton HJ; VIPS Investigators. Herpesvirus infections and childhood arterial ischemic stroke: Results of the VIPS Study. *Circulation.* 2016;133(8):732-41

**D. Research Support**

ACTIVE

1U01NS106655-01A1 Ramey, Lead PI, and Lo, MPI
Virginia Tech / NINDS/NIH
02/01/2019 – 01/31/2024 $203,569 3.00 cal.
Perinatal Arterial Stoke(PAS): A Multi-site RCT of Intensive Infant Rehabilitation (I-ACQUIRE)
Perinatal arterial ischemic stroke (PAS) occurs in an estimated 1 in 1150 livebirths and often leads to serious lifelong neuromotor impairment. This StrokeNet Phase III trial will provide definitive efficacy data about an intensive form of infant rehabilitation (Infant ACQUIRE) to transform rehabilitation and improve clinical outcomes.

5 U54 NS 065705-10 REVISED M. Lawton (UCSF PI)
University of California San Francisco / National Institutes of Health (NIH)
9/30/2014 – 7/31/2019 $14,724 0.12 cal.
Brain Vascular Malformation Clinical Research Network (BVMC)
Role: Co-investigator
The focus of this specific project is on Sturge-Weber syndrome which is a rare congenital syndrome. NCH will be part of a national consortium database which will gather clinical data and serve indirectly as a registry to foster future clinical trials; determine the usefulness of urine vascular biomarkers and identify the action of the somatic mutation causing SWS.
OVERLAP: None

U24NS107205 S. Kolb (OSU PI)
Ohio State University/NINDS
7/1/2018 – 6/30/2019 $17,392 0.36 cal.
Network of Excellence in Neuroscience Clinical Trial Center
The Network was created to provide infrastructure in the conduct of multicenter phase 2 clinical trials in neurological diseases through partnerships with academia, private foundations, and industry.
OVERLAP: None

(82146816) J. Heathcock (OSU PI)
Ohio State University Office of Sponsored Programs / Patient Centered Outcomes Research Institute (PCORI)
9/15/2016 – 8/15/2019 $409,327 0.60 cal.
A Comparison: High Intense periodic vs. Every week therapy in children with cerebral palsy (ACHIEVE)
Role: Co-investigator
The specific aims are: 1) To conduct a randomized controlled trial (RCT) with 300 children, age 2 to 8 years of age with CP, that compares the short-term and long-term effects of 2 service delivery models: 1 hour per day, 1 x week for 40 weeks (usual weekly) and 2 hours every weekday for two bouts of 10-consecutive-weekdays (total 4 weeks), for a repeated “periodic’ bout (high intensity period) of an already established clinical program; and 2) to determine individual differences in children’s response to intensity.
OVERLAP: None

R01 NS 06820 -05 H. Fullerton (UCSF PI)
University of California San Francisco / National Institutes of Health (NIH)
9/1/2017 – 6/30/2019 $5,800 0.12 cal.
VIPS II - The Vascular effects of Infection in Pediatric Stroke 2017
Role: Co-investigator
Specific Aims: 1) To identify known and novel pathogens in children with AIS, and determine whether different pathogens (including unusual strains or combinations of pathogens) are associated with arteriopathic versus cardioembolic or idiopathic stroke; 2) To determine whether children with arteriopathic AIS have a distinct analyte signature consistent with an alternative pathway of inflammation compared to children with cardioembolic or idiopathic stroke; 3) To obtain and analyze the childhood stroke transcriptome, and identify molecular correlates of stroke heterogeneity. The purpose of this study is to examine the association between infection and arterial ischemic stroke (AIS) in children.
OVERLAP: None

R01 HD 083384 -01 J. Heathcock (OSU PI)
Ohio State University Office of Sponsored Programs / National Institutes of Health (NIH)
4/1/2016 – 1/31/2020 $415,140 0.24 cal.
Frequency: Dosing for Rehabilitation Delivery in children with Cerebral Palsy
Role: Co-investigator
The specific aims are: 1) to compare short-term (6 months following initiation of therapy) and long- term (1, 1.5, and 2 years following the initiation of therapy) outcomes in terms of gross motor function, domains of development, goal attainment scaling, and spontaneous play; and 2) to identify factors that predict individual differences in outcomes for children with CP with the two dosing protocols.
OVERLAP: None

1R01HD074574-01A1 A. Darragh (OSU PI)
Ohio State University Office of Sponsored Programs / Virginia Polytechnic Institute/ NICHD/NIH
03/01/2014 – 6/30/2019 $32,279 0.12 cal
Multisite RCT of 3 Neurorehabilitation Therapies for Infants with Asymmetrical CP
Role: Co-investigator
This multisite randomized controlled trial tests 3 highly-promising new therapies for infants with asymmetrical CP (N=72) and will yield much needed data about the differential impact of these therapies on neuromotor outcomes and brain development up to 12 months post-treatment. OVERLAP: None

PENDING

C. Fox (UCSF PI)
University of California San Francisco/National Institutes of Health
9/1/2019 – 8/31/2024 $21,280 0.12 cal.
Seizures and Children's OUTcomes after Stroke (SCOUTS)
The Specific Aims are: 1) to determine the early serum inflammatory biomarker profile that predicts epilepsy after childhood AIS; 2) to determine the early serum inflammatory biomarker proile that predicts epilepsy after neonatal AIS; and 3) to identify early electrographic and imaging biomarkers of epilepsy after childhood and neonatal stroke.