

**AWARD NUMBER:** W81XWH-20-1-0560

**TITLE:** The Impact of Childhood-Onset Lupus on the Developing Brain

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**CONTRACTING ORGANIZATION:** The Hospital for Sick Children  
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<b>13. SUPPLEMENTARY NOTES</b> None					
<b>14. ABSTRACT</b>  This research study seeks to understand how and why childhood-onset lupus affects the developing adolescent brain. The study will look for better ways to identify early cognitive changes, and the factors contributing to the changes. We will use advanced magnetic resonance imaging techniques to learn about brain structure and function in adolescents newly diagnosed with lupus. We will study these adolescents over time, and compare their brain development to that of healthy peers. Initiation of the study has been delayed due to the COVID-19 pandemic. The study is currently under review for final approval by the sponsor.					
<b>15. SUBJECT TERMS</b> Lupus, childhood, adolescent, brain, cognition, development, neuroimaging					
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## 1. INTRODUCTION:

This research study seeks to understand how and why childhood-onset lupus affects the developing adolescent brain. The study will look for better ways to identify early cognitive changes, and the factors contributing to the changes. We will use advanced magnetic resonance imaging (MRI) techniques to learn about brain structure and function in adolescents newly diagnosed with lupus. This longitudinal study will examine the impact of cSLE on the developing brain in a cohort of 40 adolescents with new-onset disease, comparing to 40 age, sex, and ethnicity-matched healthy controls. The study aims to: 1) compare brain structure, function and development between adolescents with lupus and healthy peers, using measures obtained by advanced MRI over time; 2) examine relationship between the MRI findings and cognitive test performance, and ; 3) examine the relationship between the MRI findings and lupus-related factors, such as disease activity, prednisone exposure, and concurrent depression/anxiety and pain.

## 2. KEYWORDS:

Lupus, childhood, adolescent, brain, cognition, development, neuroimaging

## 3. ACCOMPLISHMENTS:

### What were the major goals of the project?

The major goals of the project and completion status of these goals are listed in the table below.

	<b>Timeline (months)</b>	<b>Completion Status</b>
<b>Major Task 1: Hire staff</b>		
Advertise, interview and hire neuroimaging scientist	Pre-award	Sept 2020
<i>Milestone Achieved: All study staff hired</i>	Pre-award	Sept 2020
<b>Major Task 2: Protocol Approval</b>		
Finalize consent form & human subjects protocol	Pre-award	Feb 2021
IRB protocol submission	Pre-award	Aug 2020
Submission for Human Research Protection Office (HRPO) Review	Pre-award	Feb 2021
<i>Milestone Achieved: IRB &amp; HRPO approvals</i>	Pre-award	Aug 2021
Submit amendments, adverse events and protocol deviations as needed	As Needed	-
Annual IRB report for continuing review	Annually	-
<b>Major Task 3: Conduct Study</b>		
Begin subject recruitment	2	Not started
<i>Milestone Achieved: 1st participant consented, screened and enrolled</i>	2	Not started

<i>Milestone Achieved: Study visit 1 completed by 80 subjects (40 new-onset lupus adolescents and 40 controls)</i>	24	Not started
<i>Milestone Achieved: Study visit 2 completed by 80 subjects</i>	36	Not started
Weekly study team meetings to discuss issues related to recruitment, enrollment, MRI data quality, data collection and management	1-36	Not started
<b>Major Task 4: Data Analysis &amp; Report Findings</b>		
Monthly meetings with co-investigators Drs. Taylor and Yeh, Ashley Danguedan and neuroimaging scientist to discuss analysis & results	7-36	Not started
Preliminary analysis of cross-sectional data from study visit 1, to examine baseline neuroimaging measures and associated cognitive function of new-onset lupus subjects, in comparison to controls	7-24	Not started
<i>Milestone Achieved: Report results from cross-sectional data analyses (abstracts, presentations, publications)</i>	18-30	Not started
Analysis of longitudinal data from study visits 1 and 2, to examine trajectories of brain development and function in new-onset lupus adolescents, and contributing cSLE disease-related factors	14-36	Not started
<i>Milestone Achieved: Report results from longitudinal data analyses (abstracts, presentations, publications)</i>	24-36	Not started

**What was accomplished under these goals?**

The major activities completed to date are hiring of the study staff, and approval from the Hospital for Sick Children Research Ethics Board (REB, equivalent to IRB) in February 2021, and approval from the HRPO in August 2021. The study is awaiting final approval from the sponsor, anticipated September/October 2021, prior to initiation of subject recruitment. Therefore, no data has been obtained to date.

Due to impact of the COVID-19 pandemic on research operations within the SickKids Research Institute and correspondingly within Dr. Knight's research team, there were significant delays in the steps for obtaining REB approval. Additionally, there was a delay in HRPO evaluation of the documents submitted for evaluation due to a possible issue with the email server preventing receipt of Dr. Knight's email containing requested documents (International form).

**What opportunities for training and professional development has the project provided?**

Nothing to report.

**How were the results disseminated to communities of interest?**

Nothing to report.

**What do you plan to do during the next reporting period to accomplish the goals?**

As final approval from the sponsor is anticipated in September/October 2021, we plan to initiate subject recruitment upon approval, with the goal of recruiting 20 lupus and 20 controls during the first year of recruitment. We will have weekly study team meetings to discuss issues related to recruitment, enrollment, MRI data quality, data collection and management. We will also have monthly co-investigator meetings to discuss preliminary data analysis and results.

#### **4. IMPACT:**

**What was the impact on the development of the principal discipline(s) of the project?**

Nothing to report.

**What was the impact on other disciplines?**

Nothing to report.

**What was the impact on technology transfer?**

Nothing to report.

**What was the impact on society beyond science and technology?**

Nothing to report.

**5. CHANGES/PROBLEMS:**

Nothing to report.

**Actual or anticipated problems or delays and actions or plans to resolve them**

Due to impact of the COVID-19 pandemic on research operations within the SickKids Research Institute and correspondingly within Dr. Knight's research team, there were significant delays in obtaining REB and HRPO approval.

As final approval from the sponsor is anticipated in September/October 2021, we plan to initiate subject recruitment upon approval. While we are hopeful that the ongoing pandemic will not impact our study recruitment goals, it is a possibility. We have developed strategies to enable virtual components of the consenting and enrollment process, thereby limiting in-person components as much as possible, to reduce patient and family anxiety related to the in-person nature of the study visits. We expect recruitment to be most challenging for controls, and plan to recruit using multiple strategies (posters, hospital website, etc).

**Changes that had a significant impact on expenditures**

Nothing to report.

**Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**

**Significant changes in use or care of human subjects**

Nothing to report.

**Significant changes in use of biohazards and/or select agents**

Nothing to report.

**6. PRODUCTS:**

- **Publications, conference papers, and presentations**

**Journal publications.**

Nothing to report.

**Books or other non-periodical, one-time publications.**

Nothing to report.

**Other publications, conference papers and presentations.**

Nothing to report.

- **Website(s) or other Internet site(s)**

Nothing to report.

- **Technologies or techniques**

Nothing to report.

- **Inventions, patent applications, and/or licenses**

Nothing to report.

- **Other Products**

Nothing to report.

## **7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS**

**What individuals have worked on the project?**

Nothing to report.

**Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

Please see below changes in Dr. Knight's active support.

**Active**

K23  
(0.24 Cal Mos)  
NIH/NHLBI  
Chang (PI) 04/01/2020-03/31/2025  
Cardiovascular health assessment & outcomes of systemic lupus erythematosus:  
bridging pediatric and adult-onset disease  
The goal of this study is to examine mechanisms of cardiovascular disease in adolescents and young adults with SLE.  
Role: Co-I

Childhood Arthritis and Rheumatology Research Alliance 07/01/2021-06/30/2024  
(1.2 Cal Mos)  
CARRA SLE Committee  
SLE Section Chair  
The position serves to oversee and coordinate CARRA lupus research workgroups, collaborating with external stakeholder groups to advance cSLE research, the CARRA mission and overall research strategy.  
Role: Chair

U01DP006490 Hersh/Knight/Schanberg/Son (MPI) 09/01/2019-08/31/2022  
(1.20 Cal Mos)  
CDC/ NCCDPHP  
This study seeks to enroll a large cohort of pediatric Lupus patients in a long-term United States registry to understand the disease, best treatments and what factors influences important outcomes including disease related damage and death.  
Role: PI

CARRA-AF Transdisciplinary Grant West (PI) 12/01/2019-11/29/2021  
(0.60 Cal Mos)  
Childhood Arthritis and Rheumatology Research Alliance  
A remotely delivered CBT intervention for youth with cSLE: A multi-site patient-engaged investigation.  
This project aims to determine: 1) the feasibility of a remotely delivered cognitive behavioral therapy intervention (TEACH) for youth with cSLE, and 2) the effect of TEACH on fatigue, depressive symptoms, and pain.

Role: Co-I

### Inactive

Childhood Arthritis and Rheumatology Research Alliance  
(0.60 Cal Mos)

10/01/2018-06/30/2021

CARRA SLE Committee  
SLE Section Vice-Chair

The position serves to oversee and coordinate CARRA research workgroups together with the SLE Chair, collaborating with external stakeholder groups to advance cSLE research, the CARRA mission and overall research strategy.

Role: Vice Chair

(Andrea Knight, Co-I)	10/01/2018 - 09/30/2020	0.3 calendar
The Children's Hospital of Philadelphia	✓ annual direct costs	
Pediatric Center for Excellence in Nephrology Pilot and Feasibility Grant (PIs: Scott Wenderfer, Meredith Atkinson)		
<i>Project Title: Learning Health Systems for Pediatric Lupus Nephritis Research</i>		
The aim of this project is to validate computable phenotypes for lupus and lupus nephritis in PEDSnet and assess the feasibility in extracting blood pressure data.		

(Andrea Knight, Co-I)	07/01/2019 - 06/30/2020	0.6 calendar
Childhood Arthritis and Rheumatology Research Alliance	✓ annual direct costs	
CARRA-AF Small Grant (PI: Kaveh Ardalan)		
<i>Project Title: Mental Health Screening in Juvenile Myositis: Pilot and Feasibility Study</i>		
This project aims to assess the feasibility of routine mental health screening and referral in a juvenile myositis specialty clinic, the prevalence of positive screens for depression/anxiety, and relationships between mental health symptoms, disease outcome measures, and pro-health behaviors.		

(Andrea Knight, Co-I)	10/01/2018 - 09/30/2019	0.6 calendar
Lupus Foundation of America	✓ annual direct costs	
Gary S. Gilkeson Career Development Grant (PI: Joyce Chang)		
<i>Project Title: Attenuated nocturnal blood pressure dipping and subclinical atherosclerosis in cSLE</i>		
This project aims to estimate the burden of nocturnal hypertension and attenuated dipping among children with SLE, and assess relationships between nocturnal blood pressure and measures of clinical atherosclerosis and organ damage.		

**What other organizations were involved as partners?**

Nothing to report.

**8. SPECIAL REPORTING REQUIREMENTS**

**COLLABORATIVE AWARDS:**

**QUAD CHARTS:**

**9. APPENDICES:**