

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

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

**PRINCIPAL INVESTIGATOR:** Andrea Knight, MD, MSCE

**CONTRACTING ORGANIZATION:** The Hospital for Sick Children, Toronto, Ontario, Canada

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# REPORT DOCUMENTATION PAGE

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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.

	Timeline (months)	Completion Status
<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	<u>started Jan 2022</u>

<i>Milestone Achieved: 1st participant consented, screened and enrolled</i>	2	<a href="#">Jan 2022</a>
<i>Milestone Achieved: Study visit 1 completed by 80 subjects (40 new-onset lupus adolescents and 40 controls)</i>	24	<a href="#">In progress</a>
<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	<a href="#">Ongoing</a>
<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	In progress
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 during this reporting period include DoD HRPO approval of the study (August 2021), initiation of study recruitment in January 2022, and enrollment of 17 lupus patients and 3 healthy controls from January 2022 to present date. Of these, 11 lupus patients and 2 controls have completed study visit 1, including completion of neuroimaging for the first timepoint. Despite significant delays in study initiation due to impact of the COVID-19 pandemic, we have made great progress in participant recruitment and visit one completion since starting recruitment 7 months ago.

Abstraction of clinical data for the enrolled lupus patients has begun. Data entry for neurocognitive data for all participants, as well as data management processes to monitor data quality and completeness is also ongoing. Pre-processing of imaging data is also ongoing.

**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?**

During the next reporting period, we plan to complete recruitment of an additional 20 SLE participants and 20 controls for study visit 1, adding to the current enrollment of 17 lupus patients and 3 healthy controls to date. This will get us close to the goal of 40 SLE and 40 controls. We will complete study visit 2 for the currently enrolled participants. We will work on strategies for retention of participants for visit 2. We will begin preliminary analysis of the cross-sectional data, with a goal of submitting an abstract to a scientific conference. 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 have been challenges with recruiting control participants. With the recent lifting of public health restrictions, we anticipate control recruitment to improve as the community begins to interface more with the Hospital for Sick Children. To facilitate control recruitment, we have prioritized matching to SLE participants on age and sex (with less emphasis on matching by race/ethnicity, although this data is still being collected). We have also boosted our recruitment efforts by encouraging SLE participants to invite health peers to join the study, and through more robust advertising of the study. All of these efforts have been approved by our IRB. We will continue to re-evaluate and optimize our recruitment processes and progress during weekly recruitment meetings.

**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?**

No change.

**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.

**New Active**

Canada Institute of Health Research Knight (PI) 04/01/2022-03/31/2027 (effort subsumed)  
Canadian Research Chair – Tier 2  
Mental Health in Childhood Chronic Disease  
The goal of this program is to support the research program of an exceptional emerging investigator.  
Role: Chair

Lupus Research Alliance Knight (PI) 07/01/2022-06/30/2026  
(1.20 Cal Mos)  
Career Development Award  
Inflammation, Brain Injury and Trajectories of Cognitive Function in Childhood-onset Lupus.  
The goal of this study is to examine trajectories of cognitive function, and investigate correlates to systemic IFN-mediated inflammation, brain injury and structural brain changes in adolescents with cSLE.  
Role: PI

Lupus Foundation of America El Tal (PI) 10/01/2022-09/30/2024  
(0.30 Cal Mos)  
Gary S Gilkeson Career Development Award  
The position serves to oversee and coordinate CARRA research workgroups, collaborating with external stakeholder groups to advance cSLE research, the CARRA mission and overall research strategy.  
Examining the Longitudinal Prevalence of Cognitive Dysfunction and Relationship to Disease and Patient-Reported Outcomes in Childhood-onset Lupus.  
Role: Mentor/Co-investigator

LADA-CARRA Award Ogbu/Rodriguez/Knight (MPI) 07/01/2022-06/30/2023  
(0.3 Cal Mos) Lupus and Allied Diseases Association  
Deriving Research Priorities in Neuropsychiatric Systemic Lupus Erythematosus in Children

The goal of this project is to develop a prioritized patient-centered research agenda for neuropsychiatric lupus.  
Role: Co-PI

**New Inactive**

None

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

Nothing to report.

**8. SPECIAL REPORTING REQUIREMENTS**

**COLLABORATIVE AWARDS:**

**QUAD CHARTS: /**

**9. APPENDICES:**