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TITLE: Mechanisms of Social Deficits in Youth with Neurofibromatosis Type 1

PRINCIPAL INVESTIGATOR: Dr. Matthew Hocking, PhD

CONTRACTING ORGANIZATION: The Children's Hospital, Philadelphia, PA

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# REPORT DOCUMENTATION PAGE

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<b>14. ABSTRACT</b> Youth with neurofibromatosis type 1 (NF1) often have difficulties with social functioning (e.g., getting along with peers). However, research evaluating the underlying mechanisms that contribute to these difficulties remains limited. Prior research suggests that the social difficulties go beyond the neurocognitive impairments often seen in NF1 and have been related to socio-emotional processes that are typically impaired in ASD. An emerging model of social skills development grounded in social cognitive neuroscience emphasizes the role of cognitive and affective functions (CAF), such as executive function, facial processing, social attention, and theory of mind (i.e., ability to understand others' perspectives), and highlights brain areas essential to CAF (e.g., facial processing) that are often disrupted in atypical brain development. The <u>objectives</u> of this research are to evaluate the CAF abilities of youth with NF1 and establish associations between CAF abilities and social adjustment outcomes. A secondary objective is to describe the neurobiological mechanisms underlying the CAF abilities of youth with NF1 using neuroimaging. The project has been significantly delayed by the COVID-19 pandemic, thus there are no findings to report at this stage.						
<b>15. SUBJECT TERMS</b> Neurofibromatosis; social functioning; cognitive; affective; social adjustment; neuroimaging						
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## 1. INTRODUCTION:

Youth with neurofibromatosis type 1 (NF1) often have difficulties with social functioning (e.g., getting along with peers). However, research evaluating the underlying mechanisms that contribute to these difficulties remains limited. The objectives of this research are to evaluate the cognitive and affective functions (CAF) of youth with NF1 and establish associations between CAF abilities and social adjustment outcomes. A secondary objective is to describe the neurobiological mechanisms underlying the CAF abilities of youth with NF1 using neuroimaging.

## 2. KEYWORDS:

Neurofibromatosis; social functioning; cognitive; affective; social adjustment; neuroimaging

## 3. ACCOMPLISHMENTS:

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

### **Major Task 1: Conduct neurobehavioral assessments with youth with NF1**

Milestone: Recruit 20 youth to complete neurobehavioral assessment

-Goal: 9 months into project

-Actual progress: 0% of goal

### **Major Task 2: Complete proposed analyses to determine group differences on CAF/neurobehavioral data**

### **Major Task 3: Complete proposed analyses to determine associations between neurobehavioral data and social adjustment data**

Milestones: Report findings from analyses

-Goal: 22-24 months into project

-Actual progress: N/A

### **Major Task 4: Conduct neuroimaging protocol (rs-fMRI, fMRI) with youth with NF1**

Milestone: Pilot neuroimaging protocol in 15 youth with NF1

Goal: 8 months into project

-Actual progress: 0% of goal

**What was accomplished under these goals?**

Major activities for this project to date have focused on study start-up, acquiring necessary equipment and technology for the project, and modifying study procedures to increase flexibility of data collection following the onset of the COVID-19 pandemic. Additionally, activities have focused on establishing a pipeline to obtain previously collected comparison data on typically developing youth and youth with autism spectrum disorder from collaborators at the Center for Autism Research at CHOP. Progress on this project has been significantly impacted by the COVID-19 pandemic and unanticipated delays. To date, no participants have been enrolled in the study. CHOP IRB approval was obtained on 7/10/2020. HRPO approval was obtained on 9/11/2020. Given the COVID-19 pandemic, we modified some procedures so that they could be conducted remotely. We received CHOP IRB approval for this amendment on 12/9/2020 and HRPO approval on 1/15/2021. We encountered delays in obtaining the eye tracking equipment from the company out of the UK, receiving this equipment on 12/24/2020, and in installing it into our dedicated research MRI. Given the high rates of COVID-19 in early 2021 in the Philadelphia area and the fact that we are recruiting a population that does not regularly need to come to the hospital, we decided to hold off on recruitment until early spring in order to reduce COVID-related declines to participate. We anticipate beginning recruitment the week of 4/19/2021.

**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?**

Recruitment will begin towards the end of April 2021. We anticipate enrolling our first participant in early May 2021 and expect an accrual rate of 2 per week, which would allow us to reach our original goal for sample size. We expect that we will be able to complete the milestones associated with Major Tasks 2 & 3 close to the original timeline (months 22-24).

**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:**

Made minor changes to protocol to allow for some study procedures to be conducted virtually, including informed consent, responses to surveys, and engagement in an unstructured social interaction. These changes were made in response to the COVID-19 pandemic.

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

The ongoing COVID-19 pandemic has significantly delayed the onset of recruitment and study accrual for this project. Due to safety concerns and challenges related to recruitment in other active studies at our institution in the late 2020 and early 2021, we chose to delay recruitment until early spring of 2021. We plan to begin recruitment the week of 4/19/2021 and will work diligently to recruit participants in this study in order to make up for time lost secondary to the pandemic.

**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?**

Name: Matthew Hocking, PhD  
Project Role: PI  
Research Identifier: [0000-0002-1368-0856](#)  
Nearest person month worked: 4  
Contribution to project: Dr. Hocking has overseen the project and the start-up activities, including obtaining of IRB and HRPO approval, directed research team meetings related to the project, and supervised the Clinical Research Assistant.

Name: May Albee  
Project Role: Clinical Research Assistant  
Research Identifier: [0000-0002-7065-3520](#)  
Nearest person month worked: 6  
Contribution to project: Ms. Albee worked on obtaining IRB and HRPO approval and obtaining needed materials to conduct the project. She also has developed the study protocol for the lab.

Name: John Herrington, PhD  
Project Role: Co-I  
Research Identifier: [0000-0002-9720-3917](#)  
Nearest person month worked: 2  
Contribution to project: Dr. Herrington has worked to develop the neuroimaging protocol and test it using phantom scans and research staff.

Name: Benjamin Yerys, PhD  
Project Role: Co-I  
Research Identifier: [0000-0002-7370-0740](#)  
Nearest person month worked: 1  
Contribution to project: Dr. Yerys has contributed to the development of the study protocol and worked to obtain the technology transfer agreement for a computerized assessment of executive function that will be used in the research.

Name: Kelly Janke, PhD  
Project Role: Co-I  
Research Identifier: [0000-0001-6595-3361](#)  
Nearest person month worked: 1  
Contribution to project: Dr. Janke has contributed to the development of the study protocol and established the study protocol for the neuropsychological assessment that will be conducted with each participant.

Name: Michael Fisher, MD  
Project Role: Co-I  
Research Identifier: N/A  
Nearest person month worked: 1  
Contribution to project: Dr. Fisher has contributed to the development of the study protocol and facilitated procedures for recruitment through NF program at CHOP, for which he is the director.

Name: Robert Schultz, PhD  
Project Role: Co-I  
Research Identifier: [0000-0001-9817-3425](#)  
Nearest person month worked: 1  
Contribution to project: Dr. Schultz has contributed to the development of the study protocol and facilitated acquisition of study materials (e.g., face processing measure) and provided access to the previously collected data that will be used for comparison with the NF data.

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

Matthew Hocking

**New Award**

1R01CA248103-01A1 (PI: Gerhardt)  
NIH/NCI

02/09/2021-1/31/2026

2.40 calendar

*Psychosocial Risk in Young Survivors of Early Onset Pediatric Cancer: The Role of Physical and Neurocognitive Late Effects*

The goal of this project is to assess the psychological risk of young cancer survivors and the role of physical and neurocognitive late effects on these survivors.

Role: Site Principal Investigator

Note: subaward agreement negotiations underway

John Herrington

**New Award**

1R01MH125958-01 (PI: Herrington)  
NIH/NIMH

04/01/2021-1/30/2026

2.40 calendar

*Optimized Affective Computive Measures of Social Processes and Negative Valence in Youth Psychopathology*

The goal of this project is to develop and validate novel facial expression and linguistic measures that can be applied to research and clinical work in youth with psychopathology.

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

Nothing to Report

**8. SPECIAL REPORTING REQUIREMENTS**

**COLLABORATIVE AWARDS:**

**QUAD CHARTS:**

**9. APPENDICES:**