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

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

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

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 objectives 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.

15. SUBJECT TERMS

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: 85% 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: 93.3% 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, participant recruitment and enrollment, and data collection. 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, 17 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 postponed recruitment until early spring in order to reduce COVID-related declines to participate. We resumed recruitment in mid-May 2021. Recruitment was again paused in December 2021 and January 2022 due to increased rates of COVID-19. In February 2022, we amended the protocol to enroll participants who cannot undergo an MRI (due to braces, metallic implants, etc) to complete only the cognitive portion of the study. To date we have contacted 53 families. Of those, 15 families declined and 11 had passive refusal. We have screened 20 potential participants and determined 1 to be ineligible. Of the 19 screened, 17 have enrolled in the study and the other two are in the process of scheduling their study visit.

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 began in mid-May 2021. Since that time, we have enrolled 17 over the course of 10 months of active recruitment. As COVID has less of an impact on daily lives, we anticipate an accrual rate of 2 per month, which bring us close to our original goal for sample size by May 2023. We expect that we will be able to complete the milestones associated with Major Tasks 2 & 3 by the end of the no cost extension year.

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

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

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 participants with braces who would be unable to undergo neuroimaging to complete the non-imaging study procedures.

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 began recruitment in mid-May 2021 and will continue to 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
1R37CA256889-01A1 (PI: Hocking) 01/01/2022-12/31/2027 3.60 calendar
NIH/NCI
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 access 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

What other organizations were involved as partners?

Nothing to Report

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS:

QUAD CHARTS:

9. APPENDICES: