

AWARD NUMBER: W81XWH-13-1-0179

TITLE: "Subtyping of Toddlers with ASD Based on Patterns of Social Attention Deficits"

PRINCIPAL INVESTIGATOR: Katarzyna Chawarska, Ph.D.

CONTRACTING ORGANIZATION: Yale University
New Haven, CT 06510

REPORT DATE: October 2015

TYPE OF REPORT: ANNUAL

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release; Distribution Unlimited

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REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. **PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.**

1. REPORT DATE October 2015	2. REPORT TYPE Annual	3. DATES COVERED 30Sep2014 - 29Sep2015
4. TITLE AND SUBTITLE “Subtyping of Toddlers with ASD Based on Patterns of Social Attention Deficits”		5a. CONTRACT NUMBER
		5b. GRANT NUMBER W81XWH-13-1-0179
		5c. PROGRAM ELEMENT NUMBER
6. AUTHOR(S) Katarzyna Chawarska, Ph.D. E-Mail: Katarzyna.chawarska@yale.edu	5d. PROJECT NUMBER	
	5e. TASK NUMBER	
	5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Yale University Toddler Developmental Disabilities Clinic 40 Temple St., Suite 7-D, New Haven, CT 06510		8. PERFORMING ORGANIZATION REPORT NUMBER
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012		10. SPONSOR/MONITOR'S ACRONYM(S)
		11. SPONSOR/MONITOR'S REPORT NUMBER(S)
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited		
13. SUPPLEMENTARY NOTES		

14. ABSTRACT

The main objective of the proposed project is to elucidate the factors that affect spontaneous dyadic orienting at the earliest stages when ASD can be reliably diagnosed in order to advance our understanding of phenotypic heterogeneity and foster identification of more homogeneous and clinically relevant subgroups within the autism spectrum. Initial major tasks of the research project included regulatory review and approval and preparation of the eye tracking experiment, both completed in Q1Y1. Subject recruitment and enrollment is ongoing. There have not been any other administrative, technical, or logistical issues that impact performance or progress of the study. As of Q4Y2, we have recruited 119 subjects and have enrolled 107 subjects. 43 subjects have ASD, 24 have DD, and 40 are TD. As we have met the study enrollment total for the TD group, in the upcoming period we will focus our efforts exclusively on recruiting into the ASD and DD groups. All enrolled subjects have complete Time 1 subject assessment and data acquisition and 3 have completed Time 2 assessment and data acquisition. Thus far there have been no dropouts or disqualifications. We have made solid progress in implementing the tasks outlined in the SOW. In the upcoming quarter we will begin preliminary analyses of our eye tracking data.

15. SUBJECT TERMS

ASD, subgrouping, toddlers, heterogeneity, eye-tracking, visual attention, dyadic orienting, hierarchical clustering, predictors of outcome

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT UU	18. NUMBER OF PAGES 7	19a. NAME OF RESPONSIBLE PERSON USAMRMC
a. REPORT Unclassified	b. ABSTRACT Unclassified	c. THIS PAGE Unclassified			19b. TELEPHONE NUMBER <i>(include area code)</i>

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

Table of Contents

	<u>Page</u>
1. Introduction.....	6
2. Keywords.....	6
3. Overall Project Summary.....	6
4. Key Research Accomplishments.....	7
5. Conclusion.....	7
6. Publications, Abstracts, and Presentations.....	7
7. Inventions, Patents and Licenses.....	7
8. Reportable Outcomes.....	8
9. Other Achievements.....	8
10. References.....	8
11. Appendices.....	8

1. INTRODUCTION:

Toddlers with ASD vary tremendously in the type and severity of symptoms they experience. Moreover, while some toddlers with ASD greatly improve in terms of their social difficulties, cognitive abilities, and language skills, for a large proportion of affected children the outcome is poor and characterized by limited gains over time. At present, we neither understand the sources of this diversity, nor can we predict outcome reliably in affected toddlers, which limits our ability to design better screening and diagnostic instruments, to develop more effective treatments for young children, as to identify the causes of the disorder. To improve this situation, we need to discover how to better classify and categorize patterns of behavior and development within the autism spectrum. Our subgrouping analysis based on visual responses to dyadic orienting tasks will be performed on 18-24 month old toddlers, at the age when the first diagnosis is made and determination of risk for poor or positive outcome is essential for treatment planning. Therefore, this work has great potential to help us understand the mechanisms underlying these social attention deficits and predictors of outcome, as well as guide the development of individualized treatments that will accommodate the specific profiles of strengths and weakness in the identified subgroups. The design of our study will permit greater understanding of the sources of variability that complicate early detection efforts and will further generate hypotheses regarding the underlying neural substrates affected at the earliest stages of ASD. The impact of this study will be fourfold: (1) identification of phenotypically homogenous groups within ASD; (2) identification of more accurate predictors of outcome; (3) facilitation of development of individualized early interventions; and (4) informing our understanding of the mechanisms underlying the emergence of social deficits.

2. KEYWORDS:

ASD, subgrouping, toddlers, heterogeneity, eye-tracking, visual attention, dyadic orienting, hierarchical clustering, predictors of outcome

3. OVERALL PROJECT SUMMARY:

Summary of Current Objectives:

The main objective of the proposed project is to elucidate the factors that affect spontaneous dyadic orienting at the earliest stages when ASD can be reliably diagnosed in order to advance our understanding of phenotypic heterogeneity and foster identification of more homogeneous and clinically relevant subgroups within the autism spectrum.

Summary of Results, Progress, and Accomplishments with Discussion:

Initial major tasks of the research project included regulatory review and approval (SOW 1.2.1), which was achieved in Q1Y1, and preparation of the eye tracking experiment (SOW 1.2.2), also completed in Q1Y1. Subject recruitment and enrollment, while ongoing, continues to lag somewhat behind projections due to a longer than expected preparatory stage with regard to other aspects of the study launch. There have not been any other administrative, technical, or logistical issues that impact performance or progress of the study. As of Q4Y2, we have recruited 119 subjects and have enrolled 107 subjects (i.e., 12 subjects are scheduled to participate in the coming weeks). 43 subjects have ASD, 24 have DD, and 40 are TD. As we have met the study enrollment milestone for the TD group, in the upcoming period we will focus our efforts exclusively on recruiting into the ASD and DD groups. All enrolled subjects have complete Time 1 (T1) subject assessment and data acquisition. T1 subject assessment includes eye tracking, Mullen Scales of Early Learning (developmental assessment), medical/family/intervention history, Vineland II (adaptive skills assessment), ADOS (diagnostic assessment), and feedback with families. Data acquisition (SOW 1.2.6) involves processing eye tracking data using custom software written in MatLab, and double-entering characterization data into the database and checking for errors

using automated programs and manual checking procedures, and has been ongoing. Thus far there have been no dropouts or disqualifications. We have made solid progress in implementing the tasks outlined in the SOW and are continuing to recruit and enroll subjects, particularly those with ASD and DD, to meet milestones. In addition, we have begun seeing children for their T2 visit (N=3) as they reach the designated age interval. In the upcoming quarter we will begin preliminary analyses of our eye tracking data.

4. KEY RESEARCH ACCOMPLISHMENTS:

Nothing to report.

5. CONCLUSION:

Lack of insight into the bases of heterogeneity in ASD constitutes a major barrier to understanding the etiology of autism and designing highly effective targeted treatments for children with a wide range of abilities. Understanding the underlying factors contributing to atypical responses to dyadic bids may both illuminate the mechanisms underlying social orienting deficits in ASD as well as help to decode the behavioral variability of later emerging, scaffolded, and higher-level skills. Through this project we will investigate factors that affect dyadic orienting in ASD as compared to non-ASD groups, identify subgroups of toddlers within ASD based on their gaze patterns in response to dyadic bids and evaluate validity of the identified subtypes, employ novel statistical approaches to identifying the most accurate predictors of outcome amongst toddlers with ASD and further refine our understanding of specific factors associated with atypical outcomes.

In the upcoming quarter (Q1 Y3), we will continue seeing children for their Time 2 visits as they turn 36-42 months of age. Statistical analyses of eye tracking and characterization data will be carried out beginning in Q1 Y3 for purposes of preliminary discussion and potential dissemination.

6. PUBLICATIONS, ABSTRACTS, AND PRESENTATIONS:

Nothing to report.

7. INVENTIONS, PATENTS AND LICENSES:

Nothing to report.

8. REPORTABLE OUTCOMES:

Nothing to report.

9. OTHER ACHIEVEMENTS:

Nothing to report.

10. REFERENCES:

None

11. APPENDICES:

None