

AWARD NUMBER: W81XWH-14-1-0526

TITLE: Precursors to the Development of Anxiety Disorders in Young Children with Autism Spectrum Disorder

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REPORT DATE: October 2015

TYPE OF REPORT: Annual

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

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REPORT DOCUMENTATION PAGE				Form Approved OMB No. 0704-0188	
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1. REPORT DATE October 2015		2. REPORT TYPE Annual		3. DATES COVERED 30 Sep 2014 - 29 Sep 2015	
4. TITLE AND SUBTITLE Precursors to the Development of Anxiety Disorders in Young Children with Autism Spectrum Disorder				5a. CONTRACT NUMBER	
				5b. GRANT NUMBER W81XWH-14-1-0526	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Geraldine Dawson, PhD; Helen Egger, MD; Grace Baranek, PhD; Kimberly Carpenter, PhD E-Mail: Kimberly.Carpenter@duke.edu				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) DUKE UNIVERSITY 2200 W MAIN ST STE 710 DURHAM NC 27708-4677				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 Anxiety disorders are extremely common among individuals with autism spectrum disorder (ASD). The presence of an anxiety disorder negatively affects family functioning, friendship development, and school functioning. Our long term goal is to be able to identify children with ASD who are at risk for anxiety as early as possible so that early intervention can address not only ASD symptoms, but also target specific symptoms that put a child with ASD at risk for developing an anxiety disorder. During the first year of funding, we have received regulatory approval for our study at Duke University, the University of North Carolina Chapel Hill, and the DOD HRP0. We have hired study personnel, as well as set-up, calibrated, and piloted our experimental measures. Furthermore, we developed a study database, launched study recruitment, and begun data collection. Finally, we have successfully competed for additional grant funding (NARSAD Young Investigator Award; PI: Carpenter) to extend the scope of the current study to include children 40 without ASD.					
15. SUBJECT TERMS Autism, anxiety, sensory over-responsivity					
16. SECURITY CLASSIFICATION OF: U			17. LIMITATION OF ABSTRACT Unclassified	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON USAMRMC
a. REPORT Unclassified	b. ABSTRACT Unclassified	c. THIS PAGE Unclassified			19b. TELEPHONE NUMBER (include area code)

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I. Introduction

Anxiety disorders are extremely common among individuals with Autism (ASD), yet we still know very little about the early risk factors for anxiety in ASD. Research is beginning to provide some clues regarding early risk factors for anxiety in individuals with ASD, suggesting that sensory over-responsivity (SOR) may be an early emerging risk factor for anxiety in individuals with ASD. Our goal is to identify early risk factors for anxiety disorders in individuals with ASD by conducting an in-depth study of the relationship between SOR, attention, and anxiety symptoms in preschool age children with ASD, using parent report, observational, and EEG measures. This project will help identify the early risk factors for anxiety disorders in ASD, which may ultimately allow interventions to focus on prevention of anxiety. If an association between SOR and anxiety symptoms is confirmed, this study will set the stage for a program of research by our group focused on early detection and prevention of anxiety disorders in young children with ASD.

II. Keywords

Autism, Anxiety, Sensory Over-Responsivity, Attention, EEG

III. Accomplishments

A. Major goals of the project

Specific Aim 1: Evaluate the relationship between Sensory Over-reactivity (SOR) and anxiety symptoms/ disorders in a sample of 3-5 year old children with ASD using parent report, observational, and neurophysiological measures.

	Statement of Work Goal Completion Date	Actual Completion Date or Progress		
		Site 1 - Duke Dawson, Initiating PI	Site 2 - Duke Egger, Partnering PI	Site 3 - UNC Baranek, Partnering PI
Major Task 1: Prepare regulatory documents and research protocol for IRB and HRPO Approval				
Milestone # 1: IRB approval received at both Duke University and UNC Chapel Hill	12/29/2014	7/21/2014	7/21/2014	6/18/2014
Milestone # 2: HRPO approval received	3/29/2015	8/8/2014	8/8/2014	8/8/2014
Major Task 2: Hiring and training of study personnel on observational measures				
Milestone # 3: Study personnel achieves reliability on the Sensory Processing Assessment, Tactile Defensiveness and Discrimination Test, PAPA, ADOS, and ADI	3/29/2015	7/1/2015	8/1/2015	6/26/2015
Major Task 3: Set up, test, calibrate and pilot experimental measures of attention and neurophysiology				
Milestone #4: Experimental paradigms set-up, tested, and calibrated	3/29/2015	1/22/2015	5/14/2015	5/14/2015

Milestone #5: Study personnel trained in administration of and data collection for attention and ERP tasks	3/29/2015	1/22/2015	5/14/2015	5/14/2015
Milestone #6: Attention and ERP tasks piloted and finalized	4/30/2015	4/3/2015	5/14/2015	5/14/2015
Milestone #7: Study is ready for implementation	4/30/2015	5/14/2015	5/14/2015	5/14/2015
Major Task 4: Participant recruitment and launch of testing				
Milestone # 8: Target enrollment of 30 participants for year 1 reached	9/29/2015	53%	53%	53%
Major Task 5: On-going enrollment and testing of participants and data collection and processing				
Milestone # 9: Target enrollment of 100 participants by end of Q1 of third year reached and data ready for analysis	12/29/2016	16%	16%	16%
Milestone # 10: EEG, eye-tracking and sensory observation task data prepared for analysis.	12/29/2016	5%	5%	5%
Major Task 6: Data analysis of SOR and anxiety measures and publication				
Milestone #11: Complete analysis of SOR and anxiety measures	6/29/2017	0%	0%	0%
Milestone #12: Publish results of study on risk factors for anxiety in young children with ASD.	9/29/2017	0%	0%	0%

Specific Aim 2 Evaluate whether anxiety symptoms/disorders mediate the relationship between SOR and a wide range of negative outcomes that have been associated with SOR, namely, levels of impaired adaptive behavior, challenging behaviors (e.g. irritability, aggression), GI symptoms and parental stress.

	Statement of Work Goal Completion Date	Actual Completion Date or Progress		
		Site 1 - Duke Dawson, Initiating PI	Site 2 - Duke Egger, Partnering PI	Site 3 - UNC Baranek, Partnering PI
Major Task 1: Data analysis of comprehensive set of measures and publication				
Milestone #13: Complete analyses on anxiety as a mediator of the impact of SOR on negative outcomes for children with ASD	6/29/2017	0%	0%	0%
Milestone #14: Publish study on the role of anxiety as a mediator of the impact of SOR on negative outcomes for children with ASD.	9/29/2017	0%	0%	0%

Specific Aim 3 Evaluate whether attentional control, as assessed by a visual attention-shifting task and event-related potentials (ERPs), moderate the relationship between SOR and anxiety symptoms/disorders.

	Statement of Work Goal Completion Date	Actual Completion Date or Progress		
		Site 1 - Duke Dawson, Initiating PI	Site 2 - Duke Egger, Partnering PI	Site 3 - UNC Baranek, Partnering PI
Major Task 1: Automated coding of visual attention task from videotapes - Work to be conducted by Jordan Hashemi under the supervision of Dr. Sapiro in collaboration with Dr. Egger				
Milestone #15: Finalize algorithm for data capture.	3/29/2016	N/A	0%	N/A
Milestone #16: Apply automated coding to videotapes (N = 100)	12/29/2016	N/A	0%	N/A
Major Task 2: Data analysis of attention measures and publication - Work to be conducted by Jordan Hashemi under the supervision of Drs. Sapiro, Egger, and Dawson				
Milestone #17: Complete data analysis of all eye-tracking and automated coding data	6/29/2017	0%	0%	0%
Milestone #18: Results of study on automated coding as a valid measure of attention in young children with ASD are published	9/29/2017	0%	0%	0%
Major Task 3: Data analysis of SOR measures (parent report, observation, ERP) and publication				
Milestone #19: Complete data analyses of SOR measures	6/29/2017	0%	0%	0%
Milestone #20: Publish results of study validating an auditory ERP measure as a biomarker of SOR in young children with ASD	9/29/2017	0%	0%	0%

B. Accomplishments under the goals of the project (9/30/2014 through 9/29/2015)

Specific Aim 1. Evaluate the relationship between sensory over-responsivity (SOR) and anxiety symptoms/disorders in a sample of 3-5 year old children with ASD using parent report, observational, and neurophysiological measures.

a. Major Task 1: Prepare regulatory documents and research protocol for IRB and HRPO Approval.

Objective 1: Obtain IRB approval from Duke University and UNC Chapel Hill.

IRB approval was obtained from Duke University on 7/21/2014 for both AR130128 (PI, Dawson) and AR130128P1 (PI, Egger). IRB approval was also obtained from the University of North Carolina at Chapel Hill on 6/18/2014 for AR130128P2 (PI, Baranek).

Objective 2: Submit amendments, adverse events, and protocol deviations as needed.

As the project develops, we will continue to amend our IRB to reflect any changes made. Once approved at both sites, amendments to the IRB will also be submitted to the HRPO.

b. Major Task 2: Hiring and training of study personnel on observational measures.

Objective 1: Hire EEG technician and research assistant.

On 8/1/2014 Mrs. Maura Tourian was hired as a Research Coordinator I to assist with all aspects of the project, including EEG data collection and analysis. Mrs. Tourian terminated her position on 2/6/2015. On 6/22/2015, Ms. Lauren DeMoss joined the team and will be replacing Mrs. Tourian.

Objective 2: Study personnel trained by Dr. Baranek in the reliable administration and coding of the Sensory Processing.

Training on the reliable administration and coding of the sensory processing assessments is a three-part process. First, each trainee must attend two training sessions that are overseen by Dr. Baranek (PI, AR130128P2). Second, study personnel are required to code training video tapes and achieve 90% reliability for the Sensory Processing Assessment (SPA) and 80% reliability for the Tactile Defensiveness and Discrimination Test (TDDT) with Dr. Baranek's team. Finally, each trainee must provide tapes of live administrations of the assessment themselves and have their administration evaluated and again must achieve 90% and 80% reliability on the SPA and TDDT, respectively, with Dr. Baranek's team on coding.

Study personnel completed orientation and training for the SPA on 10/24/14 and 10/31/14. Additionally, personnel submitted their coding tapes for the SPA on 10/29/14. Completion of the final tapes occurred on 6/26/2015.

Study personnel completed orientation and training for the TDDT on 12/5/14 and 1/23/15. Additionally, personnel submitted their coding tapes for the TDDT on 12/3/14. Completion of the final tapes occurred 6/26/2015.

Dr. Baranek and team refined SPA and TDDT manuals and scoring sheets to increase utility and accuracy for data collection and data entry. Inter-rater reliability scoring will be ongoing with live administrations and/or from video on approximately 20% of cases. Calibration of SPA and TDDT will be ongoing in Dr. Baranek's lab at UNC to ensure that assessors and coders are not drifting from procedures and scoring.

Objective 3: Study personnel trained by Dr. Egger in the reliable administration and coding of the Preschool Age Psychiatric Assessment (PAPA).

Training on the reliable administration and coding of the Preschool Age Psychiatric Assessment (PAPA) is a two-part process. First, each trainee must attend a one week training session overseen by Dr. Egger (PI, AR130128P1). Second, each trainee must provide tapes of 3 live administrations of the assessment themselves and have their administration evaluated and must achieve 80% reliability with Dr. Egger's team on coding.

Study personnel completed orientation and training for the PAPA on 9/19/14. We have one staff member who is fully trained on administration of this (Mr. Brian Small) who joined the team in August and will complete each of the PAPA assessments.

Objective 4: Initial reliability established for Autism Diagnostic Observation Schedule (ADOS) and Autism Diagnostic Interview (ADI) (already trained to research reliability by certified trainer).

Training on the ADOS-2 and the ADI-R is a multi-part process that has been overseen by Dr. Dawson (PI, AR130128). The first step is that each trainee must complete a 5-day clinical training on both the ADOS-2 and the ADI-R, which will be comprised of both didactic sessions and training video-based practice. Second, trainees must attend a 3-day research reliability training focused on hands-on practice and scoring of the ADOS-2 and ADI-R, using volunteers with ASD and their parents. In addition to these trainings, each trainee must demonstrate knowledge of the standardized administration procedures on 3 administrations of ADOS Modules T/1/2, 3 administrations of Modules 3/4, and 3 administrations of the ADI. To achieve this, each trainee must: (a) Complete video recordings of the trainee administering two different ADOS-2 modules (one Module T/1/2 and one Module 3/4) and one ADI; (b) Complete administration of two ADOS-2 and one ADI during the research training and (c) Complete post-course DVD tapings of two ADOS-2 administrations and one ADI.

Demonstrated understanding of coding rules and achievement of at least 80% agreement for the ADOS and at least 90% agreement for the ADI with a certified ADOS/ADI instructor.

Study personnel completed both the 5-day clinical training and the 3-day research reliability training prior to the awarding of this grant on Oct 17 – 25th, 2013 and Jan. 15-17th, 2014, respectively. Study personnel have completed 5 out of 6 of the ADOS/ADI administration videotapes. Completion of the ADOS Module T/1/2 reliability occurred on 2/24/15 and completion of the ADI reliability occurred on 5/14/15. Submission of the tapes required for reliability on ADOS Module 3/4 occurred in August, 2015. Completion of this objective was slowed by the loss of Mrs. Tourian.

c. Major Task 3: Set up, test, calibrate and pilot experimental measures of attention and neurophysiology.

Objective 1: Attention-shifting/eye-tracking task set-up, tested, and calibrated.

Finalization of the attention-shifting eye-tracking task has been completed. After careful consideration and discussions with the authors of the proposed task (Landry and Bryson group), we have decided to utilize a new attention-shifting task (publication currently under review) developed by Dr. Baranek, Partnering PI on this proposal, that is better suited for our target participants and targets the sensory processing deficits in addition to the attention construct of interest. John Bulluck, research associate under the direction of Dr. Baranek, provided the experimental protocol and stimuli, and assisted in calibration of procedures with Duke personnel. The programming and implementation of the attention task at the Duke Center for Autism and Brain Development occurred on 5/14/2015.

Objective 2: ERP paradigm set-up, tested, and calibrated.

Finalization of the ERP paradigm is completed. Set-up and testing have been completed.

Objective 3: Study personnel trained by Drs. Egger and Baranek in the administration of the attention-shifting task.

Training in the administration of the attention-shifting task is completed, as noted above.

Objective 4: Study personnel trained by Dr. Dawson in administration of ERP tasks and collection of EEG data.

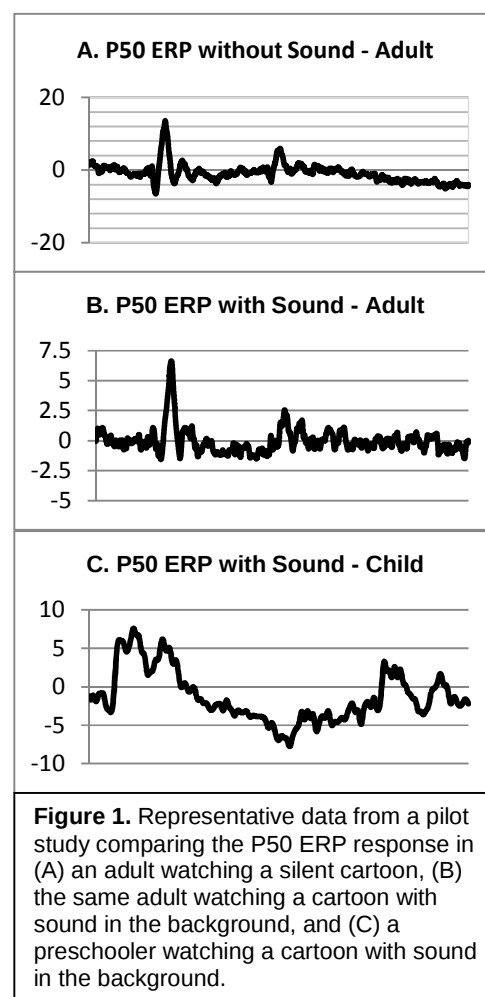
Training in the administration of the administration of the ERP tasks and collection of EEG data is completed.

Objective 5: Pilot attention and ERP tasks.

Piloting of the attention task was completed as part of a previous study. ERP task piloting was completed on 4/3/2015. Early piloting involved optimizing the ERP paradigm for use in preschoolers with ASD. A modified version of the paradigm, in which participants were allowed to watch a low volume cartoon while the ERP was designed and piloted first in young adults and then in typically developing (TD) preschoolers.

Preliminary Results and Conclusions from ERP Pilot:

The ERPs generated from the two adult pilot subjects were filtered to isolate the P50 responses to both the second and first clicks in each trial. Bad channels were replaced with an interpolation from nearby channels, and all successful trials were compiled into an aggregate, so an average response could be viewed. Representative results from one participant are shown in Figures 1A and 1B. As shown, the peaks for the first and second clicks were attenuated in the trial with sound



(click 1: 6.65 V, click 2: 2.57 V) relative to the trial with sound (13.59 V, 5.93 V), but the relative difference between the two voltage amplitudes remained essentially unchanged (with sound: 38.6%, without sound: 43.6%).

The TD preschool trials were run with the modified task design in both cases and were processed in the same way as the adult trials. Both participants demonstrated a successful measurement of sensory gating, with relative voltage amplitudes of 40% and 42%, respectively. The aggregate data, averaging both participants' ERP sessions is shown in Figure 1C.

While there is attenuation of the overall P50 signal when participants watch a low-volume cartoon, the *relative* differences in P50 ERP signals between the first and second clicks remains unchanged. These results are consistent in both young adults and TD children and indicate the feasibility of the modified version of the paired-click paradigm task. Critically, they demonstrate that low background noise does not fundamentally alter the measure of sensory gating garnered through paired-click ERPs.

The ability to play low-volume cartoons while recording an ERP signal greatly extends the utility of the paired-click paradigm as a measure of SOR in populations of preschoolers with ASD. As researchers continue to explore development of anxiety in children with autism, the ability to use the paired click paradigm to tap relevant variables will likely prove invaluable. Unlike other standard measures of SOR, the paired click paradigm taps the neurobiological basis of sensory sensitivity, and is thus an essential complement to more observational assessments.

Objective 6: Study is ready for implementation.

Data collection began on 5/14/2015.

d. Major Task 4: Participant recruitment and launch of testing.

Objective 1: Provide information and flyers about study to all recruitment sites.

We have been actively recruiting subjects through the Duke Center for Autism Subject Registry and have been distributing study brochures to local agencies and at a number of local events (e.g. Autism Speaks Walks, etc.). We have also included the brochures at our UNC site and have received approval to send an email on the UNC email listerv.

Objective 2: Begin screening and enrolling participants in study.

We have screened 31 subjects and of those families, 3 children were excluded due to not meeting eligibility criteria, 1 family did not show up to their enrollment visit and have been unreachable since that date, 16 children have been enrolled, 8 families are scheduled and 1 is waiting to be scheduled for the enrollment visit. We have an additional 5 individuals who we are trying to contact to complete a phone screen.

Objective 3: Maintain reliability and quality control on all measures.

Training to ensure reliability of the assessments is ongoing. Study staff attend monthly ADOS reliability sessions, as well as monthly reliability sessions for the sensory assessments, which take place at the UNC site for this study.

Objective 4: Target enrollment of 30 participants for year 1 reached.

We have enrolled 16 subjects and have 8 scheduled for their enrollment visit. Study visits are scheduled through the end of the year. Completion of this objective was slowed by the loss of Mrs. Tourian.

e. Major Task 5: On-going enrollment and testing of participants and data collection and processing.

Objective 1: Continue active recruitment through on-going communication with recruitment sites

We have continued to receive study referrals from the Duke Center for Autism and Brain Development subject registry and distribute study information at all local autism events (e.g. Walk Now for Autism Speaks, Autism Society of North Carolina Walk, etc.).

Objective 2: Maintain reliability and quality control on all measures.

Training to ensure reliability of the assessments is ongoing. Study staff attend monthly ADOS reliability sessions, as well as monthly reliability sessions for the sensory assessments, which take place at the UNC site for this study

Objective 3: Edit and process EEG data for analysis.

Editing and processing of the EEG data occurs as it is collected so that it is ready for analysis at the end of data collection.

Objective 4: Process eye-tracking data for analysis.

Editing and processing of the eye-tracking data occurs as it is collected so that it is ready for analysis at the end of data collection.

Objective 5: Coding of sensory observation tasks for analysis - ongoing.

Coding of the sensory observation tasks occurs as they are collected so that they are ready for analysis at the end of data collection.

Objective 6: Data entry, verification, and cleaning for analysis – ongoing.

With the help of Prometheus Research, the Duke Center for Autism and Brain Development has created a database in which all data from this study will be stored. Data from this study is entered into the Prometheus database, verified, and cleaned as it is collected, so that it is ready for analysis at the end of data collection.

C. Opportunities for training and professional development the project has provided

This project has provided training to individuals at a number of levels, including undergraduate, graduate, and post-graduate trainees.

Undergraduate Training: Logan Beyer, a Duke University undergraduate student, has been receiving course credit as an Independent Study student on this project since the beginning of the project in September 2014. Ms. Beyer has received training in autism, anxiety, sensory processing, EEG and eye-tracking data acquisition and analysis, as well as general training in the day-to-day activities associated with scientific research. Additionally, the current funding and associated project have provided Ms. Beyer with training in scientific writing and principles of scientific data dissemination.

Graduate Training: Kathryn Williams, a graduate student under Dr. Grace Baranek at UNC Chapel Hill, and Adrienne Harris, a graduate student under Drs. Helen Egger, Geraldine Dawson, and Nancy Zucker at Duke University, have received training in observational assessment of sensory processing in children with autism as a result of this award. They have also gained experience with study management and oversight.

Post-Graduate Training and Professional Development: Additional training and professional development has been provided to Kimberly Carpenter, a postdoctoral associate who oversees this project. As a result of this project, Dr. Carpenter received training in (a) observational assessment of autism symptoms (ADI and ADOS) and sensory processing (SPA and TDDT) assessment in young children, (b) parent interviewing skills (ADI and PAPA), (c) EEG and eye-tracking data collection and analysis, (d) mentorship of undergraduate and graduate students, and (d) study and personnel management. Additionally, as a direct result of the work supported by this grant, Dr. Carpenter successfully competed for a 2015 NARSAD Young Investigator Award, which supports the research and professional development of early career scientists.

D. Dissemination of results to communities of interest

Dr. Kimberly Carpenter presented a description of this study, including information about the theory behind how sensory over-responsivity may contribute to the development of anxiety in autism, at the grand opening

of the Duke Center for Autism and Brain Development reception. This event reached a diverse community of interest, including both individuals and families of individuals with autism, as well as clinicians and researchers who work with individuals with autism. The chair of the Duke Department of Psychiatry and Behavioral Sciences, the Provost of Duke University, and the Chancellor for Health Affairs and President and CEO of the Duke University medical Center attended as well.

Preliminary results from the pilot study on ERP responses were presented at the 2015 Visible Thinking event, which is put on by the Duke Undergraduate Research Support Office, by Ms. Logan Beyer in a poster entitled "Updated Methodologies and Preliminary Data Analysis of Sensory Over-Responsivity in Children with Autism" based on the pilot ERP studies. This event is meant to disseminate undergraduate research projects to undergraduates and faculty members from across the Duke University community and to promote interest in undergraduate participation in science.

E. Plans for next reporting period to accomplish goals

Specific Aim 1. Evaluate the relationship between SOR and anxiety symptoms/disorders in a sample of 3-5 year old children with ASD using parent report, observational, and neurophysiological measures.

- a. Major Task 1: Prepare regulatory documents and research protocol for IRB and HRPO Approval – completed in year 1.**
- b. Major Task 2: Hiring and training of study personnel on observational measures – completed in year 1.**
- c. Major Task 3: Set up, test, calibrate and pilot experimental measures of attention and neurophysiology – completed in year 1.**
- d. Major Task 4: Participant recruitment and launch of testing.**

Objective 1: Provide information and flyers about study to all recruitment sites.

Flyers and information about this study will be distributed throughout the enrollment period of this study.

Objective 2: Begin screening and enrolling participants in study – completed in year 1.

Objective 3: Maintain reliability and quality control on all measures.

Training to ensure reliability of the assessments is ongoing. Study staff attend monthly ADOS reliability sessions, as well as monthly reliability sessions for the sensory assessments, which take place at the UNC site for this study.

Objective 4: Target enrollment of 30 participants for year 1 reached.

We have enrolled 16 subjects and have 8 scheduled for their enrollment visit. Study visits are scheduled through the end of the year. We continue to receive study referrals from the Duke Center for Autism and Brain Development subject registry and distribute study information at all local autism events (e.g. Walk Now for Autism Speaks, Autism Society of North Carolina Walk, etc.). Subject enrollment will be maintained at a rate of approximately 5-6 subjects per month.

- e. Major Task 5: On-going enrollment and testing of participants and data collection and processing.**

Objective 1: Continue active recruitment through on-going communication with recruitment sites

We will continue to receive study referrals from the Duke Center for Autism and Brain Development subject registry and distribute study information at all local autism events (e.g. Walk Now for Autism Speaks, Autism Society of North Carolina Walk, etc.). We have also added the UNC email listserve as an added mode of recruitment. This listserve targets all individuals with a UNC email address.

Objective 2: Maintain reliability and quality control on all measures.

Training to ensure reliability of the assessments is ongoing. Study staff attend monthly ADOS reliability sessions, as well as monthly reliability sessions for the sensory assessments, which take place at the UNC site for this study

Objective 3: Edit and process EEG data for analysis.

We will edit and process the EEG data as it is collected so that it is ready for analysis at the end of data collection.

Objective 4: Process eye-tracking data for analysis.

We will edit and process the eye-tracking data as it is collected so that it is ready for analysis at the end of data collection.

Objective 5: Coding of sensory observation tasks for analysis.

We will code the sensory observation tasks as they are collected so that they are ready for analysis at the end of data collection.

Objective 6: Data entry, verification, and cleaning for analysis.

With the help of Prometheus Research, the Duke Center for Autism and Brain Development has created a database in which all data from this study will be stored. Data from this study is entered into the Prometheus database, verified, and cleaned as it is collected, so that it is ready for analysis at the end of data collection.

Objective 7: Target enrollment of 100 participants by end of Q1 of third year reached.

We have enrolled 16 subjects and have an additional 8 subjects scheduled through December, and have 5 additional individuals for whom we are trying to contact to complete a phone screen. We will increase our recruitment goals from 5 subjects per month to 6 subjects per month, which will put us back on track for reaching our final N of 100 subjects.

f. Major Task 6: Data analysis of SOR and anxiety measures and publication – begins in year 3.

Specific Aim 2 Evaluate whether anxiety symptoms/disorders mediate the relationship between SOR and a wide range of negative outcomes that have been associated with SOR, namely, levels of impaired adaptive behavior, challenging behaviors (e.g. irritability, aggression), GI symptoms and parental stress – begins in year 3.

Specific Aim 3 Evaluate whether attentional control, as assessed by a visual attention-shifting task and event-related potentials (ERPs) to a fearful facial expression, moderate the relationship between SOR and anxiety symptoms/disorders.

a. Major Task 1: Automated coding of visual attention task from videotapes - Work to be conducted by Jordan Hashemi under the supervision of Dr. Sapiro in collaboration with Dr. Egger.

Objective 1: Apply and calibrate algorithm for data capture – ongoing.

Our collaborators have been actively applying and calibrating the video coding algorithms for data capture on unrelated datasets. As we collect data as part of the current study, these algorithms will be calibrated to our subject population.

Objective 2: Apply automated coding to videotapes.

Automated coding of videotapes is slated to begin in year 2, quarter 2. All videos that have been collected as part of this study will be processed through the automated coding algorithm once that algorithm has been calibrated to our study population. Videos that are captured after algorithm calibration will be analyzed as data is collected.

Objective 3: Enter data for analysis.

The data from the automated coding analyses will be deposited in our Center database as it is acquired.

- b. Major Task 2: Data analysis of attention measures and publication – begins in year 3.**
- c. Major Task 3: Data analysis of SOR measures (parent report, observation, ERP) and publication – begins in year 3.**

IV. Impact

A. Impact on the development of the principal discipline(s) of the project

The immediate impact of this project will be the identification of early risk factors for anxiety in ASD. Currently, treatments focus on helping older children and adults with ASD who already suffer from an anxiety disorder, rather than addressing anxiety symptoms when they first begin or even preventing the onset of an anxiety disorder. In fact, very little research on anxiety in preschool age children with ASD has been conducted. If an association between SOR and anxiety is confirmed, this study may ultimately inform interventions that focus on prevention, rather than treatment, of anxiety. Specifically, early behavioral interventions could be customized for children at risk for anxiety to include strategies that could prevent the development of anxiety, offering a more positive outcome for many people with ASD and their families. This study will shed light on the specific ways such interventions should be customized for children with ASD who are at risk for anxiety.

This project will also pilot and validate new methods for measuring SOR and attention that allow for more objective measurement of these behaviors. First, our early pilot study demonstrating a negligible impact of a low-volume cartoon on the P50 ERP response greatly extends the utility of the paired-click paradigm as a measure of SOR in populations of preschoolers with ASD. As researchers continue to explore development of anxiety in children with autism, the ability to use the paired click paradigm to tap relevant variables will likely prove invaluable. Unlike other standard measures of SOR, the paired click paradigm taps the neurobiological basis of sensory sensitivity, and is thus an essential complement to more observational assessments. Second, the use of automated methods for measuring attention will allow assessment of these behaviors in a more efficient, scalable, and cost-effective manner. Both of these methodological advances will facilitate the translation of findings from the research lab into clinical and educational settings.

B. Impact on the on other disciplines

Sensory over-responsivity (SOR) is characterized by heightened and unusual reactivity to sensory stimuli, such as touch and sound. Community studies suggest that SOR affects up to 16% of school-age children. SOR is also prevalent across a number of neurodevelopmental and psychiatric disorders and recent evidence suggests that it may be a risk factor for emotion dysregulation and anxiety in not only ASD, but also other disorders such as ADHD and anorexia nervosa. This suggests that there is a shared relationship between SOR and anxiety, yet the mechanism underlying this relationship remains unknown. Thus, although the current project focuses on young children with ASD, the findings will have implications for understanding the relationship between SOR, anxiety, and negative outcomes and the development of novel approaches for treating anxiety disorders across the lifespan.

C. Impact on technology transfer

Nothing to report.

D. Impact on society beyond science and technology

Firsthand accounts from people with autism spectrum disorder (ASD) illustrate the impact of sensory over-responsivity (SOR) and anxiety on everyday life. Both SOR and anxiety are extremely common among people with ASD and both have been shown to significantly affect quality of life for the person with ASD and their families. SOR has been associated with higher rates of avoidance, aggression, food selectivity, and lower levels of social and adaptive behavior. A recent study found that early SOR symptoms in a child with ASD can lead to higher levels of family stress and restrictions in family life activities. SOR can also have an impact on oral care, both in the home and dental office. Similarly, the presence of an anxiety disorder has been shown to negatively affect family functioning, friendship development, and school functioning. Later in life, anxiety places adolescents with ASD at risk for social isolation and employment difficulties. Furthermore, higher rates of SOR and anxiety are associated with chronic GI symptoms and sleep disturbance. The results of the current study have the potential of directly influencing the policy and practice around the early identification and early treatment of SOR and anxiety in children with ASD.

V. Changes/Problems

A. Changes in approach and reasons for change

We have made 2 minor changes to the approach outlined in the original grant application.

1. After careful consideration and discussions with the authors of the proposed task (Landry and Bryson group), we decided to utilize a new attention-shifting task (publication currently under review) developed by Dr. Baranek, Partnering PI on this proposal, that is better suited for our target participants and targets the sensory processing deficits in addition to the attention construct of interest.
2. Due to the time burden associated with collecting data on young children using a wide range of assessments, we decided to focus our EEG data collection on the pre-attentive auditory P50 paradigm, which will provide data that is central to testing our hypothesis, and will not collect data on the fear face paradigm.

B. Actual or anticipated problems or delays and actions or plans to resolve them

The loss of Mrs. Tourian, who served as a study co-coordinator, hampered progress of this project. We replaced Mrs. Tourian on June 22nd, 2015. With Ms. DeMoss now part of the team, we are back on track, were able to launch the study, and are increasing our recruitment efforts in order to meet our goals.

C. Changes that had a significant impact on expenditures

There was a delay in our finding a qualified replacement for Mrs. Tourian, thus the funding allocated to the project co-coordinator position was not fully utilized. Because of this delay and a lower effort and salary for Ms. DeMoss, there are remaining funds in Award AR130128. A portion of these funds will be used to cover the effort of Mr. Brian Small, who joined the team as our Preschool Age Psychiatric Assessment (PAPA) interviewer, and to cover the increased contribution of Dr. Carpenter, project coordinator for this study. Additionally, the delay in launching subject recruitment resulted in a lower number of subject payment disbursements; however, these funds will be used in year 2 of the project.

D. Significant changes in use or care of human subjects

Nothing to Report

E. Significant changes in use or care of vertebrate animals

Nothing to Report

F. Significant changes in use or care of biohazards and/or select agents

Nothing to Report

VI. Products

A. Publications, conference papers, and presentations

a. Journal publications.

Nothing to Report

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

Nothing to Report

c. Other publications

Nothing to Report

d. Conference papers

Nothing to Report

e. Presentations

Beyer L, Dawson G, Egger HL, and Carpenter KLH (2015, April) "Updated Methodologies and Preliminary Data Analysis of Sensory Over-Responsivity in Children with Autism." Poster presented at the Visual Thinking Symposium at Duke University, Durham, NC.

Carpenter KLH, Dawson G, Egger HL, Baranek G (2015, June) "Sensory Over-Responsivity and Anxiety in Autism." Poster presented at the grand opening of the Duke Center for Autism and Brain Development, Durham, NC.

B. Website(s) or other Internet site(s)

<http://autismcenter.duke.edu/research/sensory-processing-and-anxiety-preschool-age-children-autism-spectrum-disorder>

C. Technologies or techniques

Nothing to Report

D. Inventions, patent applications, and/or licenses

Nothing to Report

E. Other Products

Nothing to Report

VII. Participants & Other Collaborating Organizations

A. Individuals that have worked on the project

Name: Geraldine Dawson, PhD, FAPA, FAPS

Project Role: Principal Investigator

Nearest person month worked: 1

Contribution to Project: Ensure the fiscal integrity of the grant; Oversee the IRB approval process and ensure compliance for Duke site; Hire, train and manage staff; Oversee the training in the autism diagnostic measures (ADOS and ADI); Design the ERP paradigms; Oversee recruitment efforts; Refine study protocol; Participate in the interpretation of data and publication/dissemination of findings; Attend weekly Duke team meetings and monthly all-site meetings.

Name: Helen Egger, MD

Project Role: Partnering Principal Investigator

Nearest person month worked: 1

Contribution to Project: Ensure the fiscal integrity of the grant; Train and manage staff involved in the early childhood mental health data collection (PAPA); Design and implement the eye-tracking attention-shifting paradigm; Participate in the interpretation of data and publication/dissemination of findings; Refine study protocol; Attend weekly Duke team meetings and monthly all-site meetings.

Name: Grace Baranek, PhD, OTR/L, FAOTA

Project Role: Partnering Principal Investigator

Nearest person month worked: 1

Contribution to Project: Ensure the fiscal integrity of the grant; Train and manage staff involved in the sensory processing data collection (SPA and TDDT); Oversee the IRB approval process and ensure compliance for UNC site; Refine study protocol; Design and implement the eye-tracking attention-shifting paradigm; Participate in the interpretation of data and publication/dissemination of findings; Attend monthly all-site meetings.

Name: Kimberly Carpenter, PhD

Project Role: Postdoctoral Associate, Project Coordinator – Duke Site

Nearest person month worked: 5

Contribution to Project: Project coordination – Duke Site; Oversee IRB submission process and maintain updated approval under the direction of Drs. Dawson and Egger; Manage DoD related activities (e.g. preparation of quarterly report, submission of human research documents to HRPO); Participate in the ongoing training in autism diagnostic evaluations, early childhood mental health assessment, sensory processing measures, and ERP/EEG data collection and analysis; Supervise undergraduate and graduate research assistants; Refine study protocol; Lead weekly Duke team meetings and monthly all-site meetings; Subject recruitment; Participate in the interpretation of data and publication/dissemination of findings; Subject assessment and data collection.

Name: Lauren DeMoss, MS, OTR/L

Project Role: Project Co-Coordinator – Duke Site

Nearest person month worked: 2

Contribution to Project: Project co-coordination – Duke Site; Contribute to DoD related activities (e.g. preparation of quarterly report, submission of human research documents to HRPO); Participate in the ongoing training in autism diagnostic evaluations, early childhood mental health assessment, sensory processing measures, and ERP/EEG data collection; Help supervise undergraduate and graduate research assistants; Coordinate recruitment efforts; Refine study protocol; Attend weekly Duke team meetings and monthly all-site meetings.

Name: Logan Beyer

Project Role: Undergraduate Student

Nearest person month worked: 2

Contribution to Project: Support research staff, including preparing materials used in refining study protocol and preparing recruitment materials. Attend weekly Duke team meetings and monthly all-site meetings as available.

Name: Maura Tourian, MS, CCC-SLP

Project Role: Project Co-Coordinator – Duke Site

Nearest person month worked: 3

Contribution to Project: Project co-coordination – Duke Site; Contribute to DoD related activities (e.g. preparation of quarterly report, submission of human research documents to HRPO); Participate in the ongoing training in autism diagnostic evaluations, early childhood mental health assessment, sensory processing measures, and ERP/EEG data collection; Help supervise undergraduate and graduate research assistants; Coordinate recruitment efforts; Refine study protocol; Attend weekly Duke team meetings and monthly all-site meetings.

Name: Adrienne Harris, BA

Project Role: Graduate RA

Nearest person month worked: 1

Contribution to Project: Contributed to IRB submission process; Participate in the ongoing training in autism diagnostic evaluations, sensory processing measures, and ERP/EEG data collection; Attend weekly Duke team meetings and monthly all-site meetings.

Name: Brian Small, MS

Project Role: Interviewer

Nearest person month worked: 1

Contribution to Project: Collect PAPA data.

Name: Ashley Freuler, PhD

Project Role: IRB coordination – UNC

Nearest person month worked: 1

Contribution to Project: Provide support for IRB submission process and maintain updated approval under the direction of Dr. Baranek.

Name: John Bulluck, BS

Project Role: Research Associate, UNC

Nearest person month worked: 1

Contribution to Project: Provide support for and coordination of training activities and scoring protocols for SPA/TDDT; Provide support and training for the attention shifting/eye tracking protocol; Participate in oversight of data security measures as outlined by UNC's IRB protocol. Attend monthly all-site meetings.

Name: Kathryn Williams, MS

Project Role: Graduate RA, UNC

Nearest person month worked: 1

Contribution to Project: Provide support for and coordination of training activities, Participate in the ongoing training in sensory processing measures and support administration/scoring of the SPA/TDDT; Attend monthly all-site meetings.

B. Changes in the active other support of the PD/PI(s) or senior/key personnel

Nothing to Report

C. Other organizations involved as partners

Organization name: Center for Autism and Brain Development, Duke University Medical Center

Location of organization: Durham, NC

Partner's contribution to the project: Collaboration

Organization name: Center for Developmental Epidemiology, Duke University Medical Center

Location of organization: Durham, NC

Partner's contribution to the project: Collaboration

Organization name: Pratt School of Engineering, Duke University

Location of organization: Durham, NC

Partner's contribution to the project: Collaboration

Organization name: Duke Pediatric Primary Care

Location of organization: Durham, NC

Partner's contribution to the project: Recruitment support

Organization name: Duke Lenox Baker Children's Health Center

Location of organization: Durham, NC

Partner's contribution to the project: Recruitment support

Organization name: Autism Society of North Carolina

Location of organization: Raleigh, NC

Partner's contribution to the project: Recruitment support