AWARD NUMBER: W81XWH-16-1-0753

TITLE: Prenatal Polyunsaturated Fatty Acid Levels and Risk of Autism Spectrum

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REPORT DATE: October 2017

TYPE OF REPORT: Annual

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

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
October 2017	Annual	30 Sep 2016 - 29 Sep 2017

4. TITLE AND SUBTITLE

Prenatal Polyunsaturated Fatty Acid Levels and Risk of Autism Spectrum

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-16-1-0753

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) AND ADDRESS(ES)

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PA 19104-2816

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 causes of autism spectrum disorder (ASD) are not well understood, but research suggests that factors influencing early brain development may be involved. Polyunsaturated fatty acids (PUFAs), which include omega 3 fatty acids, are fats obtained from the diet that play key roles in early fetal brain development. It is not known whether levels of these crucial fats during pregnancy influence risk of ASD. This project will examine the relationship between PUFA levels and ASD, addressing the role of **environmental risk factors in ASD** (a FY15 priority Area of Interest). Specifically, the goal of this project is to determine whether levels of PUFAs measured from maternal blood samples collected during pregnancy, and in a subgroup group, from newborn blood spots, differ between children with ASD and those without ASD. We will also explore whether the relationship between PUFAs and ASD differs in certain subgroups, such as by race/ethnicity, preterm birth, or child gender. Based on the importance of PUFAs in neurodevelopment, we suspect that lower levels of PUFAs may be related to ASD.

In order to address these questions, we will use data from routine screening programs in the state of California. Children with ASD (cases) will be selected from the California Department of Developmental Services (DDS), a statewide program that coordinates services for children with autism and other disabilities. Children without ASD (controls) will be selected from California birth certificates in the same year as children with ASD. PUFAs will be measured in the previously collected blood samples from pregnancy (500 cases and 500 controls), and in newborn blood spots from a subgroup (200 cases and 200 controls) using sensitive, state-of-the-art technology. Statistical analyses will examine differences in levels of maternal and newborn PUFAs between children with and without ASD, adjusting for demographic and other factors that may influence the association. Subgroup analyses will explore potential differences by major categories of race/ethnicity, gender, preterm birth, and others. Because the samples used in this study were collected during the time when PUFAs may have the greatest influence on the developing brain, associations seen here will inform on the role of PUFAs in risk of ASD

15. SUBJECT TERMS

None listed

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
Unclassified	Unclassified	Unclassified	Unclassified	38	19b. TELEPHONE NUMBER *(include area code)*

TABLE OF CONTENTS

1. **INTRODUCTION:** Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

The purpose of this project is to determine whether prenatal levels of polyunsaturated fatty acids (PUFAs), as classes (omega 3, omega 6, and total PUFA) as well as individual fatty acids, are associated with offspring autism spectrum disorder (ASD). These fats are critical in neurodevelopmental processes with evidence for disruption in ASD, and thus we hypothesize that altered levels of them during critical windows of neurodevelopment may influence risk. To address this hypothesis, we are conducting a population-based case control study, including 500 cases with ASD identified through the California Department of Developmental Services (DDS) and 500 general population controls identified through state birth certificates and matched by birth year (2011-2013), birth month, and sex, after excluding DDS clients. Using banked prenatal serum specimens collected through routine prenatal screening in California, levels of PUFAs are measured using liquid chromatography-mass spectrometry/high resolution mass spectrometry (LC-MS/MHMS). In a subset of participants (n=400), we will also examine measured levels of PUFAs in neonatal blood spots. Results from this work will provide novel information about the relationship between PUFAs and ASD, in the first study with measured levels of PUFAs during pregnancy.

2. **KEYWORDS:** Provide a brief list of keywords (limit to 20 words).

Autism, etiology, epidemiology, polyunsaturated fatty acids, prenatal risk factors, nutrition

3. **ACCOMPLISHMENTS:** The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction.

What were the major goals of the project?
List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

Major goals included in the SOW, and information on target and actual dates and percent completion, are listed below:

1. **Procurement of Maternal and Neonatal Stored Blood Samples**
   Target completion: Year 1, quarter 3-4
   Actual completion/% complete: Year 1, quarter 4- all maternal serum samples have been obtained; we are still awaiting receipt of neonatal blood spots; thus, this task is ~80% complete.
   Description: We have obtained all maternal prenatal serum samples (n=1000) and are awaiting receipt of neonatal blood spots (n=400). This major goal included the following sub-tasks: completing and submitting IRB and vital record use applications (completed by the second quarter of our first year, slightly later than expected due to California review board meeting dates); selecting cases and controls from California databases (projected for quarter 1; completed slightly later than anticipated, due to waiting for approvals); obtaining approval from the Genetic

Disease Screening Program (GDSP) for use of samples (completed as projected); requesting and obtaining samples from GDSP and sample shipment to the Snyder laboratory (maternal serum samples completed one quarter later than expected, due to delays in the California Biobank queue process. Neonatal samples not yet obtained but expected completion within this quarter, given our project is next in the Biobank queue).
Major milestones sought and achieved: Local and CPHS IRB approvals (as projected); HRPO approval (as projected); procurement of samples (majority completed, slightly later than expected due to the California Biobank Program's sample pulling process and limited resources).

2. **Measurement of PUFAs in maternal serum and newborn blood spots (Aims 1 and 3)**
   Target completion: Year 1, quarter 4- year 2, quarter 2
   Actual completion/% complete: We are on target for maternal serum samples; newborn blood spots measurements may extend into the 3rd quarter of year 2. Approximate % complete: 60%.
   Description: Measurement of PUFAs in 95% of maternal samples has been completed. As projected, final processing of the remaining maternal samples will be completed by the second quarter of the second year. As described under major goal 1 above, there has been a slight delay in obtaining bloodspots from the California Biobank, therefore delaying our analysis of these samples. However, we have confirmed shipment of these samples will soon take place.
   Major milestones sought: As stated in the SOW, completion of biosample assays is sought for the second year of our project.

3. **Data analysis of PUFAs in association with ASD (Aims 1, 2, and 3)**
   Target completion: (Year 2, quarters 2-4.)
   Actual completion/% complete: ~15% complete; on target for analyses to proceed as planned.
   Description: This major goal, as well as sub-tasks within it (analyses for Aim 1, the association between maternal PUFAs and ASD; analyses of subgroups and modifiers; and analyses of PUFAs as measured in newborn spots), is set for completion in our second year. As such, we have minimal information to report on this task in our first year. However, we have been able to conduct preliminary analyses relevant to Aim 1 (presented in Appendix as an abstract recently submitted to a major scientific conference), based on the ~95% of maternal serum samples that have been processed at this point. Thus, we are on, if not ahead of, target for this major goal.

4. **Presentation of findings**
   Target completion: (Year 3, quarters 1-4)
   Actual completion/% complete: ~10%
   Description: We have submitted preliminary results as an abstract to an international scientific conference, as mentioned in goals above, and as displayed in our Appendix.

What was accomplished under these goals?
For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

Major activities accomplished under these goals include: receipt of all necessary approvals, including local and California IRBs and GDSP for biospecimens; approval for use and receipt of all necessary data files, including outcome data from the California Department of Developmental Services, demographic, covariate, and identifying information needed for data linkage from Vital Statistics; conducting data linkage and selection of cases and controls for finalized study sample and data file; receipt and laboratory processing of the majority of biospecimens for PUFA measurement; and preliminary data analysis, including submission of these preliminary findings to a major scientific conference as an abstract (see Appendix 2). Basic statistics of covariates and characteristics of the study population have been examined and are displayed in Appendix 1, Table 1. In preliminary analyses of maternal PUFA levels, no significant associations were seen with PUFAs and ASD, but ORs were suggestive of an increased odds of ASD for individuals with very low linoleic acid (those in the lowest 5th percentile had ~50% increase in odds of ASD, though confidence intervals overlapped the null), while individuals with the highest levels of total PUFA and total omega 6 PUFAs appeared to have a reduction of risk of ASD by ~20% (though again, not statistically significant). These associations will be further examined as final samples are processed. As stated above, there has been a slight delay in receipt of neonatal samples, but we anticipate receipt of these samples shortly.

What opportunities for training and professional development has the project provided?
If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

Under funding from this project, the PI will attend the 2018 meeting of the International Society for Autism Research (INSAR), where she plans to present findings from this study (see Appendix for submitted abstract). This abstract has been submitted as part of a panel on prenatal nutrition and ASD; thus, the conference will provide opportunities for dissemination of findings from this work, gaining knowledge of other ongoing study of nutritional factors in ASD, and discussions with colleagues in the field that may serve fruitful for future collaborations.

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

Preliminary results from this work (data analysis is still ongoing, given the first lab batches have only recently been completed, and additional samples must be processed) have been submitted to the INSAR meeting as described above. As the premiere autism conference, findings will be disseminated to professionals in the field, though results may also be shared with the press. Once analyses are finalized, we plan to disseminate findings through publishing in peer reviewed journals.

What do you plan to do during the next reporting period to accomplish the goals?
If this is the final report, state "Nothing to Report."

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

Over the next reporting period, in our second year, we plan to complete laboratory analysis of all maternal serum samples, as well as obtain and process the neonatal blood spots. Upon final processing of all biosamples, we can update maternal analyses and run final analyses, while also exploring secondary analyses and conducting sensitivity analyses to ensure robust findings. Likewise, analyses using measured PUFA levels from neonatal blood spots will also be conducted. Finally, we will begin summarizing our findings and preparing them for manuscripts as the analyses are completed (with manuscript and presentation of findings to be conducted primary in the third year of the project).

4. **IMPACT:** Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

We expect that our analyses of PUFAs in neonatal bloodspots may have an impact on the potential for measuring nutritional biomarkers in these more widely-available specimens, given that such analysis has seen limited application; however, as we have not yet conducted these measurements, we cannot report on this aspect in this reporting period.

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to Report. Analyses are preliminary and ongoing at this point.

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "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:

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to Report.

What was the impact on society beyond science and technology?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

As we have not yet finalized statistical analyses, we do not have anything significant to report during this reporting period. However, we anticipate the results from this study will have an impact on improving public knowledge of the role of polyunsaturated fatty acids in the development of ASD, and the importance of intake of these fats during pregnancy.

5. **CHANGES/PROBLEMS:** The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

Changes in approach and reasons for change
Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

No significant changes in approach have been made. We did include an additional two controls in our sample given the need to balance birth years with matched cases after determining biospecimen availability. Analyses will still be conducted taking matching into account.

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

We have not experienced any major problems during this reporting period, though there were some delays in obtaining biosamples. We are still awaiting shipment of neonatal bloodspots, but are the next project in the California Biobank queue, with samples expected to ship within the next few weeks. This is not affecting our timeline, given the prioritization of processing these samples in our laboratory.

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

None.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

None.

Significant changes in use or care of vertebrate animals.

Not applicable

Significant changes in use of biohazards and/or select agents

Not applicable

6. PRODUCTS: List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

  Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to report.

Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: Author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to report.

Other publications, conference papers, and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

We have submitted the following as an abstract to the International Society for Autism Research (INSAR) 2018 Meeting, to be held in Rotterdam in May 2018:
"Prenatal levels of polyunsaturated fatty acids in association with autism spectrum disorder." Authors: Kristen Lyall, Gayle Windham, Nathaniel Snyder, Jasmine Carver, Craig Newschaffer.
We plan to submit this work as a manuscript for publication once analyses are finalized.

- **Website(s) or other Internet site(s)**
  List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to report.

- **Technologies or techniques**
  Identify technologies or techniques that resulted from the research activities. In addition to a description of the technologies or techniques, describe how they will be shared.

Nothing to report.

- **Inventions, patent applications, and/or licenses**
  Identify inventions, patent applications with date, and/or licenses that have resulted from the research. State whether an application is provisional or non-provisional and indicate the application number. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to report.

- **Other Products**
  Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment, and/or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:
  - *data or databases;*
  - *biospecimen collections;*
  - *audio or video products;*
  - *software;*
  - *models;*
  - *educational aids or curricula;*
  - *instruments or equipment;*
  - *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
  - *clinical interventions;*
  - *new business creation; and*

- *other.*

Nothing to report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?
Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change."

Name: Dr. Kristen Lyall
Project Role: Principle Investigator
Researcher Identifier
Nearest person month worked: 2
Contribution to Project: Oversaw all project activities, obtained appropriate approvals, and completed preliminary data analyses.

Name: Dr. Nathaniel Snyder
Project Role: Co-Investigator
Researcher Identifier
Nearest person month worked: 1
Contribution to Project: Performed laboratory analysis of bio specimens

Name: Dr. Gayle Windham
Project Role: Co-Investigator
Researcher Identifier
Nearest person month worked:1
Contribution to Project: Oversaw data linkage and aided in preparation of data files; helped to coordinate case control selection process.

Name: Jasmine Carver
Project Role: Data Analyst
Researcher Identifier
Nearest person month worked: 1
Contribution to Project: Under supervision of Co-I, Gayle Windham, performed data management, and data linkage.

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

If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Please see attached appendix 3. New grants are marked as "New."

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.
Provide the following information for each partnership:
Organization Name:
Location of Organization: (if foreign location list country)
Partner's contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- *Other.*

California Department of Public Health (CDPH)
Richmond, CA
Collaboration description: Our collaboration with Co-Investigator Dr. Gayle Windham and her study staff at CDPH is to ensure data linkage and study sample selection necessary for this project. Dr. Windham and her team have extensive experience with California birth certificate and DDS data, and conducting data linkages for similar projects. Dr. Windham and her staff have maintained close communication with the PI of this project, Dr. Lyall. Facilities have not been exchanged.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: For collaborative awards, independent reports are required from BOTH the Initiating PI and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to **https://ers.amedd.army.mil** for each unique award.

QUAD CHARTS: If applicable, the Quad Chart (available on https://www.usamraa.army.mil) should be updated and submitted with attachments.

N/A

9. APPENDICES:

Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.

Please see attached.

APPENDIX 1: STUDY POPULATION BASIC CHARACTERISTICS

Table 1: Basic characteristics of the study population by case status

		Cases		Controls	
		N=500		N=502	
Sex		n	(%)	n	(%)
	Male	413	(82.6)	416	(82.9)
	Female	87	(17.4)	86	(17.1)
Maternal Race					
	White	371	(74.2)	388	(77.3)
	Black	17	(3.4)	20	(4)
	Asian	89	(17.8)	67	(13.3)
	Other	5	(1.0)	3	(0.6)
	More than one race	12	(2.4)	9	(1.8)
	Not reported	6	(1.2)	15	(3)
Maternal ethnicity					
	Not Hispanic	243	(48.6)	222	(44.2)
	Hispanic	251	(50.2)	265	(52.8)
	Not reported	6	(1.2)	15	(3)
Insurance status					
	Medi-Cal	241	(48.2)	243	(48.4)
	Private Insurance	225	(45.0)	225	(44.8)
	Other	34	(6.8)	34	(6.8)
[Maternal Education					
	Less than High School	86	(17.2)	115	(22.9)
	High School	112	(22.4)	109	(21.7)
	Some College*	161	(32.2)	115	(22.9)
	College Degree	118	(23.6)	118	(23.5)
	Graduate Degree	45	(9.0)	46	(9.2)
Smoking					
	Preconception	12	(2.4)	10	(2)
	First Trimester	5	(1.0)	5	(1)
	Second Trimester	3	(0.6)	2	(0.4)
	Third Trimester	4	(0.8)	2	(0.4)
Maternal Birthplace					
	U.S.	272	(54.4)	279	(55.6)
	Mexico	115	(23.0)	138	(27.5)

	Philippines	16	(3.2)	9	(1.8)
	Vietnam	27	(5.4)	14	(2.8)
	Other (Outside U.S.)	70	(14.0)	62	(12.4)
		Mean (std. dev)		Mean (std. dev)	
Maternal Age (years)		29.46 (5.8)		28.30 (5.82)	
Paternal Age (years)		32.55 (6.9)		31.13 (6.7)	
Gestational Age (weeks)		38.78 (1.6)		38.73 (1.6)	
Birthweight (grams)		3382 (496)		3382 (538)	
Prenatal Visits		13.13 (3.8)		13.14 (3.5)	

Appendix 2: SCIENTIFIC ABSTRACT SUBMISSION

Abstract submitted to International Society for Autism Research (INSAR) Annual Meeting 2018, to be held in Rotterdam, Netherlands, May 9-12

Title: Prenatal polyunsaturated fatty acid levels in association with autism spectrum disorder

Authors: Kristen Lyall[1], Gayle Windham[2], Nathaniel Snyder[1], Jasmine Carver[3], Craig Newschaffer[1]
Author affiliations:
[1]AJ Drexel Autism Institute, Drexel University, Philadelphia, PA, USA
[2]California Department of Public Health, Environmental Health Investigations Branch, Richmond, CA
[3]Sequoia Foundation, La Jolla CA

Background: Polyunsaturated fatty acids (PUFAs) are critical to neurodevelopment. Though emerging work has identified associations between certain prenatal nutrients and reported supplements in association with autism spectrum disorder (ASD), and suggested altered levels of PUFAs in individuals already diagnosed with ASD, no prior study has examined the association between measured levels of prenatal PUFAs and ASD in order to determine potential etiologic involvement of these fats.

Objectives: To determine whether levels of PUFAs, measured in stored mid-pregnancy serum samples, differ in mothers who go on to have a child with ASD as compared to those who have an unaffected child.

Methods: This population-based statewide case-control study includes approximately 500 cases and 500 general population (GP) controls, matched on sex and month and year of birth (2011-2013). Cases of ASD were identified from the California Department of Developmental Services (DDS), and GP controls were randomly selected within strata of matching factors from birth certificate files after excluding DDS clients. Prenatal serum samples were drawn from the California Biobank Program, and levels of specific omega 3 and omega 6 PUFAs were measured using liquid chromatography-mass spectrometry/high resolution mass spectrometry (LC-MS/HRMS). Conditional logistic regression analyses, accounting for matching factors and adjusted for potential confounders, were used to examine the association between PUFAs (as individual fatty acids and as classes) and ASD.

Results: In preliminary analyses, mean levels of PUFAs did not significantly differ. In adjusted analyses examining associations with extremes of the distribution, there was a suggestion of an increase in odds of ASD for individuals in the lowest 5th percentile of linoleic acid levels (OR=1.57, 95% CI 0.90-2.76), relative to those with mid-distribution levels. Reductions of approximately 20% in odds of ASD for those in the highest 5th percentile of total PUFAs and total omega 6, were also observed, though these associations also did not reach statistical significance (OR=0.83, 95% CI 0.44, 1.56, respectively). Analyses will be updated as final samples are processed. Additional analyses will also investigate potential non-linear relationships between these fats and ASD using cubic splines, as well as associations with PUFAs measured in neonatal bloodspots in a subset of 400 cases and controls. Secondary analyses will examine the odds of ASD with and without comorbid intellectual disability (ID), relative to GP controls.

Conclusions: Preliminary findings from this large population-based case control study did not reveal significant associations between prenatal PUFA levels and ASD. However, associations similar in direction and magnitude for extremes of total PUFA, as well as linoleic acid specifically, are generally consistent with our previous results based on reported maternal diet, suggesting potential influences of very high and very low levels of these fats. Given the critical role of PUFAs in fetal brain development, and their influence on mechanisms with evidence for involvement in ASD etiology (inflammation and oxidative stress), further exploration of these potential associations is needed. Findings here will be updated using the full study group, exploring more complex exposure distribution relationships, and considering additional outcome subtypes.

APPENDIX 3

OTHER RESEARCH SUPPORT: Kristen Lyall, Sc.D.

Research Support: Since the last reporting period, Dr. Lyall has received additional support from grants R01ES026903, R01ES025531, and UG3OD023342; full support information is provided below.

CURRENT SUPPORT
TITLE: N/A - New Investigator Start-up Funding
FON: N/A
ROLE: PI
EFFORT: N/A
SUPPORTING AGENCY: Drexel University
GRANTS OFFICER: N/A
PERFORMANCE PERIOD: 07/01/2015-06/29/2018
FUNDING AMOUNT: $30,000
GOALS: Funding to be used for generation of preliminary data and associated costs to enable research program start-up.
SPECIFIC AIMS: N/A
OVERLAP: None

(NEW)
TITLE: An ASD Enriched (ASD-ER) ECHO Cohort (Grant # UG3OD023342)
EFFORT: 15%
SUPPORTING AGENCY: NIH
GRANTS OFFICER: N/A
PERFORMANCE PERIOD: 09/01/2016-08/31/2023
FUNDING AMOUNT: $11,378,719
PROJECT GOALS: In order to facilitate the study of environmental risk factors for ASD and related developmental delays in ECHO, this proposes to assemble a cohort of cohorts from 14 sites that include more than 1,000 siblings of confirmed ASD cases who are at markedly higher risk for ASD. Approximately 500 lower risk subjects will also be enrolled. Subjects were either pre- or postnatally enrolled and prospectively followed.
SPECIFIC AIMS: UG3 Phase (Years 1-2) 1. Establish and implement initial processes supporting both the overall ECHO initiative and the specific ASD ER aims, including: i. develop participant re-contact and consent procedures; ii. create a protocol for the collection of shed deciduous teeth; iii. re-contact ASD-ER subjects; and iv. collect shed deciduous teeth. 2. Validate quantification of prenatal deposition of selected (organochlorine pesticides, PCBs, and phthalates) persistent organic pollutants (POPs) in dental tissues as an exposure biomarker.
UH3 Phase (Years 3-7) For the ASD-ER Cohort: 3. Estimate associations of individual POP exposure levels and POP mixture exposure as measured in dental tissue with continuous, dichotomous, and trajectory ASD-related phenotypes. The Aim 2 validation study can be used for exposure measurement error correction, if the needed. 4. Estimate associations of individual metal exposure levels and metal mixture exposure with continuous, dichotomous, and trajectory ASD-related phenotypes. 5. Use polygenic risk scores (PRS) to explore the role of genetic susceptibility in modifying the effect of prenatal POP and metal and exposure on the expression of ASD-related phenotypes. For the full ECHO cohort (in the Neurodevelopmental Focus Area) 6. Screen a range of environmental exposures for indications that exposure effects are magnified by specific susceptibility genotypes in the enriched risk ASD-ER cohort (using gene-environment wide interaction study, GEWIS, approaches) then replicate GEWIS analyses for exposures flagged in ASD-ER in the remaining ECHO cohort. The approach can be used for ASD and broader developmental delay outcomes.
ROLE: Co-Investigator

OVERLAP: None

(NEW)
TITLE: Prenatal exposure to metals and risk for ASD in MARBLES and EARLI (Grant # R01ES025531)
EFFORT: 4.7%
SUPPORTING AGENCY: NIH, Subcontract to Drexel; Prime Institution: Johns Hopkins
GRANTS OFFICER: N/A
PERFORMANCE PERIOD: 07/01/2016-06/30/2021
FUNDING AMOUNT: $181,845
PROJECT GOALS: Estimate the prospective associations between directly measured prenatal and birth exposure to five metals (Pb, Hg, Cd, Se, Mn) and subsequent risk for ASD and related quantitative phenotypes. Examine the utility of epigenetic DNA methylation measurement in characterizing the ASD risk associated with prenatal metals exposure.
SPECIFIC AIMS: 1) Estimate prospective associations between directly measured prenatal and birth exposure to each of five metals (Pb, Hg, Cd, Se, Mn), and to pooled metals, and subsequent risk for ASD and related quantitative phenotypes; 2) Maximize ability to detect risk due to metals exposure by incorporating maternal and child genetic susceptibility; 3) Integrate epigenetic DNA methylation in the examination of prenatal metals exposure ASD risk.
ROLE: Co-Investigator
OVERLAP: None

(NEW)
TITLE: Prenatal Exposure to Endocrine Disrupting Chemical Mixtures and ASD Risk (Grant # R01ES026903)
EFFORT: 7.5%
SUPPORTING AGENCY: NIEHS
GRANTS OFFICER: Molly E. Puente; Puentem@mail.nih.gov; 919-541-1373
PERFORMANCE PERIOD: 9/15/2017-8/31/2021
FUNDING AMOUNT: $242,276
GOALS: Prenatal brain development is heavily influenced by hormonal mechanisms, and endocrine disrupting chemicals (EDCs) cross the placenta to reach the particularly vulnerable fetus. In this project, we measure EDC exposure from blood and urine samples collected from pregnant women to study the effect of a woman's exposure to complex mixtures of these chemicals on the behaviors in their child that are related to autism spectrum disorders (ASD). We will determine whether and how much exposure to EDC mixtures increases ASD behaviors and will identify any particular EDCs that are driving effects we observe, in order to inform possible approaches to reduce pregnant women's exposure to EDCs that may be increasing their children's ASD risk.
SPECIFC AIMS: Aim 1: (a) characterize the cumulative effect of prenatal exposure to complex EDC mixtures on ASD related phenotype and (b) identify specific EDCs driving any observed mixture effect. Aim 2: Explore whether EDC mixture effects vary across subgroups defined by sibling ASD status, sex, and cognitive status. Aim 3: Explore whether prenatal exposure to complex EDC mixtures affects maternal prenatal thyroid hormone levels, biomarkers for one candidate mechanism by which EDCs may influence ASD risk.
OVERLAP: None.
Role: Co-Investigator
OVERLAP: None

PAST SUPPORT

TITLE: Autism Risk, Prenatal Environmental Exposures, and Pathophysiologic Markers
FON: R01ES020392 (Hertz-Picciotto, Ozonoff, Pessah)
ROLE: Postdoctoral fellow
EFFORT: 50%

SUPPORTING AGENCY: NIH/NIEHS
GRANTS OFFICER: Cindy Lawler, Ph.D.
P.O. Box 12233
Mail Drop K3-15
Research Triangle Park, NC 27709
PERFORMANCE PERIOD: 08/24/11 - 02/28/16
FUNDING AMOUNT: $1,198,254 (annual direct)
GOALS: This 5-year study extends the MARBLES (Markers of Autism Risk in Babies: Learning Early Signs) Study, a prospective investigation of a high-risk cohort that begins during pregnancy and seeks to identify environmental exposures that increase risk for childhood autism.
SPECIFIC AIMS:

1) To assess associations of self-reported exposure, measurements of internal dose, and toxicologically-derived estimates of biologically effective dose, on the one hand, with risk for ASD or other impairments in neurobehavioral development on the other
2) To examine whether the exposure or dose estimates are associated with markers of aberrant immune responses or mitochondrial dysfunction and whether these markers predict clinically confirmed child developmental status at three years of age.

OVERLAP: None

TITLE:The UC Davis Center for Children's Environmental Health & Disease Prevention
FON: 2P01ES011269 and 83543201 (van de Water)
ROLE: Post-doctoral fellow
EFFORT: 50%
SUPPORTING AGENCY: NIH/NIEHS and EPA
GRANTS OFFICER: Kimberly Gray, Ph.D.
530 Davis Dr
Keystone Building
Durham, NC 27713
PERFORMANCE PERIOD: 06/01/13 - 05/31/18
FUNDING AMOUNT: $1,000,000 (annual direct)
GOALS: The principal concern of the UC Davis Center for Children's Environmental Health and Disease Prevention (CCEH) is to identify and understand environmental, immunologic, and genetic risk factors contributing to the incidence and severity of childhood autism. This project leverages existing resources from two large epidemiologic studies to address the potential contribution from several common household exposures to risk for an autism spectrum disorder (ASD), separately and in combination with certain genomic or epigenetic profiles. The two existing investigations are: the population-based case-control CHARGE (CHildhood Autism Risk from Genetics and Environment) Study, and MARBLES (Markers of Autism Risk in Babies Learning Early Signs), a cohort study following pregnant women who previously delivered a child that developed autism to understand what influences the outcome of the younger sibling and to identify early markers of ASD.
SPECIFIC AIMS:

1) To examine polybrominated diphenyl ethers (PBDEs, used as flame retardants), their hydroxylated metabolites, perfluorinated compounds and pyrethroid insecticides in relation to a) child's developmental status (ASD, developmental delay (DD), specific speech /language delay) and other trajectories, and b) with markers of immune function and c) epigenetic markers.
2) To examine the differential impact of the PBDEs, PFCs, and pyrethroids based on relevant genetic polymorphisms, CNVs, or measures of global DNA methylation, considering mechanistic pathways that link to these compounds.

3) To explore, in discovery-oriented mode, a wide array of exposures from biologic specimens, interviews, and medical records, along with the genetic and epigenetic data from these projects.

OVERLAP: None

TITLE: Interdisciplinary Training for Autism Researchers
FON: MH073124-07 (PI Rogers and Amaral)
ROLE: Trainee
SUPPORTING AGENCY: NIH, NIMH
GRANTS OFFICER: Christopher S Sarampote, Ph.D.
Division of Developmental Translational Research (DDTR)
National Institute of Mental Health
6001 Executive Boulevard, Room 7164, MSC 9617
Bethesda, MD 20892-9617
PERFORMANCE PERIOD: 09/29/2004-07/31/2019
FUNDING AMOUNT: Variable; Approx. $250,000-350,000 per year
PROJECT GOALS: The primary, long-term goal of this training program is to prepare a diverse pool of highly trained scientists to conduct interdisciplinary biological, behavioral, and clinical research to understand, treat, and prevent autism spectrum and related neurodevelopmental disorders.
SPECIFIC AIMS:

1) Provision of 24 months of postdoctoral interdisciplinary research training to 8 NIH-funded MD and PhD trainees from diverse scientific fields and from cultural backgrounds under-represented in science.
2) Development and delivery of an interdisciplinary curriculum that imparts to trainees the current research questions, methods, and findings on autism spectrum and related neurodevelopmental disorders in diverse fields of study, including genetics, animal models, epidemiology, immunology, cultural competency and health disparities, neuroanatomy, neuroimaging, metabolomics/proteomics, neurochemistry/psychopharmacology, neurophysiology, and research design and analysis.
3) Development and delivery of training content that grounds trainees in the ethics of research involving children, persons with disabilities, family members, and research access by underrepresented groups.
4) Delivery of training that provides experiential and conceptual understanding of the clinical and psycho-social effects of autism and related disabilities on persons with the disorders and on their families.

OVERLAP: None

PENDING SUPPORT

TITLE: A pooled cohort investigation of comprehensive prenatal diet and autism phenotype
ROLE: Principal-Investigator
EFFORT: 25%
SUPPORTING AGENCY: NIH
GRANTS OFFICER: N/A
PERFORMANCE PERIOD: 4/1/2018-3/31/2023
FUNDING AMOUNT: $ 22,159,125
PROJECT GOALS: Despite the known importance of maternal diet in fetal development, relatively few studies have focused on its role in autism spectrum disorder (ASD). The proposed project will merge data from three longitudinal cohorts with validated prenatal dietary data in order to examine nutrients with evidence for a role in neurodevelopment, including a focus on polyunsaturated fatty acids, vitamin D, and folate, as well as objective markers of these nutrients or their related pathway as measured in prenatal biosamples, in association with ASD phenotype. This work will also more comprehensively assess the role of prenatal diet in ASD by conducting state-of-the-art Bayesian analyses to determine combined effects of a larger set of nutrients and examine the relative roles of suspected mechanistic pathways.
SPECIFIC AIMS:

1) Examine associations between ASD phenotype and specific nutrients measured from a validated Food Frequency Questionnaire (FFQ): **A)** long-chain PUFAs, as a class as well as by n-3, n-6, and specific fatty acids; **B)** Vitamin D; and **C)** maternal folate, adjusting for other dietary factors, in the pooled cohort (n~5,000). We will examine intake of these nutrients during pregnancy, and explore, for the subset of ~2,000 participants with available information, lactational exposure during the first postnatal year (as a period of rapid brain growth and potential ASD susceptibility).
2) Estimate associations between ASD-related phenotype and available objective biomarkers of maternal prenatal nutritional status: circulating levels of **A)** PUFAs (n~800); and **B)** vitamin D (25OHD) (n~1000).
3) Explore whether prenatal and cord blood global methylation, a mechanism of etiologic interest in ASD that is influenced by maternal nutrition, measured as %5-methyl cytosines in Long-Interspersed Nuclear Element (LINE-1), is associated with ASD-related phenotype (n~800). We will also examine whether these methylation scores are associated with other nutrients with neurodevelopmental potential (listed in 4A).
4) Conduct data-driven Bayesian analyses of multiple maternal dietary factors measured by prenatal FFQ in the pooled cohort (n~5,000).
5) OVERLAP: None

TITLE: Oxidative stress pathways and placental pathology in association with autism spectrum disorder and neurodevelopment

ROLE: Principal-Investigator
EFFORT: 20%
SUPPORTING AGENCY: NIH
GRANTS OFFICER: N/A
PERFORMANCE PERIOD: 7/1/2018-6/30/2023
FUNDING AMOUNT: $ 331,488
PROJECT GOALS: Oxidative stress (OS, the state of imbalance between antioxidants and reactive oxidant species) can cause damage to proteins, lipids, and DNA; with both the developing brain and placenta particularly susceptible to such imbalance, OS may have lasting impacts on the developing fetus. The proposed project, which uses data from a high-risk pregnancy cohort of mothers who have had a child with an autism spectrum disorder (ASD), will examine prenatal levels of key oxidative stress biomarkers as well as placental measures in association with ASD phenotype and neurodevelopment as captured by validated continuous scales (the Social Responsiveness Scale and the Mullen Scales of Early Learning). By using biomarkers of OS-induced DNA damage (8-OHdG), protein oxidation (tyrosines), and lipid peroxidation (8-isoprostane), antioxidant balance (glutathione and the GSH/GSSG ratio), and exploring mediation through placental morphology and vascular pathology, this study will provide novel information about potential OS pathways that may lead to adverse neurodevelopmental outcomes.
SPECIFIC AIMS:

1. Examine associations between prenatal maternal OS biomarkers and ASD/neurodevelopment
2. Examine placental morphology in association with OS and ASD/neurodevelopment
3. Examine placental vascular pathology in association with OS and ASD/neurodevelopment

OVERLAP: None

PREVIOUS/CURRENT/PENDING SUPPORT
NEWSCHAFFER, CRAIG

Research Support: Since the last reporting period, Dr. Newschaffer has received additional support from grants R01ES026903, R01ES025531, U01DD001214, and UG3OD023342; full support information is provided below.

CURRENT

TITLE: Early Detection of Autism Spectrum Disorder (Robins)
EFFORT: 3%
SUPPORTING AGENCY: NIH
GRANTS OFFICER: Saiyda Khan; Email: khansa@mail.nih.gov; Phone: (301) 496-5001
PERFORMANCE PERIOD: 09/25/2014-05/31/2015
FUNDING AMOUNT: $3,029,559 total costs
PROJECT GOALS: To examine the optimal schedule for routine ASD screening, and the integration of screening with surveillance and other strategies to detect autism.
SPECIFIC AIMS: 1) Determine the most appropriate schedule for ASD screening (12, 15, or 18 mos); 2) Examine the effect of a brief training on the accuracy of physician surveillance in identifying ASD during pediatric well-child care visits; 3) Identify factors that influence ASD screening and surveillance
OVERLAP: None

TITLE: Mobilizing Community Systems to Engage Families in Early ASD Detection & Services
EFFORT: 5%
SUPPORTING AGENCY: NIH; Subaward to Drexel, Prime Institution: Florida State University
GRANTS OFFICER: Jackie Chia; Email: Jackie.Chia@nih.gov; Phone: 301-443-1341
PERFORMANCE PERIOD: 08/25/2014-06/30/2019
FUNDING AMOUNT: $10,439,836 total costs
PROJECT GOALS: the overarching purpose of this collaborative research investigation is to document the effectiveness of an online automated universal screen for communication delay and autism initially at 18 months of age and decision rule for referral to an ASD evaluation and study an evidence-based intervention to increase family engagement and expedite receipt of screening, diagnosis, eligibility for early intervention (EI), and EI services.
SPECIFIC AIMS: 1) Test effectiveness of universal ASD screening at 18mos and referral for evaluation; 2) Test effectiveness of family engagement intervention; 3) Explore mediators and moderators of intervention; 4) monitor implementation of evidence-based EI; 5) improve uptake of evidence-based EI.
OVERLAP: None.

TITLE: Perspective Evaluation of Air Pollution, Cognition, and Autism from Birth Onward (Volk)
EFFORT: 5%
SUPPORTING AGENCY: NIH; Subaward to Drexel, Prime Institution: Johns Hopkins University
GRANTS OFFICER: N/A
PERFORMANCE PERIOD: 06/10/2014-04/30/2016
FUNDING AMOUNT: $88,627 total costs
PROJECT GOALS: Determine if air pollutant exposure is associated with ASD risk.
SPECIFIC AIMS: 1) Assign air pollution exposure using modeling techniques; 2) Examine effects of exposure on cognative development; 3) Evaluate the effect of pollutant exposures on ASD traits and diagnoses.

OVERLAP: None (Directly complementary project that will provide air pollutant measures to be used to develop exposure response biomarkers here)

TITLE: Prenatal Antimicrobial Agent Exposure, Fetal Androgens and ASD Risk
EFFORT: 1%
SUPPORTING AGENCY: NIH
GRANTS OFFICER: James R Williams; Email: williamsjr@niehs.nih.gov; Phone: 919-541-1403
PERFORMANCE PERIOD: 08/01/2015-06/30/2017 (1 year NCE)
FUNDING AMOUNT: $430,375
PROJECT GOALS: Investigate the association between prenatal antimicrobial exposure and ASD risk.
SPECIFIC AIMS: 1) Estimate the association between biomarkers of prenatal maternal TCS/TCC exposure and sibling ASD-related outcomes at 12 and 36 months; 2) Assess whether fetal testosterone levels mediate and/or modify the association between prenatal maternal TCS/TCC exposure and sibling ASD-related outcomes at 12 and 36 months
OVERLAP: None.

TITLE: Folic Acid Prevention Pathways for ASD in High Risk Families
EFFORT: 5%
SUPPORTING AGENCY: NIH
GRANTS OFFICER: E-mail: Cindy Lawler lawler@niehs.nih.gov
PERFORMANCE PERIOD: 8/1/15-7/30/20
FUNDING AMOUNT: $172,790
PROJECT GOALS: Examine pathways for prevention of ASD through folate intake.
SPECIFIC AIMS: 1) Examine association between folate intake and ASD; 2) Investigate whether associations between periconceptional folate and ASD risk is altered by methylation-altering genotypes.
OVERLAP: None.

TITLE: Lipidomics of meconium in neurodevelopment (Snyder)
EFFORT: 5%
SUPPORTING AGENCY: NIH/NICHD
GRANTS OFFICER: Saiyda Khan; Telephone: 301-496-5001; E-mail: khansa@mail.nih.gov
PERFORMANCE PERIOD: 04/22/2016-03/31/2018
FUNDING AMOUNT: $275,000 Direct Costs
PROJECT GOALS: This proposal will quantify and compare the lipid content of meconium in typically developing versus neurodevelopmentally delayed children from a prospective enriched risk cohort of early events in autism spectrum disorder.
SPECIFIC AIMS: Specific Aim 1. Identify unknown chromatographic features with differential abundance between ASD and controls in a prospective enriched risk cohort. Specific Aim 2. Structurally elucidate the putative biomarkers of ASD and compare the lipid content of meconium, placenta, and cord blood. Specific Aim 3. Develop and validate a targeted method for the quantitation of putative biomarkers of ASD.
OVERLAP: No overlap.

(NEW)
TITLE: Component A: MD CADDRE: Study to Explore Early Development, SEED Phase III (Grant # U01DD001214)

EFFORT: 3%
SUPPORTING AGENCY: NIH, Subcontract to Drexel; Prime Institution: Johns Hopkins
GRANTS OFFICER: N/A
PERFORMANCE PERIOD: 07/01/2016-06/30/2017
FUNDING AMOUNT: $11,540
PROJECT GOALS: Continue SEED 2 recruitment at Maryland Site – conducted primary and other approved analyses using SEED 1 data.
SPECIFIC AIMS: Build a large multisite case-control ASD study. Evaluate association between a range of risk factors and ASD occurrence.
OVERLAP: None

(NEW)
TITLE: Prenatal Exposure to Endocrine Disrupting Chemical Mixtures and ASD Risk (Grant # R01ES026903)
EFFORT: 5%
SUPPORTING AGENCY: NIH
GRANTS OFFICER: Molly E. Puente; Puentem@mail.nih.gov; 919-541-1373
PERFORMANCE PERIOD: 09/15/2017 – 08/31/2021
FUNDING AMOUNT: $242,276
GOALS: Prenatal brain development is heavily influenced by hormonal mechanisms, and endocrine disrupting chemicals (EDCs) cross the placenta to reach the particularly vulnerable fetus. In this project, we measure EDC exposure from blood and urine samples collected from pregnant women to study the effect of a woman's exposure to complex mixtures of these chemicals on the behaviors in their child that are related to autism spectrum disorders (ASD). We will determine whether and how much exposure to EDC mixtures increases ASD behaviors and will identify any particular EDCs that are driving effects we observe, in order to inform possible approaches to reduce pregnant women's exposure to EDCs that may be increasing their children's ASD risk.
SPECIFC AIMS: Aim 1: (a) characterize the cumulative effect of prenatal exposure to complex EDC mixtures on ASD related phenotype and (b) identify specific EDCs driving any observed mixture effect. Aim 2: Explore whether EDC mixture effects vary across subgroups defined by sibling ASD status, sex, and cognitive status. Aim 3: Explore whether prenatal exposure to complex EDC mixtures affects maternal prenatal thyroid hormone levels, biomarkers for one candidate mechanism by which EDCs may influence ASD risk.
OVERLAP: None.

(NEW)
TITLE: An ASD Enriched (ASD-ER) ECHO Cohort (Grant # UG3OD023342)
EFFORT: 20%
SUPPORTING AGENCY: NIH
GRANTS OFFICER: N/A
PERFORMANCE PERIOD: 09/01/2016-08/31/2023
FUNDING AMOUNT: $11,378,719
PROJECT GOALS: In order to facilitate the study of environmental risk factors for ASD and related developmental delays in ECHO, this proposes to assemble a cohort of cohorts from 14 sites that include more than 1,000 siblings of confirmed ASD cases who are at markedly higher risk for ASD. Approximately 500 lower risk subjects will also be enrolled. Subjects were either pre- or postnatally enrolled and prospectively followed.

SPECIFIC AIMS: UG3 Phase (Years 1-2) 1. Establish and implement initial processes supporting both the overall ECHO initiative and the specific ASD ER aims, including: i. develop participant re-contact and consent procedures; ii. create a protocol for the collection of shed deciduous teeth; iii. re-contact ASD-ER subjects; and iv. collect shed deciduous teeth. 2. Validate quantification of prenatal deposition of selected (organochlorine pesticides, PCBs, and phthalates) persistent organic pollutants (POPs) in dental tissues as an exposure biomarker.
UH3 Phase (Years 3-7) For the ASD-ER Cohort: 3. Estimate associations of individual POP exposure levels and POP mixture exposure as measured in dental tissue with continuous, dichotomous, and trajectory ASD-related phenotypes. The Aim 2 validation study can be used for exposure measurement error correction, if the needed. 4. Estimate associations of individual metal exposure levels and metal mixture exposure with continuous, dichotomous, and trajectory ASD-related phenotypes. 5. Use polygenic risk scores (PRS) to explore the role of genetic susceptibility in modifying the effect of prenatal POP and metal and exposure on the expression of ASD-related phenotypes. For the full ECHO cohort (in the Neurodevelopmental Focus Area) 6. Screen a range of environmental exposures for indications that exposure effects are magnified by specific susceptibility genotypes in the enriched risk ASD-ER cohort (using gene-environment wide interaction study, GEWIS, approaches) then replicate GEWIS analyses for exposures flagged in ASD-ER in the remaining ECHO cohort. The approach can be used for ASD and broader developmental delay outcomes.
OVERLAP: None

(NEW)
TITLE: Prenatal exposure to metals and risk for ASD in MARBLES and EARLI (Grant # R01ES025531)
EFFORT: 4%
SUPPORTING AGENCY: NIH, Subcontract to Drexel; Prime Institution: Johns Hopkins
GRANTS OFFICER: N/A
PERFORMANCE PERIOD: 07/01/2016-06/30/2021
FUNDING AMOUNT: $181,845
PROJECT GOALS: Estimate the prospective associations between directly measured prenatal and birth exposure to five metals (Pb, Hg, Cd, Se, Mn) and subsequent risk for ASD and related quantitative phenotypes. Examine the utility of epigenetic DNA methylation measurement in characterizing the ASD risk associated with prenatal metals exposure.
SPECIFIC AIMS: 1) Estimate prospective associations between directly measured prenatal and birth exposure to each of five metals (Pb, Hg, Cd, Se, Mn), and to pooled metals, and subsequent risk for ASD and related quantitative phenotypes; 2) Maximize ability to detect risk due to metals exposure by incorporating maternal and child genetic susceptibility; 3) Integrate epigenetic DNA methylation in the examination of prenatal metals exposure ASD risk.
OVERLAP: None

PENDING
TITLE: The impact of early prenatal exposure to metals on placental development and subsequent health outcomes
EFFORT: 2.5%
SUPPORTING AGENCY: NIH; Subcontract to Drexel, Prime Institution: Johns Hopkins University School of Medicine
GRANTS OFFICE: N/A
PERFORMANCE PERIOD: 03/01/2018-02/28/2023
FUNDING AMOUNT: $15,944

PROJECT GOALS: The AJ Drexel Autism Institute will provide the PI with access to data from the EARLI study. In Year 1 we will provide the PI with de-identified data files including subject outcome and covariate data items. We will also conduct inventories and sample selection from our biorepository database and will send the EARLI Biorepository information needed to ship samples to the PI's laboratory. In Year 2, Dr. Newschaffer will assist in the interpretation of data analyses and will contribute to the co-authorship of any study publications and presentations.
OVERLAP: None.

TITLE: Mycotoxins as an environmental influence on development of autism spectrum disorder
EFFORT: 2.5%
SUPPORTING AGENCY: NIH; Subcontract to Drexel, Prime Institution: Oregon State University
GRANTS OFFICER: N/A
PERFORMANCE PERIOD: 07/01/2018-06/30/2020
FUNDING AMOUNT: $16,040
PROJECT GOALS: The AJ Drexel Autism Institute will provide the PI with access to data from the EARLI study. In Year 1 we will provide the PI with de-identified data files including subject outcome and covariate data items. We will also conduct inventories and sample selection from our biorepository database and will send the EARLI Biorepository information needed to ship samples to the PI's laboratory. In Year 2, Dr. Newschaffer will assist in the interpretation of data analyses and will contribute to the co-authorship of any study publications and presentations.
OVERLAP: None.

TITLE: Metals Dysregulation, Brain Development, and Autism Spectrum Disorder
EFFORT: 5%
SUPPORTING AGENCY: NIH; Subcontract to Drexel, Prime Institution: Johns Hopkins University School of Medicine
GRANTS OFFICER: N/A
PERFORMANCE PERIOD: 07/01/2018-06/30/2023
FUNDING AMOUNT: $34.241
PROJECT GOALS: The AJ Drexel Autism Institute will provide the PI with access to data and biosamples from the ASD-ER cohort. In Year 1 we will provide the PI with data files including subject outcome and covariate data items. We will also conduct inventories and sample selection from our biorepository database and will select samples for analysis at the Arora laboratory. In subsequent years, Drs. Newschaffer and Hamra will assist in planning, implementing and disseminating data analyses, with Dr. Hamra focusing on metal mixture models, and will contribute to the co-authorship of any study publications and presentations.
OVERLAP: None.

PAST SUPPORT

TITLE: MCH Health Care Transitions Research Network (HCT-RN) for Youth and Young Adults with ASD
EFFORT: 2%
SUPPORTING AGENCY: HRSA; Subcontract to Drexel, Prime Institution: University of California, Los Angeles
GRANTS OFFICER: N/A
PERFORMANCE PERIOD: 09/01/2014-08/31/2016
FUNDING AMOUNT: $106,507

PROJECT GOALS: To support the creation of an interdisciplinary, multi-center research forum for scientific collaboration and infrastructure-building, with a focus on research designed to improve health care transitions and promote an optimal transition to adulthood among youth and young adults with ASD, including optimal physical, psychosocial, educational, and vocational outcomes
SPECIFIC AIMS: No specific research aims – just sub-goals for achieving the above
OVERLAP: None.

TITLE: Early life vitamin D levels and risk of autism spectrum disorders
EFFORT: 2.5%
SUPPORTING AGENCY: NIH
GRANTS OFFICER: E-mail: Cindy Lawler lawler@niehs.nih.gov
PERFORMANCE PERIOD: 7/1/14-6/30/16
FUNDING AMOUNT: $172,790
PROJECT GOALS: Study the potential effect of vitamin D on ASD risk.
SPECIFIC AIMS: 1) Describe vitamin D status in prenatal and neonatal blood samples in ASD cases and controls; 2) Determine the associations of prenatal vitamin D concentrations and risk of ASD; 3) Determine the associations of neonatal vitamin D concentrations and risk of ASD.
OVERLAP: No overlap.

TITLE: Prenatal PBDE exposure and ASD-related developmental outcomes in the EARLI cohort
SUPPORTING AGENCY: Autism Speaks
PERFORMANCE PERIOD: 02/01/2013 – 01/31/2015
PROJECT GOALS: This project involves analyses of biomarkers of prenatal maternal PBDE exposure, thyroid hormone levels, epigenetic profiles and 12 month AOSI scores in a cohort of high-risk infant siblings.
OVERLAP: None. (Complementary as this project provided the PBDE exposure measures proposed for use here)

TITLE: Early Autism Risk Longitudinal Investigation (EARLI) Network
SUPPORTING AGENCY: NIH
PERFORMANCE PERIOD: 04/01/2008 – 3/31/2015
PROJECT GOALS: To implement a multisite (4 sites) NIH Autism Center of Excellence study to establish and prospectively follow a cohort of mothers of children with an autism spectrum disorder (ASD) at the start of a subsequent pregnancy.
OVERLAP: None. (Original grant creating the cohort whose data will be used in the proposed study.)

TITLE: Environment, the Perinatal Epigenome and Risk for Autism
SUPPORTING AGENCY: NIH; Subcontract to Drexel; Prime organization: Johns Hopkins
PERFORMANCE PERIOD: 09/01/2009-6/30/2014
PROJECT GOALS: This project will take a comprehensive genome-wide approach to understand the interplay between genetics, epigenetics, and in utero environment in birth and early development phenotypes that are important predictors of adverse outcomes generally, and are related to ASD specifically.
OVERLAP: None.

TITLE: Genome-wide Environmental Interaction Study for Autism: The SEED Study.
SUPPORTING AGENCY: CDC; Subcontract to Drexel; Prime organization: Johns Hopkins

PERFORMANCE PERIOD: 09/28/2009-6/30/2012
PROJECT GOALS: This project is identifying SNPS whose effects on autism spectrum disorders may vary across exposure categories, including maternal medication use in pregnancy.
OVERLAP: None.

TITLE: IBIS-EARLI Collaboration
SUPPORTING AGENCY: Autism Speaks
PERFORMANCE PERIOD: 01/01/2009 – 12/31/2014
PROJECT GOALS: This project involves analyses of pooled samples from the EARLI and IBIS studies intended to discover genetic and environmental risk factors for quantitative developmental trajectory outcomes related to ASD.
OVERLAP: None.

TITLE: Development and Validation of an Autism Case Confirmation Approach for Use in the National Children's Study
SUPPORTING AGENCY: NIH; Subcontract to Drexel; Prime Institution: Westat
PERFORMANCE PERIOD: 09/28/2010-9/27/2014
PROJECT GOALS: Formative, multisite (11 sites) research in the NCS to test performance of three alternative approaches to confirming ASD case status that can be administered by study staff without background in child development in 30 minutes or less.
OVERLAP: None.

TITLE: Study of Health Outcomes in Children with Autism and Their Families
SUPPORTING AGENCY: NIH; Subcontract to Drexel; Prime Institution: Lewin and Associates
PERFORMANCE PERIOD: 09/20/2010-2/28/2014
PROJECT GOALS: Project involves analysis of a large private insurance administrative data base to describe trajectories of health outcomes and utilization in children with ASD and their families as well as explore the potential utility of this datasource for etiologic research.
OVERLAP: None.

PREVIOUS/CURRENT/PENDING SUPPORT

ROBINSON, LUCY F.

Research Support: Since the last reporting period, Dr. Robinson has received additional support from grant R01ES02690; full support information is provided below.

ACTIVE

TITLE Structure and Growth of the Thoracolumbar Spine and Ribs in Normative Pediatric and AIS subjects - A Comprehensive Multi-Center and multi-Modal Validation Study
EFFORT: 3%
SUPPORTING AGENCY: Scoliosis Research Society
GRANTS OFFICER: N/A
PERFORMANCE PERIOD: Jan 1, 2015 – Dec 31, 2017
FUNDING AMOUNT: $50,000
PROJECT GOALS: Describe growth of lumbar spine (vertebrae and intervertebral discs) 4%for normative and adolescent idiopathic scoliosis (AIS) subjects.
SPECIFIC AIMS: 1. Quantify the 3D geometry of the lumbar spine (vertebrae and intervertebral discs) and growth rates based on retrospective abdominal computed tomography (CT) scans from 100 normative male and female subjects, ages 1 – 18 years. All the subjects will be within the 5th and 95th percentiles of height, weight, and body mass index (BMI). Hypothesis 1: Structural morphology and growth rates of the lumbar spine will vary with age and gender in the pediatric population.2. Characterize the 3D thoracolumbar vertebra morphology, 3D rib position and geometry, and 3D geometric morphology of the costovertebral articulations at each thoracic level using biplanar radiographic image-based reconstructions obtained using EOS (EOS imaging Inc, Cambridge, MA) from 120 AIS subjects (ages 10-18 years) displaying a right curvature, with varying Lenke curve types and Cobb angle. The total number of subjects will be evenly distributed among the six Lenke curve types, with each group further sub-divided by Cobb angle of greater than and less than 45 degrees. 3. Use Generalized Procrustes Analysis (GPA) and Multi-level Functional Principal Component Analysis (MFPCA) based regression to create average shape models and predictive equations that describe Lenke curve type and Cobb angle-dependent spine and rib cage shape changes in AIS subjects.
OVERLAP: None.

(NEW)

TITLE: Prenatal Exposure to Endocrine Disrupting Chemical Mixtures and ASD Risk (Grant # R01ES026903)
EFFORT: 5%
SUPPORTING AGENCY: NIH
GRANTS OFFICER:
PERFORMANCE PERIOD: 09/15/2017 – 08/31/2021
FUNDING AMOUNT: $242,276
GOALS: Prenatal brain development is heavily influenced by hormonal mechanisms, and endocrine disrupting chemicals (EDCs) cross the placenta to reach the particularly vulnerable fetus. In this project, we measure EDC exposure from blood and urine samples collected from pregnant women to study the effect of a woman's exposure to complex mixtures of these chemicals on the behaviors in their child that are related to autism spectrum disorders (ASD). We will determine whether and how much exposure to EDC mixtures increases ASD behaviors and will identify any particular EDCs that are driving effects we observe, in order to inform possible approaches to reduce pregnant women's exposure to EDCs that may be increasing their children's ASD risk.

SPECIFC AIMS: Aim 1: (a) characterize the cumulative effect of prenatal exposure to complex EDC mixtures on ASD related phenotype and (b) identify specific EDCs driving any observed mixture effect. Aim 2: Explore whether EDC mixture effects vary across subgroups defined by sibling ASD status, sex, and cognitive status. Aim 3: Explore whether prenatal exposure to complex EDC mixtures affects maternal prenatal thyroid hormone levels, biomarkers for one candidate mechanism by which EDCs may influence ASD risk.
OVERLAP: None.

PENDING
TITLE: Clinical Implications of Cerebral Deoxygenation During Hemodialysis Treatment: A Pilot Study
EFFORT: 10%
SUPPORTING AGENCY: NIH,
GRANTS OFFICER: N/A
PERFORMANCE PERIOD: 1/12018-12/31/2019
FUNDING AMOUNT: $275,021.21
PROJECT GOALS: The central premise of this proposed study is that noninvasive monitoring of brain oxygenation during HD represents a promising strategy to detect poor tolerance to HD treatments, which can result in functional deficits and poor quality of life. Therefore, the goal of this NIDDK R-21 application is to identify patterns of brain oxygenation during HD that are associated with the following patient-centered outcomes: 1) long recovery time from HD, 2) cognitive function instability, and 3) increased risk of hospitalization..
SPECIFIC AIMS:
Aim 1: To determine the association of cerebral deoxygenation during HD, measured by NIRS, with patient-reported time to recovery from HD and cognitive instability during HD.
Aim 2: To compare time to hospitalization among patients with and without cerebral deoxygenation during HD.
OVERLAP: None

TITLE Prevalence and profile of treatment non-responders in Autism Early Intervention
PERFORMANCE PERIOD: 07/01/2018 – 06/3/2021
SUPPORTING AGENCY: NIH
EFFORT: 10%
FUNDING AMOUNT: $917,453.27
PROJECT GOALS: Estimate prevalence of children responding sub-optimally to ASD early intervention and create a detailed profile of non-responders.
SPECIFIC AIMS: Aim 1. We will determine the prevalence of children who remain minimally verbal despite receiving evidence-supported early intervention targeting language
Aim 2. We will outline an empirically-derived profile of ‘suboptimal responders’ in the language domain through the analysis of child and family variables that distinguish treated minimally verbal children who show language improvements versus those who show minimal progress in this area despite receiving the same amount of evidence-based intervention.

PREVIOUS

TITLE: Prospective Evaluation of Air Pollution, Cognition, and Autism from Birth Onward, Supplement to R01
EFFORT: 5%
SUPPORTING AGENCY: NIH, Subcontract to Drexel; Prime Institution: Johns Hopkins

GRANTS OFFICER: N/A
PERFORMANCE PERIOD: 07/01/2016-04/30/2017
FUNDING AMOUNT: $74,605
PROJECT GOALS: Provide untargeted metabolomics analysis on samples provided by the prime institution.
SPECIFIC AIMS: (1) to assign air pollutant exposure using state of the art modeling techniques for multi- site studies estimating TRP and PM as well as measure novel biomarker measurements of nitro-PAH exposure to freeway-based diesel exhaust and gaseous nitro-PAH pollutants from vehicular and other sources; (2) examine the effect of these exposures on the trajectory of cognitive development using repeated administrations of the Mullen Scales of Early Learning (MSEL); and (3) evaluate the effect of these exposures on autistic traits and ASD diagnoses.

TITLE: Evaluation of Scientific Literature on Turbidity Associated with the Risk of Gastrointestinal (GI) Illness
EFFORT: 5%
SUPPORTING AGENCY: Water Research Foundation
GRANTS OFFICER: N/A
PERFORMANCE PERIOD: 01/01/2015-12/31/2015
PROJECT GOALS: Several epidemiological studies indicate turbidity as a significant risk factor for acute GI illness. However, issues in the collective research such as modeling strategies, exposure and illness measurements, and potential confounding require thorough examination to weigh the overall evidence. The goal of this project is to evaluate the available evidence on this relationship.
OVERLAP: None.

TITLE: Neighborhoods and cardiovascular risk in a multiethnic cohort
EFFORT: 10%
SUPPORTING AGENCY: National Heart, Lung, and Blood Institute (NHLBI)
GRANTS OFFICER: N/A
PERFORMANCE PERIOD: 05/01/2014-05/31/2015
FUNDING AMOUNT: $66,170.00
SPECIFIC AIMS: (1) examine the relationship between neighborhood socioeconomic characteristics and the prevalence and progression of subclinical atherosclerosis; (2) examine associations of neighborhood socioeconomic characteristics with specific individual-level factors which may mediate neighborhood differences in disease risk; (3) develop measures of specific characteristics of neighborhood environments (such as measures of resource availability, neighborhood social cohesion and neighborhood stress) and examine their relation to selected individual-level risk factors; (4) determine if these specific neighborhood characteristics explain differences in cardiovascular risk between socioeconomically advantaged and socioeconomically disadvantaged neighborhoods; and (5) examine if neighborhood characteristics contribute to race/ethnic differences in cardiovascular risk.
OVERLAP: None.

TITLE: Effects of Spinal Fusion and Instrumentation on Rib Position, Costovertebral Joint Geometry and Vertebral Morphology in Adolescent Idiopathic Scoliosis
EFFORT: 4%
SUPPORTING AGENCY: Scoliosis Research Society
GRANTS OFFICER: N/A
PERFORMANCE PERIOD: 06/01/2014-12/31/2015
FUNDING AMOUNT $30,000

PROJECT GOALS: In Adolescent Idiopathic Scoliosis (AIS), the three-dimensional (3D) characterization of positional-rib deformity (i.e. rib droop) and associated structural changes in the costovertebral articulations and vertebral morphology with varying Lenke curve types and degrees of curvature (determined by Cobb angle) are yet to be comprehensively studied. Consequently, the long-term effects of corrective spinal fusion surgery on the structural morphology of the ribs, costovertebral joints and vertebrae are also unknown. Such knowledge could help develop patient-specific modeling tools to better guide the timing and method of scoliosis treatment, i.e. non- operative bracing versus surgical procedures using thoracic enlargement or spinal fusion for improved quality and functional outcomes.
SPECIFIC AIMS: 1. Characterize the effects of pre- and two year post-spinal fusion ('treatment status') on bilateral (left versus right) 3D rib position and geometry at each thoracic level using EOS-based (EOS imaging Inc, Cambridge, MA) biplanar radiographic reconstructions obtained from 60 AIS subjects (ages 10-18 years) displaying a right curvature, with varying Lenke 'curve types' and pre-op Cobb angle greater than 45 degrees. The total number of subjects will be evenly distributed among the three common Lenke curve types [2], namely type 1AN (main thoracic curve), type 2AN (double thoracic) and type 5CN (thoracolumbar), respectively. Hypothesis 1: No significant bilateral differences will be observed in rib length, rib enclosed area and rib apparent curvature within the treatment status for each curve type, while positional and structural morphology of the ribs will vary between curve types and between treatment status for each curve type.
2. Describe the 3D geometric morphology of the costovertebral articulations at each thoracic level for all the subjects pre- and post-spinal fusion. Hypothesis 2: Structural morphology of the costovertebral joints will vary bilaterally between the different vertebral levels, Lenke curve types and treatment status. 3. Quantify the 3D geometry of the vertebrateach thoracic level for all the subjects. Hypothesis 3: Structural morphology of the vertebra will vary at each vertebral level between Lenke curve types and between the treatment status for each curve type.
OVERLAP: None

TITLE: Translational Effectiveness of Large Scale Simulations (TELSS)
EFFORT: 5%
SUPPORTING AGENCY: Independence Blue Cross
GRANTS OFFICER: N/A
PERFORMANCE PERIOD: 09/01/2015-09/01/2016
FUNDING AMOUNT: $50,000
PROJECT GOALS: High fidelity simulation based education has already been proven to be an effective teaching tool that can complement standard medical education.1 The ability to "practice without risk" has been positively received by students and educators alike. The preliminary goal of this study is to determine whether a large group simulation training experience produces equivalent debriefing/ feedback experiences as small group simulation based training
SPECIFIC AIMS: Study aim# 1- the preliminary goal of this study is to determine whether a large group simulation training experience produces equivalent debriefing/ feedback experiences as small group simulation based training.
Study aim# 2- the second goal of this study is to determine whether a large group simulation training experience produces equivalent outcomes to small group simulation based training for clinical process outcomes during decompensating patient manikin simulation sessions.
Study aim# 3- lastly, the goal of this study is to determine whether a large group simulation training experience produces equivalent knowledge retention of skills at 6 months following the intervention.
OVERLAP: None.

TITLE Implications of Cognitive Variation with Hemodialysis
EFFORT: 0%
SUPPORTING AGENCY: Drexel University
PERFORMANCE PERIOD: 11/01/2015-10/29/2016
FUNDING AMOUNT: $19,700
PROJECT GOALS: Recent studies have highlighted the high prevalence and prognostic implications of poor cognitive function among hemodialysis (HD) patients.[1-3] The relationship between cognitive dysfunction and poor outcomes may be multifactorial; for example, the finding of cognitive impairment may be a signal of systemic vascular disease,[4-6] and may also be on the causal pathway to poor medication and treatment adherence by impacting learning or decision-making ability. The goal of this study is to further explore and describe the relationship between cognitive variability and poor health outcomes in a cohort of prevalent hemodialysis patients in an urban dialysis center.
SPECIFIC AIMS: Aim 1: To characterize the prevalence and nature of cognitive function variability in a cohort of prevalent urban HD patients.Aim 2: To characterize modifiable dialysis therapy-related risk factors for cognitive function variability in HD patients.Aim 3: To examine the association between cognitive function variability and short-term health outcomes in dialysis patients including risk of hospitalization.
OVERLAP: None.

PREVIOUS/CURRENT/PENDING SUPPORT

SNYDER, NATHANIEL

Research Support: Since the last reporting period, Dr. Snyder has received additional support from grants R03CA211820 and R03HD092630; full support information is provided below.

ACTIVE

TITLE: Prenatal biomarkers of exposure and individual susceptibility to endocrine disrupting compounds
EFFORT: 75%
SUPPORTING AGENCY: NIH/NIEHS
GRANTS OFFICER: James R. William; Telephone: 919-541-1403; E-mail: williamsjr@niehs.nih.gov
PERFORMANCE PERIOD: 02/01/2016-01/31/2019
FUNDING AMOUNT: $149,750 Direct Costs
PROJECT GOALS: This project will overcome major challenges in quantitation of exposure during gestation and develop the independent research career of a young investigator focused on environmental health sciences.
SPECIFIC AIMS: Specific Aim 1. Quantify internal dose of prototypical EDC exposures (BPA, methylparaben, bis (2-ethylhexyl) phthalate, and vinclozolin) in controlled exposures in mice and human variable population exposures using developmentally relevant blood, urine, placenta, meconium and fetal tissue. Specific Aim 2. Elucidate the influence of endogenous metabolic mediators of EDC exposure (sex hormones and folates) on a known biologically relevant exposure response (DNA methylation) during critical neurodevelopmental windows in EDC exposed mice and humans. Exploratory Aim. Identify additional candidate biomarkers of biological response to EDC exposure.
OVERLAP: No overlap.

TITLE: Lipidomics of meconium in neurodevelopment
EFFORT: 15%
SUPPORTING AGENCY: NIH/NICHD
GRANTS OFFICER: Saiyda Khan; Telephone: 301-496-5001; E-mail: khansa@mail.nih.gov
PERFORMANCE PERIOD: 04/22/2016-03/31/2018
FUNDING AMOUNT: $275,000 Direct Costs
PROJECT GOALS: This proposal will quantify and compare the lipid content of meconium in typically developing versus neurodevelopmentally delayed children from a prospective enriched risk cohort of early events in autism spectrum disorder.
SPECIFIC AIMS: Specific Aim 1. Identify unknown chromatographic features with differential abundance between ASD and controls in a prospective enriched risk cohort. Specific Aim 2. Structurally elucidate the putative biomarkers of ASD and compare the lipid content of meconium, placenta, and cord blood. Specific Aim 3. Develop and validate a targeted method for the quantitation of putative biomarkers of ASD.
OVERLAP: No overlap.

(NEW)

TITLE: The influence of prenatal maternal exposures on fetal sterol metabolomics (Grant # R03CA211820)
EFFORT: 5%
SUPPORTING AGENCY: NIH
GRANTS OFFICER: Tawana Mckeither; mckeitherta@mail.nih.gov; 240-276-6300

PERFORMANCE PERIOD: 09/15/2016-08/31/2017 (1 year NCE)
FUNDING AMOUNT: $100,000 Direct Costs
PROJECT GOALS: This project will use cutting edge analytical and statistical methods to examine the effects of exposure to two major classes of environmental compounds on prenatal sterol metabolism.
SPECIFIC AIMS: Specific Aim 1. Identify unknown chromatographic features with differential abundance by maternal exposure to PBDEs and phenols. Specific Aim 2. Conduct structural elucidation of sterols of interest identified in specific aim 1. Specific Aim 3. Explore effects of maternal PBDE and phenol exposure as mixtures on compounds measured in specific aim 2.
OVERLAP: No overlap.

(NEW)
TITLE: Metabolism of propionic acid (Grant # R03HD092630)
EFFORT: 2.5%
SUPPORTING AGENCY: NIH
GRANTS OFFICER: Saiyda Khan; lhansa@mail.nih.gov; 301-496-5001
PERFORMANCE PERIOD: 09/01/2017-08/31/2019
FUNDING AMOUNT: $50,000 Direct Costs
PROJECT GOALS: Propionic acidemia (PA) is the manifestation of a set of inborn errors of metabolism that still result in significant morbidity and mortality despite detection by newborn screening. The recent discovery of a metabolite of excess propionic acid indicates that biomarkers with diagnostic, prognostic, and therapeutic potential may be possible. This research will quantify and describe the metabolism of this new metabolite for further investigation in PA patients and model systems.
SPECIFIC AIMS: Specific Aim 1. Characterize and quantify metabolites of propionate through 2M2PE. Specific Aim 2. Identify cellular localization and putative enzymology of metabolism through 2M2PE. Specific Aim 3. Establish and validate a quantitative method for biomarkers of dysregulated propionate metabolism in urine, saliva and serum.
OVERLAP: No overlap.

<u>PAST</u>
TITLE: CURE: Metabolic Control of Neurogenesis
EFFORT: 5%
SUPPORTING AGENCY: Pennsylvania Department of Health
GRANTS OFFICER: Violet Witmer; E-mail: vwitmer@pa.gov
PERFORMANCE PERIOD: 01/01/2015-12/31/2015
FUNDING AMOUNT: $75,000 Direct Costs
PROJECT GOALS: The immediate goal of this proposal is to elucidate the modulation of metabolic pathways by the histone acetyltransferase Tip60 during neurogenesis.
SPECIFIC AIMS: Specific Aim 1.Elucidate metabolic substrate utilization during neurogenesis in dTip60 WT versus dTip60E431Q. Specific Aim 2. Correct defective neurogenesis in Tip60 Mutants by metabolite replacement or rescue dTip60.
OVERLAP: No overlap.