

AWARD NUMBER: W81XWH-15-1-0354

TITLE: Neural correlates of the Y chromosome in autism: XYY Syndrome as Genetic Model

PRINCIPAL INVESTIGATOR: Timothy Roberts

CONTRACTING ORGANIZATION: Children's Hospital of Philadelphia, Research Institute  
Philadelphia, PA 19104

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Fort Detrick, Maryland 21702-5012

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| REPORT DOCUMENTATION PAGE                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |              |                          |                               | Form Approved<br>OMB No. 0704-0188            |                                           |
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| 1. REPORT DATE<br>September 2017                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |              | 2. REPORT TYPE<br>Annual |                               | 3. DATES COVERED<br>15 Aug 2016 - 14 Aug 2017 |                                           |
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| 6. AUTHOR(S)<br>Timothy Roberts<br>Judith Ross<br><br>E-Mail: robertstim@email.chop.edu; Judith.Ross@jefferson.edu                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |              |                          |                               | 5d. PROJECT NUMBER                            |                                           |
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| 7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)<br>CHILDREN'S HOSPITAL OF PHILADELPHIA,<br>THE3615 CIVIC CENTER BLVD<br>PHILADELPHIA PA 19104-4318                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |              |                          |                               | 8. PERFORMING ORGANIZATION REPORT<br>NUMBER   |                                           |
| 9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)<br><br>U.S. Army Medical Research and Materiel Command<br>Fort Detrick, Maryland 21702-5012                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |              |                          |                               | 10. SPONSOR/MONITOR'S ACRONYM(S)<br>USAMRMC   |                                           |
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| 13. SUPPLEMENTARY NOTES                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |              |                          |                               |                                               |                                           |
| 14. ABSTRACT<br><br>A multimodal MRI, MRS and MEG (magnetoencephalography) design is employed in cohorts of boys with XYY, who are symptomatic for ASD and control cohorts of idiopathic ASD (ASD-I) and typical development (TD). Targeted recruitment for year 1 totaled 30 enrolled. At the point of this report, 25 subjects have been enrolled, 5 were eliminated for not meeting inclusion criteria upon clinical assessment, 19 have completed data acquisition, and 1 is pending imaging completion. Three of the 19 are pending confirmation of ASD diagnosis. Several more are in various stages of recruitment, scheduling, neuropsychological evaluation or imaging. MRI, MRS and MEG examinations have been conducted in the 17 subjects above with confirmed diagnoses (8TD, 8XYY+ASD, 1 ASD-I). QA suggests in general that complete studies have been tolerated and that data quality is good in the majority of cases. Additional steps to remove MEG trials corrupted by excessive head motion are underway to improve further the evaluable data yield. Data analysis is ongoing, priority having been given to standard approaches for MEG (source localization in BESA followed by consensus "peak" picking), MRS (alignment of "on" and "off" spectra, then subtraction and Gaussian modeling of the GABA and Cr resonances in GANNET) and DTI/HARDI. As mentioned above, about 50% of the data tolerated this strategy robustly. The remaining data are undergoing "scrubbing" to eliminate motion-related artifacts and reduce noise, to accommodate comparable analysis – these data are likely evaluable, but are not reported herein. Dependent variable extraction is underway and preliminary data are shown for illustration of feasibility. It is premature to conduct formal statistical analyses. Recruitment, acquisition and analysis is on track and completion is anticipated in the remaining 12 months of this award. |              |                          |                               |                                               |                                           |
| 15. SUBJECT TERMS<br>Autism spectrum disorder, ASD; 47,XYY syndrome (XYY); neuroimaging; MRI; MEG; Comorbid behaviors                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |              |                          |                               |                                               |                                           |
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| a. REPORT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | b. ABSTRACT  | c. THIS PAGE             |                               |                                               | USAMRMC                                   |
| Unclassified                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Unclassified | Unclassified             | Unclassified                  | 15                                            | 19b. TELEPHONE NUMBER (include area code) |

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## 1. INTRODUCTION

**(Technical abstract from application):** This proposal addresses two topics of great importance to the ASD community: **mechanisms of heterogeneous clinical expression of ASD** and **mechanisms underlying conditions co-occurring with ASD**, including seizures, attention, and anxiety disorders. Autism affects ~1% of the population (4:1 male pre-dominance) and is heterogeneous with regard to etiological/risk factors, pathogenesis, and clinical presentations. Heritability studies have shown that genetic factors are important in ASD, but dissecting out the relationships among genes, imaging biomarkers, and behavioral phenotypes of ASD is confounded by both genetic heterogeneity and the paucity of neurobiological models. These problems can be circumvented by studying genetically defined ASD subgroups such as 47,XYY syndrome (XYY). XYY occurs in ~0.1% of the male population but has been reported in up to 1% of males with ASD. Approximately 33% of males with XYY satisfy diagnostic criteria for ASD (**XYY+ASD**). The behavioral and neuroimaging biomarkers of XYY+ASD identified in our preliminary studies overlap with those described in ASD-I and, similarly, comorbidities (seizures, attention, and anxiety disorders) exhibited in XYY+ASD are representative of those described in ASD-I. In this proposed study, we will examine the behavioral, neurophysiological and neuroimaging markers of ASD, and specifically compare the variance (**heterogeneity**) of these measures in XYY+ASD versus ASD-I. Having established the level at which XYY+ASD confers imaging/phenotypic heterogeneity reduction, the **mechanism** underlying these measures will be probed via neurochemical magnetic resonance spectroscopy of key neurotransmitters and myelin mapping. Clinically meaningful associations between such measures and behavioral ASD phenotypes will be identified.

A multimodal MRI, MRS and MEG (magnetoencephalography) design is employed in cohorts of boys with XYY, who are symptomatic for ASD and control cohorts of idiopathic ASD (ASD-I) and typical development (TD).

## 2. KEYWORDS

Autism spectrum disorder, ASD  
47,XYY syndrome (XYY)  
Neuroimaging  
MRI  
MEG  
Comorbid behaviors

### 3. ACCOMPLISHMENTS

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

**Major Task 1:** Regulatory review and approval processes for studies involving human subjects at 2 sites (CHOP and Nemours/DuPont).

**Major Task 2:** Recruitment

**Major Task 3:** Data Acquisition

**Major Task 4:** Data Analysis

#### What was accomplished under these goals?

**Major Task 1:** Regulatory review and approval processes for studies involving human subjects at 2 sites (CHOP and Nemours/DuPont Hospital for Children).

All study protocols have been submitted reviewed and approved by both local IRB's (CHOP / Nemours/DuPont Hospital for Children) as well as central DoD ethics review. Furthermore, since the co-PI Dr. Judith Ross moved to Nemours/DuPont Hospital for Children prior to commencement of this grant funding, approval was obtained by Nemours/DuPont Hospital for Children and all materials were reviewed by DoD. Where appropriate continuing renewal submissions have been submitted and approved in a timely fashion.

**Major Task 2:** Recruitment

Recruitment for year 2 totaled 46 enrolled (out of a target of 60). 11 were eliminated for not meeting inclusion criteria upon clinical assessment, namely XYY subjects not meeting clinical ASD criteria. While these are, by inclusion criteria, not consistent with the goals of the written grant proposal, we found them to be a highly relevant control group and have indeed included them in the protocol (under separate funding). Several more are in various stages of recruitment, scheduling, neuropsychological evaluation or imaging, under the goals of the no-cost extension.

| Group                                                              | N  |
|--------------------------------------------------------------------|----|
| TD                                                                 | 16 |
| XYY+ASD                                                            | 13 |
| ASD-I                                                              | 6  |
| XYY not meeting inclusion criteria<br>(Enrolled but not evaluable) | 11 |

### **Major Task 3: Data Acquisition**

MRI, MRS and MEG examinations have been conducted in the 46 subjects above with confirmed diagnoses (16TD, 13XYY+ASD, 6 ASD-I). QA continues to suggest that imaging protocols have been tolerated and that data quality is good in the majority of cases. Additional steps are being investigated to further improve evaluable data yield, via the removal of artifacts such as excessive head motion during MEG or DTI acquisitions and frequency drift during MR spectroscopy experiments.

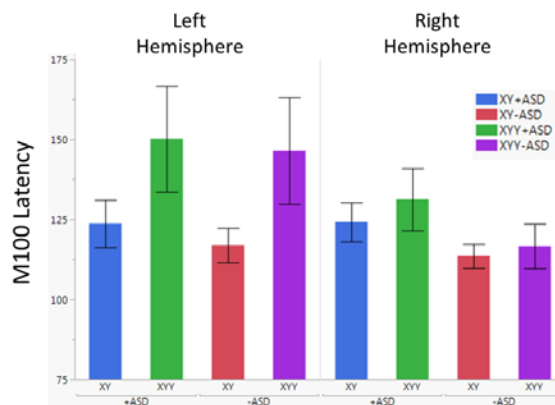
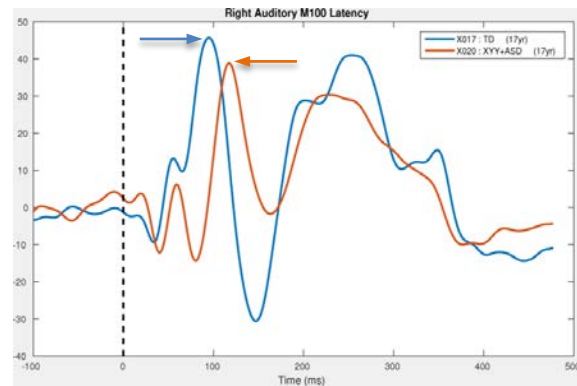
### **Major Task 4: Data Analysis**

Data analysis is ongoing, priority having been given to standard approaches for MEG (source localization in BESA followed by consensus “peak” picking), MRS (alignment of “on” and “off” spectra, then subtraction and Gaussian modeling of the GABA and Cr resonances in GANNET) and DTI/HARDI. As mentioned above, about 50% of the data tolerated this strategy robustly. The remaining data are undergoing “scrubbing” to eliminate motion-related artifacts and reduce noise, to accommodate comparable analysis – these data are likely evaluable, but are not reported herein.

As suggested during the DoD scientific review process we have included, where possible, data acquired from additional subjects (notably an XYY-ASD cohort – see major task 2) acquired under other projects. While full statistical analysis is premature, where appropriate some preliminary statistics are presented.

## Preliminary Analysis and Trend Observation of Dependent Variables acquired under Major Task 3 and Analyzed in Major Task 4:

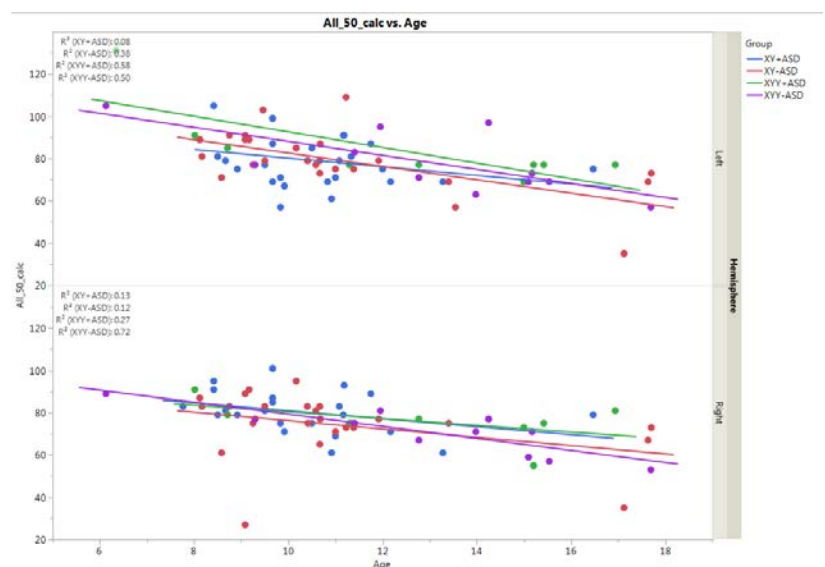
*Fig. 1a MEG recorded auditory evoked field source waveforms from right hemisphere Heschl's gyrus in a representative 17-year old with typical development (blue) vs. an XYY participant on the autism spectrum (XYY+ASD), who exhibits a profound delay in the M100 peak (arrows).*



*Fig. 1b M100 Latency Prolongation in XYY. Linear mixed models (Main effects of hemisphere, XYY and ASD status with age and NVIQ as covariates), Found significant ( $P < 0.01$ ) delays (24ms Full model, 39ms Left hemisphere) in XYY. While failing to reach significance a 12ms delay in right M100 was observed in ASD).*

| M100 Effects | Full Model | Left Hemisphere | Right Hemisphere |
|--------------|------------|-----------------|------------------|
| XYY          | +24ms      | +39ms           | +10ms            |
| ASD          | +12ms      | +1ms            | +12ms            |

*Fig. 1c Age dependence of M50 latency in XY-ASD (red), XY+ASD (blue), XYY+ASD (green) and XYY-ASD (purple) shows maturational trajectory towards shortening (as has been previously reported in both TD and ASD-I). Note that, similar to fig1b, genetic effects on latency (XYY prolongation) are more pronounced in the left hemisphere.*



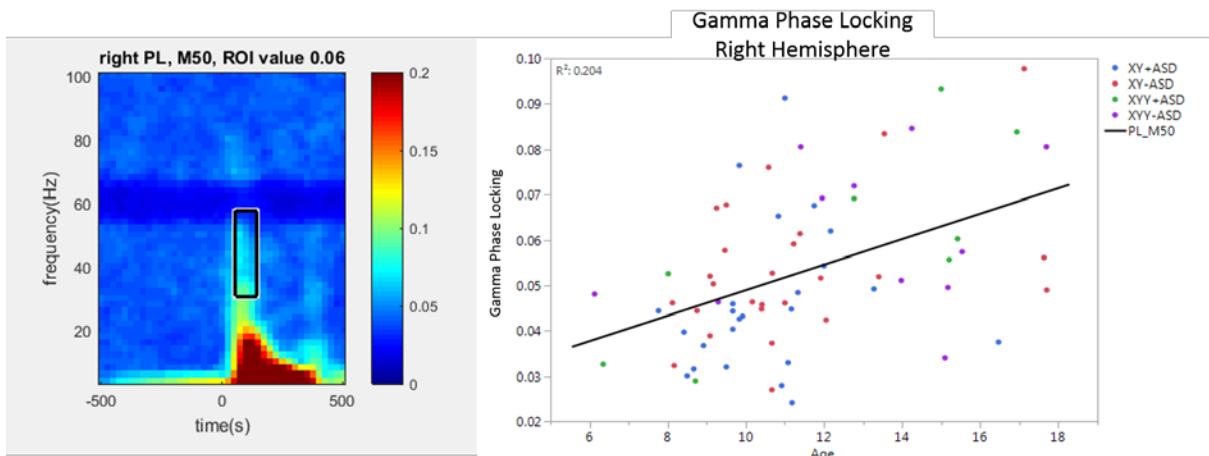


Fig. 2. Gamma band (30Hz-60Hz) phase locking value measured from the right auditory evoked response shows the expected maturational trajectory of increasing gamma synchrony with age. Similar relationships are visible in Left auditory phase locking (not shown)

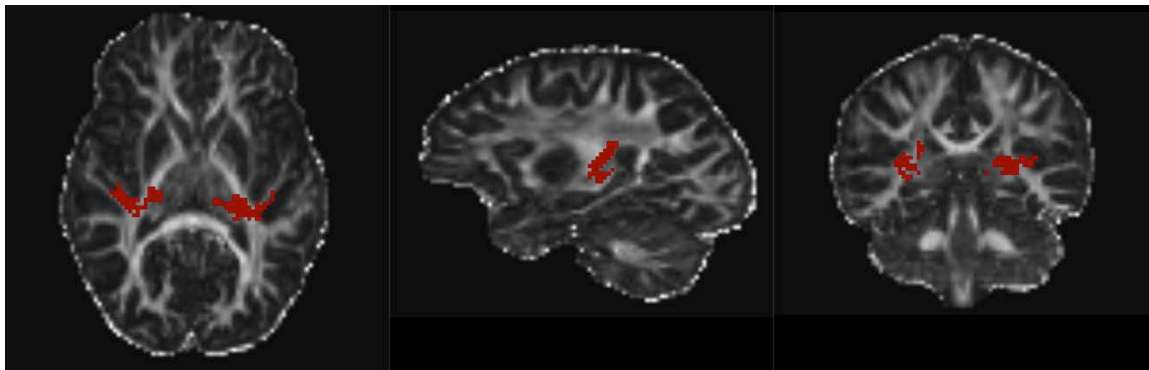


Fig. 3a High Angular Resolution Diffusion Imaging (HARDI) allows depiction of the thalamocortical projections of the white matter auditory pathway – the acoustic radiations (red) without the confounds of fiber crossing and complex white matter architecture that limit typical DTI. These masked regions can then be interrogated to reveal parameters (e.g. fractional anisotropy, FA, and mean diffusivity, MD, associated with local white matter microstructure.

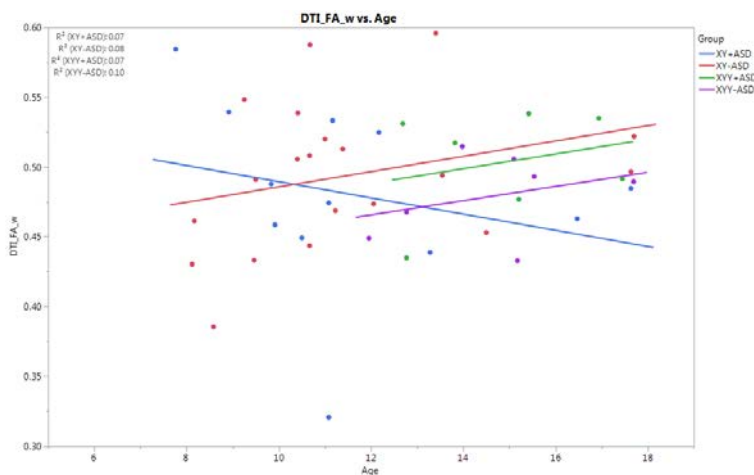


Fig. 3b Interrogating a HARDI-defined mask in the left acoustic radiation shows an anticipated maturational trend towards increasing fractional anisotropy (FA) in each group except (XY+ASD) – it is premature to assess Group differences in the slope of this trajectory. Analogous data (not shown) show maturational trajectories for the right hemisphere acoustic radiations and for mean diffusivity.

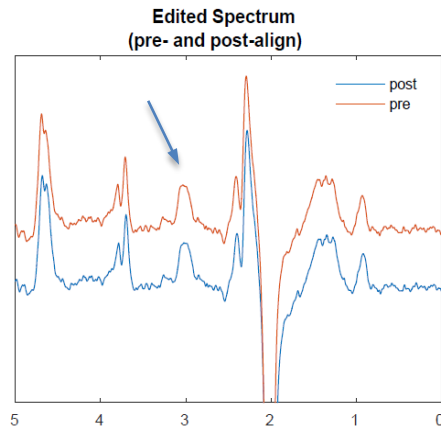


Fig. 3a Edited magnetic resonance spectra are acquired using the modified (macromolecular-suppressed) MEGAPRESS sequence from a voxel in left superior temporal gyrus and aligned to improve editing subtraction using the GANNET software package. A GABA resonance can be identified in the subtracted spectrum at 3.01 ppm (arrow).

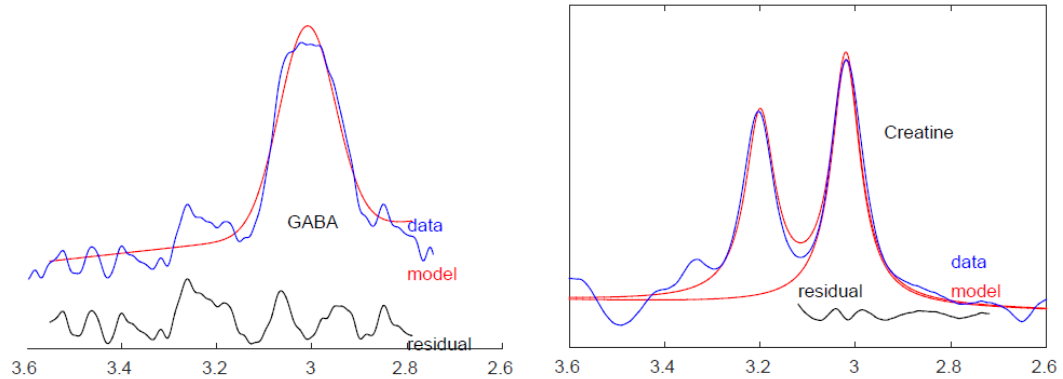


Fig. 3b The GABA resonance in the raw subtracted spectrum (blue) is fit with a single Gaussian resonance (red) using GANNET (right, upper). The integral of this fit is then normalized to the intrinsic Cr resonance at 3ppm in the unsubtracted spectra (right, lower).

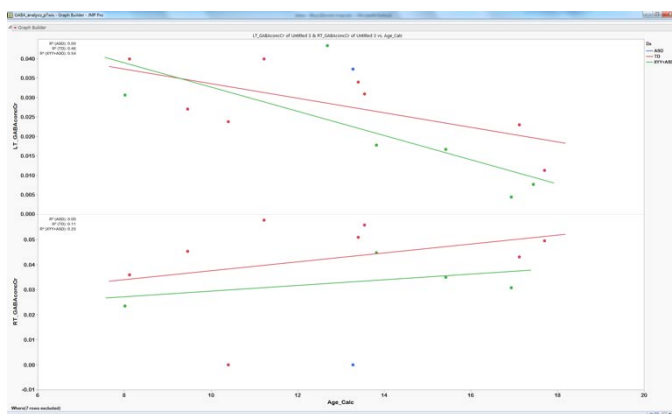


Fig. 3c The GABA/Cr ratio (obtained from ROI's in both left (upper) and right (lower) STG shows a consistently diminished level of GABA in XYY+ASD versus TD (as has been reported in ASD-I).

**Table 2. Co-morbidities associated with XYY+ASD**

| Medical and Psychiatric diagnoses or clinically significant findings | XYY+ASD (n=8) | TD (n=8) | Childhood Prevalence | Prevalence in ASD-I |
|----------------------------------------------------------------------|---------------|----------|----------------------|---------------------|
| <b>FEATURES</b>                                                      |               |          |                      |                     |
| Hypotonia                                                            | 7 (88%)       | 0        |                      | 51%                 |
| Tremor                                                               | 2 (25%)       | 0        | 0.1 – 22%            |                     |
| <b>MEDICAL DIAGNOSES</b>                                             |               |          |                      |                     |
| Motor Delay/Dyspraxia                                                | 6 (75%)       | 0        | < 5%                 | 34%                 |
| Seizures                                                             | 0             | 0        | 1%                   | 14-35%              |
| <b>PSYCHIATRIC DIAGNOSES</b>                                         |               |          |                      |                     |
| ADD or ADHD                                                          | 5 (63%)       | 0        | 2 – 16%              | 28%                 |
| Verbal or Motor Tic                                                  | 2 (25%)       | 0        | 5 – 10%              | 9%                  |
| Oppositional Defiant                                                 | 4 (50%)       | 0        | 1 – 16%              | 30%                 |
| Depression                                                           | 2 (33%)       | 0        | <1%                  | 1.4%                |
| Anxiety                                                              | 6 (75%)       | 0        | 15 – 20%             | 42%                 |
| Bipolar/mood disorder                                                | 1 (13%)       | 0        | 0.4 – 6.3%           | 26%                 |

*Table 2. XYY is associated with significant occurrence of co-morbid behaviors/diagnoses. Although stratified analyses is premature, a later goal of this study is to identify neural features relating to such behaviors*

**What opportunities for training and professional development has the project provided?**

Nothing to report

**How were the results disseminated to communities of interest?**

Initial analysis were presented at the recent International Meeting for Autism Research (*Structural and Functional Characteristics of XYY - Relationship to ASD*, L. Bloy et al, IMFAR, 2017).

Additionally two papers are currently being prepared for submission. The first, titled “*Auditory Evoked Response Delays in Children with 47,XYY syndrome*” presents the M50 and M100 findings. The second, a case report titled “*NLGN4Y copy number variations and neurocognitive/autism phenotypes: Behavioral Phenotype In Male With XYY and absent NLGN4Y Expression*” discusses the behavioral and neuroimaging phenotype of an individual with 47,XYY who is missing the NLGN4Y gene.

**What do you plan to do during the next reporting period to accomplish the goals?**

Continue / complete recruitment, acquisition and analysis. Perform statistical analyses and prepare manuscripts.

#### **4. IMPACT**

**What was the impact on the development of the principal discipline(s) of the project?** - Nothing to report yet

**What was the impact on other disciplines?** - Nothing to report yet

**What was the impact on technology transfer?** - Nothing to report yet

**What was the impact on society beyond science and technology?** - Nothing to report yet

#### **5. CHANGES/PROBLEMS**

**Changes in approach and reasons for change** - none

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

Although there have been no significant problems encountered and no study design changes made, at present we are currently behind our enrollment targets. For this reason, in June we requested and were granted a 12 month No-Cost Extension extending the project completion date to 8/14/2018. Given this extra time and our current recruitment rates we are confident that we will reach our enrollment target by the end of the project.

**Changes that had a significant impact on expenditures** – none

**Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents** – none

#### **6. PRODUCTS**

**Publications, conference papers, and presentations** – none yet

**Website(s) or other Internet site(s)** – none

**Technologies or techniques** – none

**Inventions, patent applications, and/or licenses** – none

**Other Products** – none

## **7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS**

**What individuals have worked on the project?**

No change: Roberts, Miller, Bloy, Ross

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

See appended current "Other Support" documentation from Drs. Roberts and Ross.

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

Nemours / Dupont Hospital for Children

**8. SPECIAL REPORTING REQUIREMENTS:** None

**9. APPENDICES:** None

## Roberts, Timothy OTHER SUPPORT

### ACTIVE

#### **2U54HD086984-25 (Yudkoff, Neuroimaging/circuitry Core Director: Roberts)**

08/01/1997 – 10/31/2020

0.6 calendar

NIH/NICHD

\$102,065

*Intellectual and Development Disabilities Research Center*

The overall goal of this project is to support research at the Children's Hospital of Philadelphia/University of Pennsylvania that is relevant to intellectual disabilities. Dr. Roberts serves as Director of the Neuroimaging/Neurocircuitry core and provides expertise with multi modal imaging and quantitative analyses of pre-clinical (micro) and clinical level images.

#### **2U54HD086984-25 (Yudkoff, Project PI: Roberts)**

11/01/2015 – 10/31/2020

1.08 calendar

NIH/NICHD

\$151,647

*Intellectual and Development Disabilities Research Center: MEG Studies in Minimally/Non-verbal Children with ASD*

This study examines brain activity in low functional children with ASD and low IQ controls to explore the extension of biomarkers associated with autism *per se*, and language impairment in particular, in lower functioning populations, not typically served by research studies.

#### **R01DC008871-08 (Roberts)**

09/18/2014-08/31/2019

1.8 calendar

NIH/NIDCD

\$212,500

*Electrophysiological signatures of language impairment in autism spectrum disorder*

The major goal of this study is to explore candidate biological bases for stratification of the heterogeneous ASD population according to a "dominant deficit" classification in which both thalamocortical white matter maturation and excitation/inhibition imbalance are considered components of a delayed electrophysiological response, M100.

#### **R01HD073258-05 (Embick, subaward PI: Roberts)**

09/01/2012 – 05/31/2018

1.2 calendar

NIH/NICHD

\$123,877

*Magnetoencephalographic studies of lexical processing and abstraction in autism*

The goal of this study is to identify features in the acoustic properties of words that diminish capability for abstraction in ASD, using MEG as a surrogate for characteristic brain activity, and to remediate them with signal processing.

#### **R21-MH109158 (Roberts)**

07/01/2016-06/30/2018

1.2 calendar

NIH/NIMH

\$150,000

*Structural and functional characteristics of XYY – Relationship to ASD*

Goal: to compare the imaging phenotype of boys with 47,XYY syndrome +/- ASD diagnosis

#### **#276932/#412802 (Roberts)**

11/01/2015-6/30/2018

0.6 calendar

Clinical Research Associates

\$248,061

*MEG / MRS Study of STX209*

The goal of this study is to test MEG and MRS candidate biomarker responses to acute administration of a GABA-B agonist in a dose escalation trial

#### **#345621(Sherr, subaward PI: Roberts)**

09/01/2015-08/31/2018

0.6 calendar

Simons Foundation

\$21,672

*Brain Imaging and Cell Signaling: Insights into the Biology of Autism*

|                                                                                                 |                       |              |
|-------------------------------------------------------------------------------------------------|-----------------------|--------------|
| <b>R01MH107506-01 (Edgar)</b>                                                                   | 03/01/2016–02/28/2021 | 1.2 calendar |
| NIH/NIMH                                                                                        | \$499,851             |              |
| <i>A longitudinal study of brain development in children with autism. Role: co-investigator</i> |                       |              |
| <b>R01MH092535-06 (Huang)</b>                                                                   | 9/26/2016-8/31/2021   | 1.2 calendar |
| NIH/NIMH                                                                                        | \$304,117             |              |
| <i>Structural Development of Human Infant Brain</i>                                             |                       |              |

The goal is to establish next-generation diffusion MRI atlases (quantitative UPenn-CHOP infant brain atlases) and to harness a more advanced cortical microstructural measurement by delineating its 4D spatiotemporal frameworks as well as uncovering its relationship to brain function and behavior during infancy (0-2 years). Role: co-investigator

**ROSS, JUDITH, M.D.**  
**OTHER SUPPORT**

**ACTIVE**

1. NIH/NICHD 1R01HD091251-01 (PI: Tartaglia, co-I Ross) 9/06/2017 – 06/30/2022 1.8 calendar  
*The eXtraordinary Babies Study: Natural History of Health and Neurodevelopment in Infants and Young Children with Sex Chromosome Trisomy* \$2,340,911

The aims are to describe the natural history of young children with SCT from infancy to 5 years, with a focus on early predictors of neurodevelopmental and cardiometabolic outcomes.

2. NIH/NICHD 1UG1HD090915-01 (PI: Ross) 9/21/16-8/31/20 2.4 calendar  
*Delaware Nemours/duPont Hospital for Children Site for the IDeA States Pediatric Clinical Trials Network.* \$1,732,499

The IDeA States Pediatric Clinical Trials Network will function as one component of the overall Environmental influences on Child Health Outcomes (ECHO) Program.

3. AR140197 (MPI: Roberts, Ross) 08/15/2015-08/14/2017 1.2 calendar  
US Department of Defense CDMRP \$153,479

*Neural correlates of the Y chromosome in autism: XYY Syndrome as Genetic Model*

Project goals are to evaluate the structural and functional determinants of autism in boys with 47,XYY compared to matched idiopathic ASD and typically-developing control groups. Although there is considerable scientific synergy with the R21 (#4 below), the recruited cohorts differ. There is no budgetary overlap.

4. R21 MH109158-01A1 (MPI: Roberts, Ross) 04/01/16-3/31/18 1.2 calendar  
NIH/NIMH \$192,758

*Structural and Functional Characteristics of XYY - Relationship to ASD*

The goal of this project is to compare structural and functional neuroimaging findings in boys with XYY who meet diagnostic criteria for autism versus those who do not (please see above #3).

5. 1P30GM114736-01 (PI: Shaffer, co-I: Ross) 08/01/2015 – 07/31/2020 1.2 calendar  
NIH/NIGMS \$750,000 Center for Pediatric Research (CPR)

This COBRE Phase III grant builds on the success of COBRE Phase I and II and will sustain the infrastructure cores, mentorship program and pilot project programs to provide the Center for Pediatric Research with the resources to drive translational research programs focused on pediatric diseases at Nemours.

6. R01 HD04965305 (Ross: co-I, PI: Reiss) 07/01/2012-06/30/2017 0.3 calendar  
NIH \$64,555

*Genes, Brain and Behavior in Turner Syndrome*

The goal of this project will use advanced, multi-modal magnetic resonance imaging (MRI) techniques, to elucidate the effects of X monosomy and X-linked imprinting on neurodevelopment and neural function in young girls with TS.

**PENDING: None**

**OVERLAP: None**