AWARD NUMBER: W81XWH-15-1-0212

TITLE: "Cognitive and Neural Correlates of Aging in Autism Spectrum Disorder"

PRINCIPAL INVESTIGATOR: Smith, Christopher J.

CONTRACTING ORGANIZATION: Southwest Autism Research and Resource Center

REPORT DATE: September 2018

TYPE OF REPORT: Final Report

PREPARED FOR: U.S. Army Medical Research and Materiel Command

Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;

Distribution Unlimited

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	**2. REPORT TYPE**	**3. DATES COVERED**
Sept 2018	Final	07/01/2015 - 06/30/2018

4. TITLE AND SUBTITLE

"Cognitive and Neural Correlates of Aging in Autism Spectrum Disorder"

5a. CONTRACT NUMBER
W81XWH-15-1-0212

5b. GRANT NUMBER
AR140105

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

Christopher J. Smith, Ph.D.

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

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

Southwest Autism Research and Resource Center
2225 North 16th Street
Phoenix, Arizona 85006

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

Purpose: As the first diagnosed ASD individuals are now reaching old age, it is imperative that we understand the impact of aging on individuals with ASD. We developed a model predicting greater executive dysfunction and frontal lobe susceptibility in ASD beyond normal aging. Scope: This study, which is a collaborative study of the Southwest Autism Research and Resource Center the Barrow Neurological Institute and Arizona State University, produces comprehensive cognitive, behavioral, and neuroimaging data on a set of well-characterized older ASD individuals who can be used as a reference for clinical diagnosis, therapeutics, and care plans. The **scope** of the third year was to continue with recruitment and data collection, produce results from cross-sectional analyses of the initial assessment, and begin longitudinal analyses. **Results and significance:** We published our first in a series of studies from the initial cross-sectional data analysis in a high impact Autism journal (Autism Research), and were a highlighted project on the DoD website. We presented new analyses at the International Meeting for Autism Research in Rotterdam, Netherlands. We have two papers submitted on cross-sectional data, and a third manuscript that will be submitted in the coming month. We have obtained a no-cost extension to finish collecting our second timepoint; we have a **94% retention rate** thus far. Based on the discoveries we have made from this study, we have planned a personalized, behavioral intervention program; we received approval from the DoD to submit an application on this in October 2018.

15. SUBJECT TERMS

Autism, aging, functional MRI, fMRI, neuroimaging, executive functioning, memory, cognition, cortical thickness, connectivity, white matter, sparse Bayesian networks, machine learning

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

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

Table of Contents

Page

1. **INTRODUCTION:**

As the first diagnosed Autism Spectrum Disorder (ASD) individuals are now reaching old age, it is imperative that we understand the impact of aging on individuals with ASD. Given the striking parallels in ASD of deficits in executive function, subserved by the frontal lobe, and that the frontal lobe is susceptible to normal age-related changes, we combine neuroimaging, cognitive assessments and behavioral measures to examine aging in ASD compared to Typically Developed (TD) adults. We **hypothesize** that individuals with ASD will have an exacerbation of deficits beyond normal aging, as evidenced in significantly lower scores on tests affected by aging (e.g., executive) along with neuroanatomical markers of dysfunction, and relative preservation of function subserved by more posterior brain regions (memory and local detail processing). Our **objective** is to produce comprehensive cognitive, behavioral, and neuroimaging data on a group of well-characterized older individuals with ASD who can be used as a reference for clinical diagnosis, therapeutics, and care plans. To achieve this goal, our three year project involves longitudinal assessment of aging (40–60 y.o.) ASD individuals versus age-matched TD. In addition to commonly used statistical methods, we will use innovative machine learning and sparse Bayesian networks to combine structure, function, cognition, and symptom profiles to specifically address contributions to accelerated aging in ASD.

2. **KEYWORDS:** Autism, aging, functional MRI, fMRI, neuroimaging, executive functioning, cognition, memory, white matter, cortical thickness, connectivity

3. **ACCOMPLISHMENTS:**

- **What were the major goals of the project?**

The major goals for the project in the third year of funding were:

A) **To continue obtain cognitive and MRI data from ASD and control participants (Major Task 2 and Subtask 3).**

B) **Analyze and synthesize data to address all specific aims (Major Task 3, Milestones 2).**

What was accomplished under these goals?

A) **<u>Obtaining cognitive and MRI data from ASD and control participants:</u>** We continued to collect new participants to obtain our target enrollment of 70 participants (35 per group). At

the time of this writing, we have all procedures for Time 1 for 49 participants. We have also performed the second time point for the participants who have reached their 2 year interval. We have completed all the procedures for 32 of a possible 34 participants who have reached the two year return. Two of the ASD participants list above were not scanned because they were uncomfortable in the scanner, but we obtained cognitive and other data. The rest of the participants tolerated the scanning procedure well; none of those participants has required any alteration of the MRI or cognitive protocols. Since the beginning of recruitment in August 2014, we have had only two older adults from this study withdraw; one control/TD participant withdrew because of a change in demands in his job; an ASD individual was withdrawn because he had significant health problems (back problems) that did not allow him to undergo testing and the MRI. We are very pleased with our current 94% retention. We have developed a foundation of respect within the group of individuals we recruit, and as the PI and a Clinical Neuropsychologist, I offer feedback to all participants regarding their findings in order to "give back" as much useful information as possible, which keeps them engaged in the project.

In our original Statement of Work, recruitment was scheduled for 3-18 months. Since recruitment lagged somewhat behind our anticipated schedule, we have 14 participants that are scheduled for their second time point in the upcoming year. Therefore, we have received permission to continue as a no-cost extension for the remaining funds of this study so that we can obtain the second time points for these participants. Through additional funding (see below), we have funding to continue our longitudinal data acquisition of these participants beyond the second time point. We have begun obtaining the third time points for our early recruits.

This DoD funding helped us build a strong platform that has allowed us to successfully expand our research scope. Dr. Braden has received funding through NIMH K01 and Arizona Biomedical Research Commission to expand our study to include aging women with and without ASD who will be used with the data from the core DoD study to investigate gender differences in brain, cognition and symptoms. Further, through funding from the State of Arizona and other sources, we have established a young adult ASD cohort (18-25; men and women) who undergo the same procedures as the older cohort. Finally, Dr. Braden spearheaded a Mindfulness Based Stress Reduction intervention (no age or gender constraints), based on our findings from our ancillary study examining mood status in ASD, which has just completed. Taken together, we now have **150** individuals participating in our ASD research program.

C) **Analyze and synthesize data to address all specific aims (Major Task 3, Milestones 2).**

Our first publication from our initial cross-sectional analyses in Autism Research, the official journal of the International Society for Autism Research (Impact factor: 3.765; ranked 5/51 for Behavioral Sciences and 9/70 for Psychology Developmental journals), was published on September 21, 2017. There have been three citations since this article was published: one that incorporates our study in a review of structural biomarkers of ASD (Pagnozzi et al., 2018), a survey study of aging well with ASD (Hwang, et al., 2018), and a study examining executive functions in adults with ASD (Abbott et al, 2018). This demonstrates that there is a strong interest in our research among the ASD research community.

We have submitted additional papers based on this study during the past year. These papers are still under review at the time of this writing. A summary of the results from these cross-sectional studies are presented below.

Significant results from cross-sectional analyses under review:

a) "Autism and age-related network differences in verbal fluency" Leslie C. Baxter, PhD[1], Ashley Nespodzany, MS[1], Emily Wood, Christopher J. Smith, PhD[2] , and B. Blair Braden, PhD[3] (under review: for Special Issue on Aging: Research in Autism Spectrum Disorders).

[1]Department of Neuroimaging Research, Barrow Neurological Institute, St. Joseph's Hospital and Medical Center, 350 W Thomas Rd, Phoenix, AZ 85013

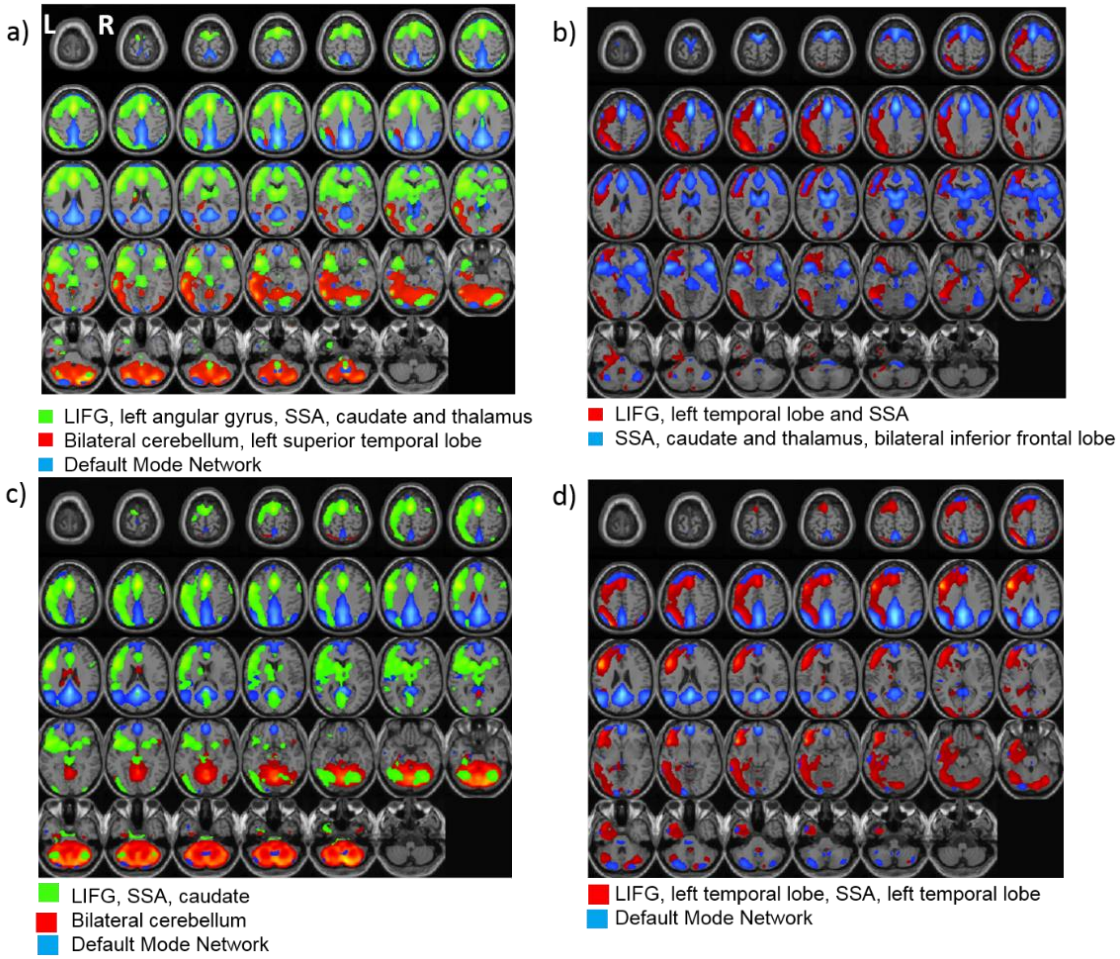
[2]Southwest Autism Research & Resource Center, 2225 N 16th Street, Phoenix, AZ 85006

[3]Department of Speech and Hearing Science, Arizona State University, 976 S Forest Mall, Tempe, AZ 85281

Summary: We have previously investigated cross-sectional differences in executive functioning but other cognitive domains, especially language, also depend in part on frontal lobe networks. An fMRI fluency task was included in our study to determine if a language task subserved in part by the frontal lobe would show a larger aging effect in ASD individuals than TDs. In this cross-sectional study, we used a network approach to investigate the influence of age and the diagnosis of ASD on language networks. The integrity and connectivity of the frontal lobe, which subserves fluency, may be compromised by both ASD and aging. Alternate networks often integrate to help compensate for compromised functions during aging. We used network analyses to study how compensation may be involved in age-related changes in language processing in individuals with ASD.

We analyzed fluency networks from both middle-aged (40-60) and young (18-25) men who have a diagnosis of ASD, and age- and IQ-matched TDs. We first used group individual component analysis (ICA) for each of the 4 groups to determine whether different networks were engaged. An SPM analysis was then used to compare activity in the network nodes from the ICA analyses.

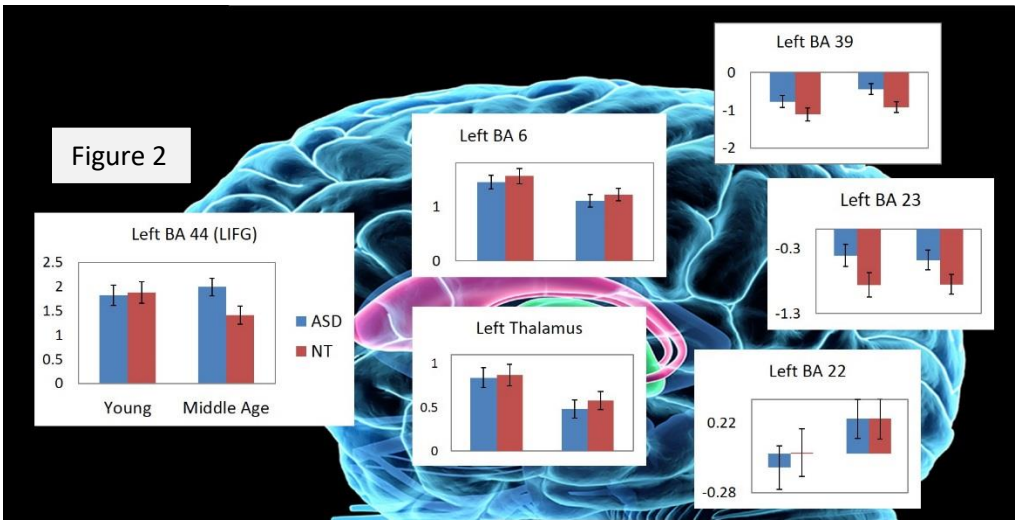
Figure 1 shows the networks generated when the participants were silently generating words to letter prompts. Figure 1 a) Young NT; b) Young ASD; c) Middle-aged NT; d) Middle-aged ASD. Group and age differences were observed in the networks engaged during the fluency task. (Colors for networks are arbitrarily assigned by the ICA program, so similar networks may have different colors).



The SPM-generated activation from the major nodes from each of these networks were extracted and compared between groups. Network nodes represent both anterior and posterior cortical language nodes, as well as more medial and subcortical nodes that are involved in processing speed and motor aspects of language. The default network, involved in the rest condition was also extracted. Figure 2 shows the group and age differences for these network nodes. Both age and group differences were observed. Strong age-related changes were observed for regions associated with speed of response (left thalamus and BA 6/Supplementary Speech Area). The large, age-related decreases in these regions suggest possible weakening in frontal-subcortical connectivity in older adults, or differences in processing efficiency of internally directed task demands. We found that both young and

middle-aged adults with ASD showed less “deactivation” during the word generation condition compared to the NT groups. There is considerable interest in gaining a better understanding of how individuals with ASD transition between fMRI conditions because activation patterns during the low-level, or baseline condition is often more telling than the more demanding condition. This failure to release from the active condition may be related to behavioral difficulties with flexible thinking.

Interestingly, the superior temporal lobe (left BA 22) showed increased engagement during word generation for all older adults, suggesting that the older individuals may have relied more heavily on lexical processing than younger adults as speed of processing decreases. This differential engagement of brain regions beyond the LIFG was observed in light of similar performance in all groups, suggesting that the challenges associated with aging, and possibly ASD, results in recruitment of neural networks to support effective performance. These findings are in alignment with the model of the “adaptive brain” described by Park and Reuter-Lorenz (the STAC model; 2009). Based primarily on working memory and executive functioning **compensatory mechanisms**, they hypothesize that maintaining behaviors at a higher level in older adults (and other conditions that involve neural challenges, like ASD) are related to the brain’s ability to use compensatory scaffolding, or “recruitment of additional circuitry that shores up” against neural changes that can negatively affect functioning.



b) "Age-related Differences in Executive Network Functional Connectivity and Relationships with Social Communication Impairments in Autism Spectrum Disorder" (under review: for Special Issue on Aging: Research in Autism Spectrum Disorders)

Melissa Walsh, MS[1], Leslie C. Baxter, PhD[2], Christopher J. Smith, PhD[3], and B. Blair Braden, PhD[1]

[1]Department of Speech and Hearing Science, Arizona State University, 976 S Forest Mall, Tempe, AZ 85281

[2]Department of Neuroimaging Research, Barrow Neurological Institute, St. Joseph's Hospital and Medical Center, 350 W Thomas Rd, Phoenix, AZ 85013

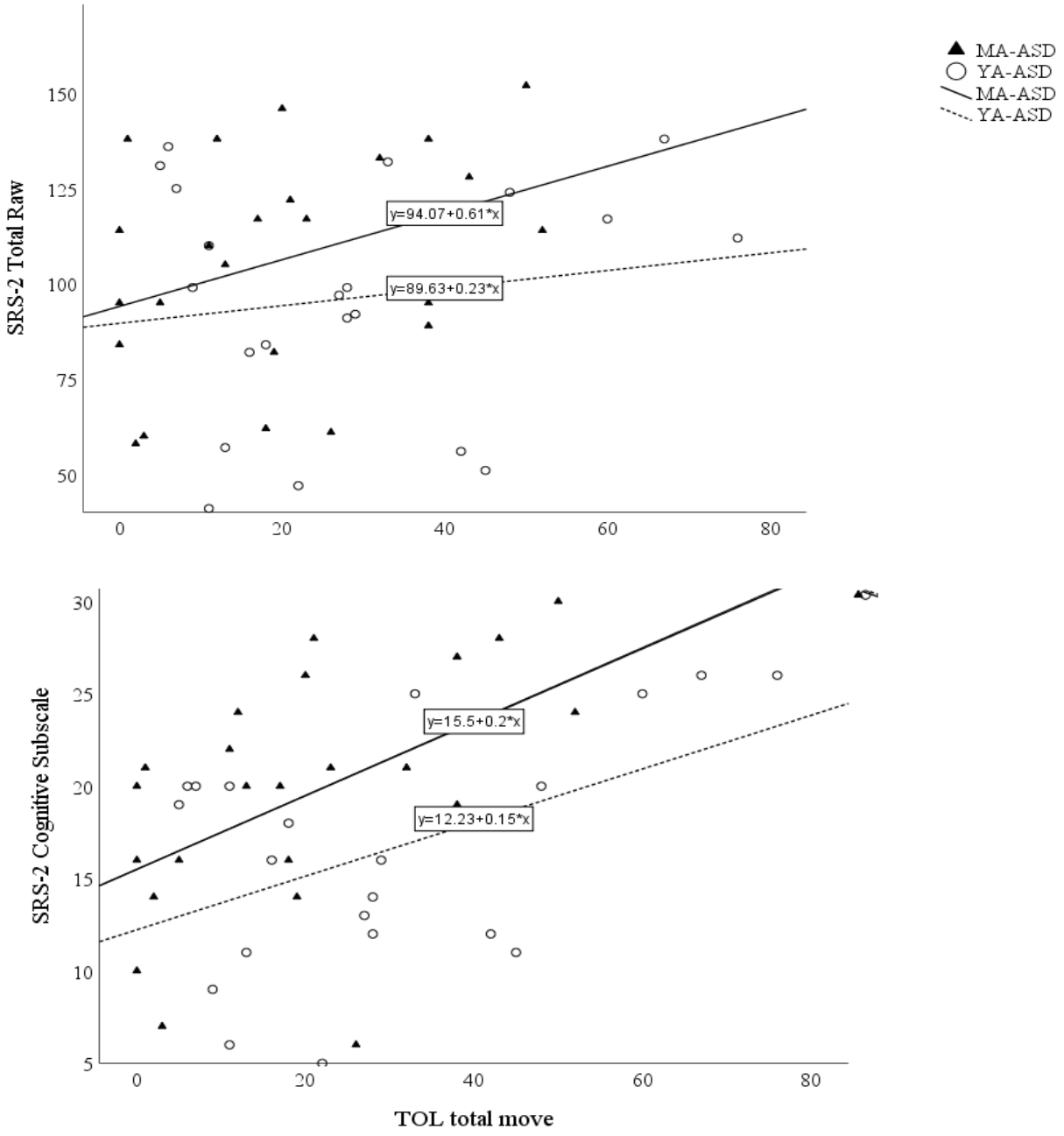
[3]Southwest Autism Research & Resource Center, 2225 N 16th Street, Phoenix, AZ 85006

Summary: The first author of this study is Dr. Braden's graduate student. She conducted her study under the supervision of Dr. Braden, her primary mentor, and Dr. Baxter, who is a member of her graduate school committee). Ms. Walsh examined the how social communication abilities may be altered with aging in ASD, and to better understand the neural basis for these changes. She examined the correlation of social communication abilities (Social Responsiveness Scale-2; SRS-2) and executive function (Tower of London; ToL) and found a stronger relationship between these two factors in the older adults with ASD.

Comparing the resting state fMRI-derived EN of young (YA) and older adult (OA) TD and ASD individuals, there was a greater degree of hypoconnectivity in OA vs YA ASD than was observed for OA vs YA TDs, suggesting an exacerbated age-related decline in functional connectivity of the left dorsolateral prefrontal cortices in adults with ASD. (Figure 1). Furthermore, there was a significant correlation between hypo-connectivity of the EN and higher SRS-2 scores in middle-aged adults with ASD (Figure 2).

This study suggests that executive control and planning plays a role in social communication problems in ASD, and that these abilities and the underlying hypoconnectivity of the Executive Network may explain why these abilities may become more troublesome with age in adults with ASD

Figure 1. Correlation between Tower of London Total Moves and SRS-2 (a) Total and (b) Cognitive Subscale Raw scores. *p<0.05; Middle-Age (MA); Young-Adult (YA)



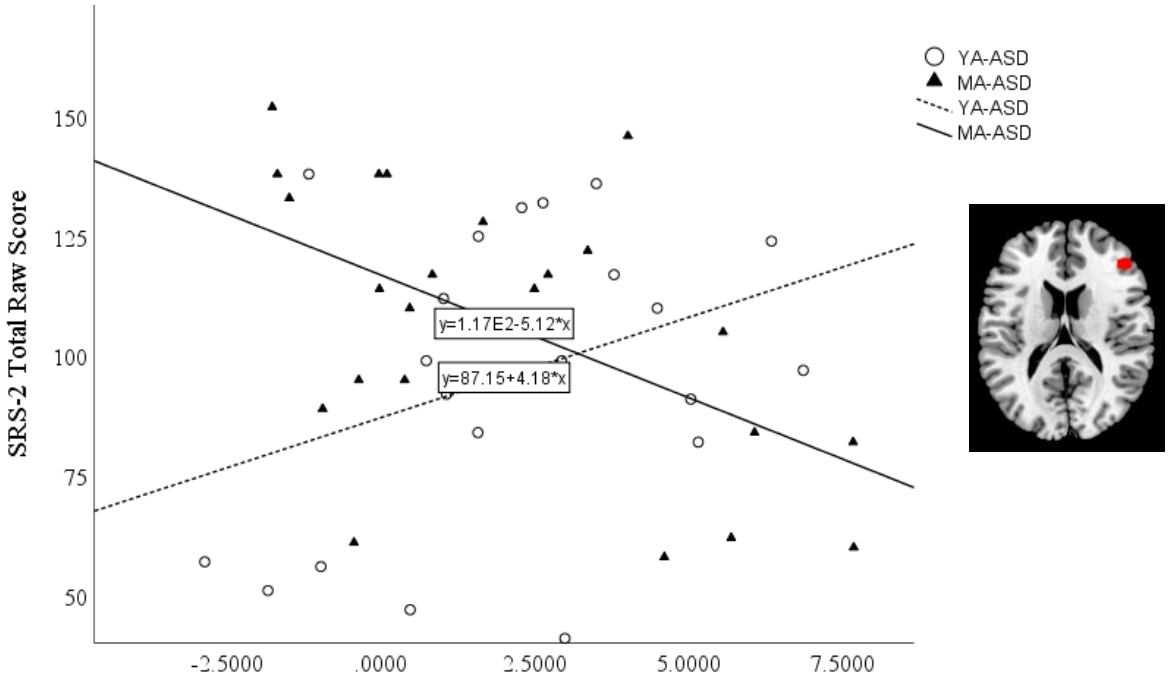


Figure 2. Correlation between functional connectivity of the right Dorsolateral Prefrontal Cortex (ROI inset) and SRS-2 scores.

Significant results from cross-sectional analyses manuscript in prep:

a) **"Taking Time to Prepare: Planning and Efficiency on the Tower of London Test in ASD"**
Ashley Nespodzany, MS[1], B. Blair Braden, PhD[3], Christopher J. Smith, PhD[2], and Leslie C. Baxter, PhD[1]
[1]Department of Neuroimaging Research, Barrow Neurological Institute, St. Joseph's Hospital and Medical Center, 350 W Thomas Rd, Phoenix, AZ 85013
[2]Southwest Autism Research & Resource Center, 2225 N 16th Street, Phoenix, AZ 85006
[3]Department of Speech and Hearing Science, Arizona State University, 976 S Forest Mall, Tempe, AZ 85281

Brief Summary: The first author is a research assistant in the Baxter Lab. This study investigates planning abilities in ASD. Planning—defined as identifying goals, formulating strategies to achieve them, and then organizing and monitoring the implementation of those strategies to reach those goals—is a particular EF subdomain that may be compromised in ASD. The current

literature on planning abilities in ASD is predominantly focused on child and adolescent individuals and inconsistently finds lower performance by ASD individuals on these tasks.

The aim of this study was to examine differences in planning ability between ASD and TD adults, and attempt to explain the inconsistencies in findings that occur in the literature. We examined group differences in planning performance between ASD and TD groups in a cross-sectional analysis of young adults and middle-aged adults using a Tower of London (ToL) task. While we predicted that the group with ASD would be outperformed by the TD on ToL performance, we further examined the mediating and moderating effects of time spent planning, learning rates, trial complexity, processing speed, and working memory to explain differences in ToL measures between ASD and TD adults.

ToL performance was evaluated from 41 Adult NT and 56 Adults with ASD. The ToL test measures of total moves, initiation time (time spent planning), execution time, and total number of correct trials were recorded. Linear modeling was used to compare the relationship between initiation time and number of trials completed correctly for each group.

Figure 1 shows that, as a group, the ASD group required more moves to solve the test and had fewer correct trials; however, no differences were observed for initiation or execution times. Figure 2 shows that the ability to perform the test well depends on the amount of time taken to plan the move. Even though both groups had similar ranges of times used to plan moves, this factor had little effect on how well TD individuals do, but greatly affected the performance of individuals in the ASD group. In the ASD group, those individuals that quickly make a move without time planning had worse scores than those that took time to plan the move. In fact, there are no differences between ASD and TD individuals who have the longest planning time; rather, the group differences in total move score and correct trials can be explained by the ASD individuals who quickly make moves without planning. These results are important for developing interventions that will help improve executive functioning in ASD individuals, and we will use these insights when planning our individualized intervention program.

Figure 1: Group Differences on common measures of ToL test

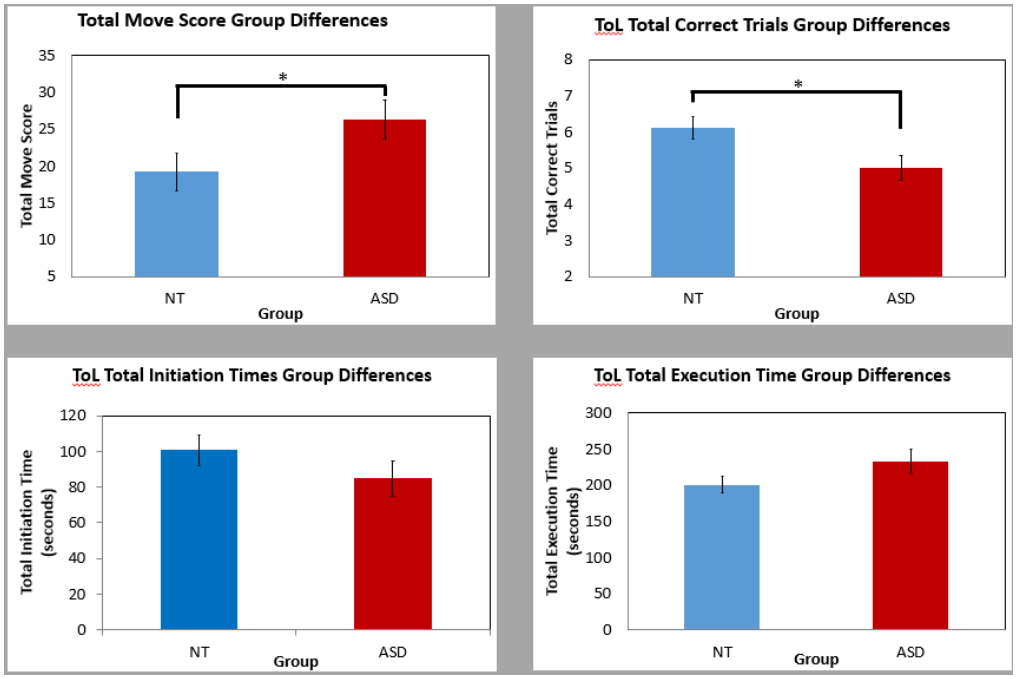
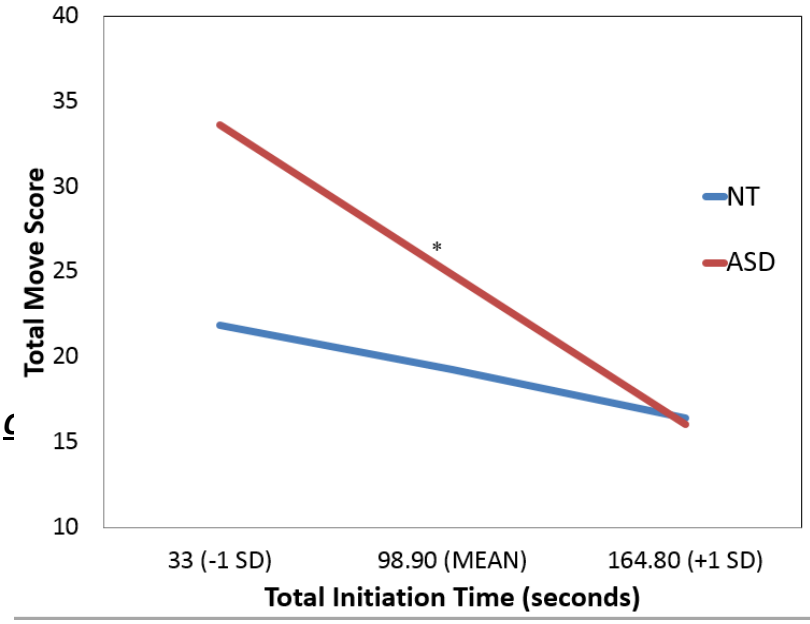


Figure 2: The relationship between TOL Initiation Time and Total Move Score Moderated by Presence of ASD Diagnosis



As noted in prior reports, we received a grant from the Institute for Mental Health Research to study emotional aspects of aging and ASD. The literature indicates that ASD individuals have greater rates of comorbid anxiety and depression. Our assessment in the parent DoD study includes self-report measures of anxiety and depression self-report at the time of cognitive testing and MRI scanning. Data from the baseline assessment of some of our participants showed that 88% of the middle-age ASD group reported significant levels of anxiety and 44% reported significant depression, as compared to 45% of a group of 8 young-adult ASD for both anxiety and depression. Social network measures did not significantly correlate with mood measures in either middle-age or young-adult ASD, and the report of caregivers was not correlated with the symptom severity reported by the participants. Interestingly, anxiety and depression symptoms correlated with several cognitive measures for the young ASD group, but there was no correlation in the older ASD group with cognition. This suggests that the cognitive deficits observed in the older ASD participants are not due to the presence of anxiety and depression but instead anxiety and depression may independently be affected in aging. In this study, we recruit the same participants who contributing to the MRI/cognition study. To date, we have evaluated 21 participants using a combination of clinical interview by a psychiatrist structured interview (via the Structured Clinical Interview for DSM Disorders (SCID for DSM-IV) and self-report measures to better understand how individuals with ASD express/self-report anxiety and depression. By far, the most common symptom that is observed in these ASD individuals is anxiety (rather than depression). Interestingly, many have difficulties articulating their emotional state, raising the question of difficulties with interoception. Interoception, or the ability to sense the internal state of the body, has been implicated as an area of impairment in autism, even on a neural basis via the insula and Salience Network (Uddin and Menon, 2009). We plan on using these data to help guide the mood component of our proposed intervention trial.

References

References:
Abbott, P., Happé, F.G. & Charlton, R.A. Exploratory Study of Executive Function Abilities Across the Adult Lifespan in Individuals Receiving an ASD Diagnosis in Adulthood. J Autism Dev Disord (2018). https://doi.org/10.1007/s10803-018-3675-x

Calhoun VD, Adali T, Pearlson GD, Pekar JJ. A method for making group inferences from functional MRI data using independent component analysis. Hum Brain Mapp 2001;14:140-151.

Gordon EM, Devaney JM, Bean S, Chandan JV, 2015. Resting-state striato-frontal functional connectivity is sensitive to DAT1 genotype and predicts executive function. Cerebral Cortex. 25:226-345.

Hwang, Y.I., Foley, KR. & Trollor, J.N. Aging Well on the Autism Spectrum: An Examination of the Dominant Model of Successful Aging. J Autism Dev Disord (2018). https://doi.org/10.1007/s10803-018-3596-8.

Kim DI, Mathalon Dignity Health, Ford JM, Mannell M, Turner JA, Brown GG, Belger A, Gollub R, Lauriello J, Wible C, O'Leary D, Lim K, Toga A, Potkin SG, Birn F, Calhoun VD. Auditory oddball deficits in Schizophrenia: An independent component analysis of the fMRI multisite function BIRN study. Schizophr Bull 2009;35(1): 67-81.

McKeownM, Handsen LK, Sejnowsk TJ. Independent component analysis of functional MRI: what is signal and what is noise? Curr Op in Neurobiology 2003;13(5):620-629.

Miller EK, Cohen JD. 2001. An integrative theory of prefrontal cortex function. Annu Rev Neurosci. 24:167.

Pagnozzi, A.M., Conti, E., Calderoni, S., Fripp, J., Rose, S.E. A systematic review of structural MRI biomarkers in autism spectrum disorder: A machine learning perspective. International Journal of Developmental Neuroscience (2018), 71: 68-82. https://doi.org/10.1016/j.ijdevneu.2018.08.010.

Park, D. C., & Reuter-Lorenz, P. The adaptive brain: aging and neurocognitive scaffolding. Annual review of psychology, 2009, 60, 173-196.

Uddin LQ, Menon V. The anterior insula in autism: Under-connected and under-examined. Neuroscience and Biobehavioral Reviews. 2009;33(8):1198-1203. doi:10.1016/j.neubiorev.2009.06.002.

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

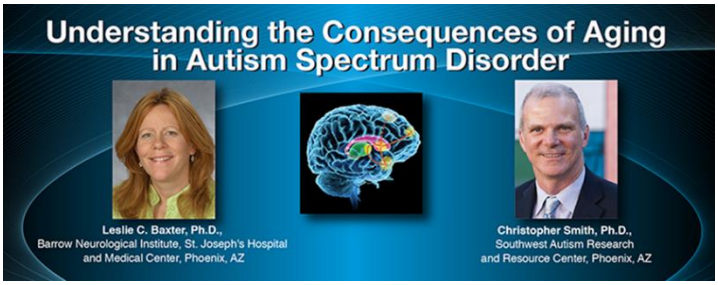
Training and professional development was not a major goal of this project; however, this project provided the environment to train and promote Dr. Baxter's post-doctoral resident, Dr. Blair Braden, who is one of the key personnel in this study. She has transitioned to a tenured-track position at Arizona State University and has established the Autism and Brain Aging Laboratory. She has obtained a K-01 award and other external funding in Autism. We will continue to collaborate on this project together, and we are incorporating another young investigator from SARRC (Nicole Mathews) in our upcoming DoD intervention application.

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

Autism Brain Imaging Data Exchange: The Autism Brain Imaging Data Exchange II is large-scale data repository of ASD and TD controls from 17 sites. Our contribution of 58 samples (which includes participants that are part of the DoD study) include the oldest sample in the group (aged 64 years old) and represents the first substantial set of older adults in the exchange. Our contribution to this high-profile, international group of researchers helps us to disseminate our study to the ASD research community. We will continue to contribute to this data exchange.

Aging in Autism Special Interest Group, International Society for Autism Research (INSAR). Both Drs. Baxter and Braden are members of the group of Autism researchers dedicated to the study of older individuals with Autism. The group was formed by Hilde Geurts, PhD of the University of Amsterdam to work towards common goals for studying older adults with ASD. Both Drs. Baxter and Braden are part of the founding members and will contribute to the establishment of a core set of cognitive tests and other data that can be collated across studies from around the world.

Our research was highlighted on the Department of Defense website in the past year.



Presentation to the Autism Community

Dr. Baxter and Dr. Smith were speakers at a Autism Speaks event on 8/3/18, discussing new frontiers in research (Phoenix, Arizona). Event attended by family members and professional caregivers.

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

d. Continue second time point evaluations of those participants who are two years from their original study, examine longitudinal analyses

B) **IMPACT:**

a. **What was the impact on the development of the principal discipline(s) of the project?**

We have significantly increased the number of older adults to a national data exchange. Our study is complementing the established cognitive studies in older individuals with Autism to emphasize the importance of developing a greater understanding of aging in Autism to inform treatment. We are now planning to use the information we have found to develop a unique intervention that is personalized to address the specific needs of the individual with ASD.

What was the impact on other disciplines?

Nothing to Report.

b. **What was the impact on technology transfer?**

Nothing to Report.

What was the impact on society beyond science and technology?

i. An intent of our study is to develop a plan of action to help keep older adults with ASD as independent as possible for as long as possible. We foresee that the results of our study, which is one of the first of its kind, will be able to inform state agencies and community aging programs to develop interventions that will help keep older ASDs independent. We plan on continuing to publish our results, and becoming a voice for the older ASD population, to help form effective and meaningful supports and treatments for this group. Based on the data obtained through this and ancillary studies, we are designing an innovative **personalized medicine approach intervention trial**, and hope to receive funding via the FY18 ARP Clinical Translational Research Award.

C) **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:*

a. **Changes in approach and reasons for change**

Received approval for a no-cost extension to complete second timepoint evaluations of participants.

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

Obtaining institutional and HRPO approval for the study took longer than expected, so recruitment of our cohort was somewhat behind schedule. Our current goals are to continue to have a high rate of return visits.

Changes that had a significant impact on expenditures

Our expenditures for MRI scans and patient reimbursement is less than expected over the grant period because of the delays in obtaining institutional approval, and patient recruitment.

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

i. We changed our local consent and HIPAA forms to allow us to share anonymized data with the Autism Brain Imaging Date Exchange (detailed above). This was approved by our institution. We informed the HRPO, who also approved this. Current approval dates are: Informed Consent: 4/20/16; HIPAA: 3/02/16

d. **Significant changes in use or care of human subjects:** Nothing to Report

e. **Significant changes in use or care of vertebrate animals. N/A**

f. **Significant changes in use of biohazards and/or select agents N/A**

D) **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."*

a. **Publications, conference papers, and presentations**
Nothing to Report

i. **Journal publications.** Nothing to Report

ii. **Books or other non-periodical, one-time publications.** Nothing to Report

b. **Other publications, conference papers, and presentations.** Nothing to Report

c. **Website(s) or other Internet site(s)**
Website/link to our media coverage: http://abc7.com/health/adult-men-with-autism-participate-in-one-of-a-kind-study/1429782/

d. ***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.*** Nothing to report

e. **Technologies or techniques**
None to report

f. **Inventions, patent applications, and/or licenses**

None to report

g. **Other Products**

None to report

E) PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

a. What individuals have worked on the project?

Name:	*Christopher J. Smith, Ph.D.*
Project Role:	*PI*
Researcher Identifier (e.g. ORCID ID):	0000-0003-4736-4701
Nearest person month worked:	*2*
Contribution to Project:	*Dr. Smith oversaw recruitment, diagnosis, assisted with data analysis and manuscript/poster presentation.*
Funding Support:	*1R01 MH104446, NIMH, 79772148, Simons Foundation, 3R44MH112470-02S1, multiple pharmaceutical trials*

Name:	*Anthony Sziklay*
Project Role:	Research Coordinator
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	8

Contribution to Project:	*Recruitment of subjects and coordination of evaluations*
Funding Support:	Internal support

b. **Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?** Yes, Dr. Braden has obtained a K-01 award and an Arizona Biomedical Research Committee award.

c. **What other organizations were involved as partners?** BNI, ASU (see below)

1. **Organization Name**: Barrow Neurological Institute

- **Location of Organization:** 350 West Thomas Road Phoenix, AZ 85013
- **Partner's contribution to the projec**t Partnering PI
- **Collaboration** Further testing and scanning of participants, collaboration with data interpretation and manuscript preparation

2. **Organization Name**: Arizona State University

- **Location of Organization:** 975 S Myrtle Ave P.O. Box 870102, Tempe, AZ 85287
- **Partner's contribution to the projec**t Co-investigator
- **Collaboration** with data interpretation and manuscript preparation