



CDMRP



Department of Defense

Autism Research Program



U.S. Army Medical Research and Materiel Command



Vision:

Improve the lives of individuals with autism spectrum disorder now

Mission:

Promote innovative research that advances the understanding of autism spectrum disorder and leads to improved outcomes for Service members, their families, and the American public

Application Review Process

The CDMRP uses a two-tier review process for application evaluation, with both tiers involving dynamic interaction among scientists and disease survivors.

The first tier of evaluation is a scientific peer review of applications measured against established criteria for determining scientific merit. The second tier is a programmatic review conducted by the Integration Panel, which is composed of leading scientists, clinicians, and consumer advocates. The Integration Panel compares applications to each other and makes recommendations for funding based on scientific merit, potential impact, adherence to the intent of the award mechanism, relevance to program goals, and portfolio composition.

Congressionally Directed Medical Research Programs

Autism Research Program

Background and History

The office of the Congressionally Directed Medical Research Programs (CDMRP) was created in 1992 from a powerful grassroots effort led by the breast cancer advocacy community that resulted in a Congressional appropriation of funds for breast cancer research. This initiated a unique partnership among the public, Congress, and the military. Since then, the CDMRP has grown to encompass multiple targeted programs and has received over \$7.5 billion in appropriations from its inception in Fiscal Year 2007 (FY07) through FY18. Funds for the CDMRP are added to the Department of Defense (DoD) budget, in which support for individual programs, such as the Autism Research Program (ARP), is allocated via specific guidance from Congress.

Autism Spectrum Disorder (ASD) encompasses a range of complex developmental disorders characterized by mild to severe challenges to social, emotional, and communication abilities. Recent reports by the Centers for Disease Control and Prevention (CDC) indicate that the prevalence of ASD may be as high as 1 in 59 children. According to one report (CDC Morbidity and Mortality Weekly Report. 2018. 67:1-23), an estimated 1 in 38 boys and 1 in 152 girls are affected and, thus, are identified as living with ASD. The associated national cost of ASD is estimated to be \$35-90 billion dollars. The causes of ASD are unknown; however, progress is being made on several fronts, and the answers related to autism will likely be as multifaceted as the disorder itself. The ARP is focused on improving the lives of those living with ASD by funding innovative and highly impactful research. Through the program's Areas of Interest, the ARP seeks to improve the study, diagnosis, and treatment of the psychosocial factors that affect key lifetime transitions to independence, resulting in a better life for those with autism and their families.

Research Portfolio

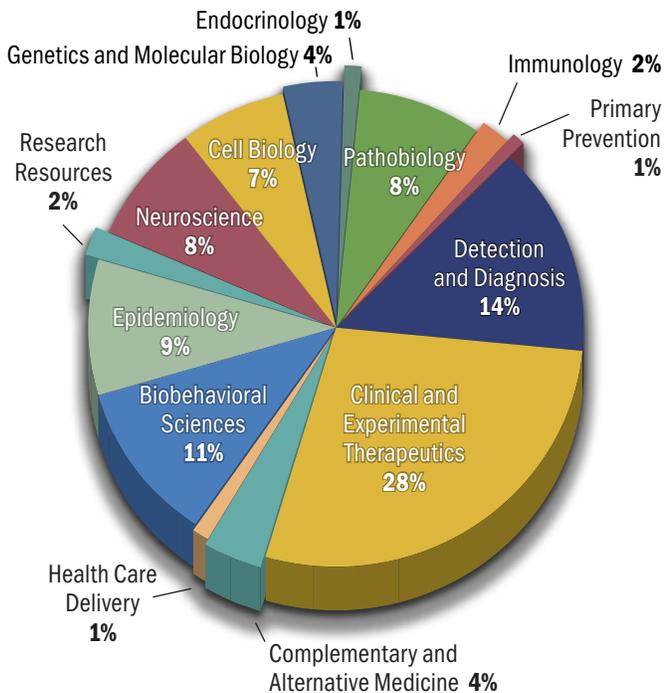
The ARP strives to fund a balanced research portfolio composed of studies focused on gaps defined by the scientific and consumer communities. The Areas of Interest (shown at the top of the next page) are topics that have been identified for increased emphasis, based on their importance to scientific research and their potential to improve consumers' daily lives. The Areas of Interest are revisited every fiscal year and are changed according to the current state of need. Additionally, the Areas of Interest differ, depending on the type of solicitation. For example, the Areas of Interest for the Clinical Trial and Clinical Translational Research Awards are related to dissemination and implementation of clinically validated interventions, whereas the Areas of Interest for the Idea Development Award are focused on the use of preclinical models for assessments of novel therapeutics.

ARP FY07-FY18 Portfolio by Area of Interest

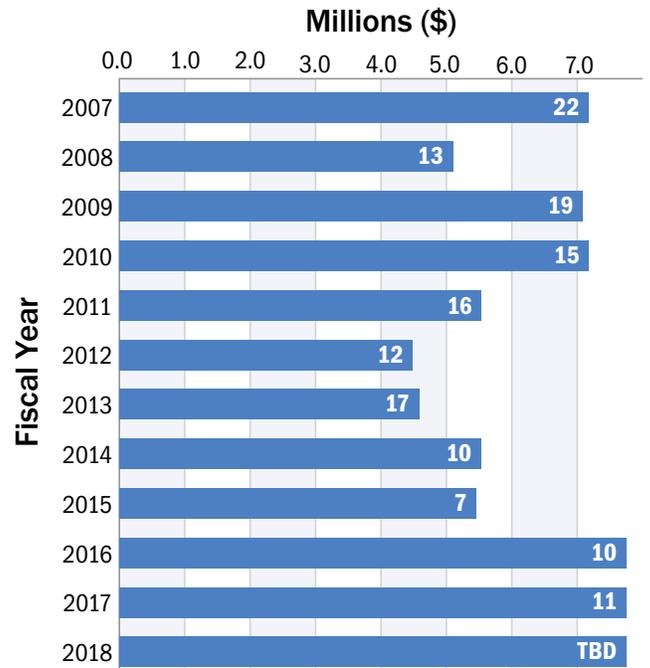
	FY07	FY08	FY09	FY10	FY11	FY12	FY13	FY14	FY15	FY16	FY17	FY18
Co-morbidity or co-occurring conditions	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓
Subgrouping and mechanisms of heterogeneous clinical expression						✓	✓	✓	✓	✓	✓	✓
Identification and/or validation of therapeutic targets	✓	✓		✓	✓*	✓*	✓*	✓**	✓**	✓**	✓**	✓**
Biomarkers and/or treatment predictors	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓
Environment	✓	✓		✓				✓	✓	✓	✓	✓
Clinical resource development	✓				✓							
Pharmacological treatments/interventions				✓	✓			✓	✓	✓	✓	✓
Psychosocial research and/or interventions				✓		✓	✓	✓				
Complementary and alternative medicine				✓	✓							
Behavioral and/or other non-pharmacological therapies/interventions					✓			✓	✓	✓	✓	✓
Dissemination/implementation of behavioral interventions								✓	✓	✓	✓	✓
Encouraged multidisciplinary collaborations					✓							
Family/caregiver well-being							✓					
Key transitions to independence									✓	✓	✓	✓
Healthcare provider-focused training or tools							✓				✓	✓

*Excluding gene discovery | **In preclinical models

ARP FY07-FY16 Portfolio Categorized by Research Area (by Dollars)



ARP Appropriations and Number* of Awards



* The number of awarded projects is anticipated for FY17, pending final negotiations, and is to be determined for FY18.

ARP Research in Depth



“I was honored to represent the Ken Anderson Alliance on FY17 ARP peer review research panel as an autistic adult consumer advocate. My experience with the ARP from the DoD’s CDMRP has been tremendous. This organization has impressed me and impressed upon me their commitment to including and advancing the conversations and cooperative endeavors between the scientists and the community their work is meant to serve. Improving our immediate quality of life is high on the autism community’s list of goals. The ARP heard this, which was reflected in this past year’s funding application submissions and directed conversations.”

Lori Hogenkamp
Ken Anderson Foundation
Consumer Peer Reviewer



Cognitive Enhancement Therapy: A Promising Approach for Adults with Autism Spectrum Disorder

Nancy J. Minshew, M.D., Shaun M. Eack, Ph.D., University of Pittsburgh

ASD-related neurocognitive impairments typically result in significant functional disability that persists throughout the lifetimes of those affected and impacts employability and relationship development, thereby diminishing overall quality of life. Drs. Nancy Minshew and Shaun Eack, with support from an FY10 ARP Clinical Trial Award, conducted the first randomized, controlled clinical trial evaluating the efficacy of Cognitive Enhancement Therapy (CET) on cognitive and behavioral deficits in verbal adults with ASD. CET was compared to Enriched Supportive Therapy (EST), an active comparison condition that is focused on psychoeducation and stress management, in 54 verbal adults with ASD. After 18 months of treatment, both therapies demonstrated gains, although CET produced more substantial

improvements in social and non-social cognition, specifically attention and processing speed. Participants who received CET were more likely to be employed at the end of treatment compared to EST. Approval from the Centers for Medicare and Medicaid Services to utilize CET as a standardized therapy for ASD requires confirmation of these results in a second, larger clinical trial funded by the National Institute of Mental Health; this trial is due for completion in 2020. Drs. Minshew and Eack are hopeful that a combination of centers can deliver CET and EST to facilitate development and maintenance of the expertise and cross-talk needed to address diagnostic difficulties and reduce social and cognitive impairments in adults with ASD through effective, evidence-based treatments.



Understanding the Consequences of Aging in Autism Spectrum Disorder

Leslie C. Baxter, Ph.D., Barrow Neurological Institute, St. Joseph’s Hospital and Medical Center; Christopher Smith, Ph.D., Southwest Autism Research & Resource Center

There is a pressing need to characterize the effects of brain aging in persons diagnosed with ASD to determine optimal treatment and care, as these individuals are now reaching old age. With support from an FY14 ARP Idea Development Award, Drs. Leslie Baxter and Christopher Smith sought to understand the cognitive, behavioral, and neurological aspects of ASD in middle-aged men through neuropsychological tests to examine the differences between a group of high-functioning ASD men (aged 40-62 years) and a group of neurotypical (NT) men matched by age, IQ, and education. Results demonstrated that men in the ASD group made more errors than men in the NT group during the performance of executive function-related tasks. Functional magnetic resonance (fMR) neuroimaging of



task-related brain networks revealed that functional connectivity in the working memory, default mode, and salience networks was equivalent between the ASD and NT groups. However, fMR neuroimaging showed that the cortico-striatal-thalamic-cortical circuitry network, which is involved in regulating attention and activity, was engaged in the NT group, but only minimally engaged in the ASD group. A model of ASD in older persons predicts greater impairment in executive function and frontal lobe susceptibility to dysfunction. This understanding can aid in developing care and treatment for the aging population of persons with ASD.

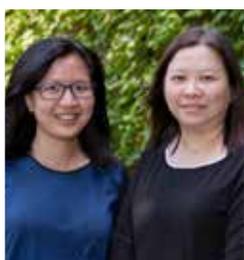
Transitioning to Adulthood with ASD

Young adults living with ASD represent a growing population at risk for poor outcomes associated with employment and independence during their transition from adolescence to adulthood. In the United States, the cost of supporting an individual with ASD during his or her lifespan is roughly \$1.4 million, and \$2.4 million if the individual has an intellectual disability.¹ Approximately 50,000 students with ASD exit high school each year in the United States, and roughly 500,000 are expected to enter into adulthood over the next decade.² As available services decrease after high school, many adolescents with ASD experience difficulties adapting to their new roles and responsibilities as they transition into adulthood. According to data from the National Longitudinal Transition Study-2, only 58% of young adults with ASD were employed between high school and their early 20s.³ The ARP is dedicated to improving the lives of individuals with ASD now and has a special focus on their quality of life. The ARP-funded studies described below are investigating ways to promote success in the transition to adulthood of adolescents with ASD.



Amie Duncan, Ph.D., Children's Hospital Medical Center

High-functioning adolescents with ASD have impaired daily living skills (DLS) that can affect their ability to flourish in the areas of education, employment, and independent living. With an FY17 Clinical Translational Research Award, Dr. Amie Duncan will conduct a clinical trial assessing the effects of *Surviving and Thriving in the Real World*, a group-based intervention for high-functioning adolescents with ASD that targets the development of DLS such as hygiene and self-care, laundry, cooking, grocery shopping, and money management. The effects of social communication skills, executive functioning abilities, and parenting factors on the ability to acquire DLS will also be explored. This project will provide initial steps in the development of an evidence-based DLS intervention package for teaching high-functioning adolescents with ASD the age-appropriate DLS to improve their current and future adult outcomes.



Ka Lai Gloria Lee, Ph.D., Ying Yuk Connie Sung, Ph.D., Michigan State University

Deficits in social skills have consistently been cited as a substantial barrier to maintaining employment and advancing within a job for young adults with ASD. Empirically supported interventions that enhance social and adaptive functioning are needed to promote the key skills necessary for a successful transition for adolescents with ASD. With an FY16 Clinical Trial Award, Drs. Ka Lai Gloria Lee and Ying Yuk Connie Sung will conduct a randomized controlled trial to evaluate the effectiveness of the *Assistive Social Skills and Employment Training* program, a manualized, work-related social skills training intervention for transition-age youth with ASD. The intervention is a 10-week group-based program that aims to improve work-related social skills and self-efficacy. Findings from this work will provide an intervention manual to assist transition-age individuals with ASD in becoming more successful at work-related responsibilities.



Ned Sahin, Ph.D., Brain Power, LLC

Individuals with ASD who have the technical talent for a job may struggle with anxiety and social-emotional skills crucial for a successful interview and navigating workplace dynamics. Though advances are evident in career-readiness services and special needs placement programs, on-the-job coaching by a trainer is costly, and teaching job skills through theoretical scenarios may overlook aspects of real-life situations. Dr. Ned T. Sahin has developed a Google Glass-based, social-emotional skills training platform and demonstrated in clinical and real-world trials as well as peer-reviewed publications that autistic youth happily wear, use, and benefit from this technology. With the support of an ARP FY16 Idea Development Award, Dr. Sahin and the Brain Power team are refining a jobs-focused version of this platform, with emphasis on immersive simulated

work settings to serve as exposure therapy and gamified training for future job-related environments. The wearable remote coach sees and hears what the individual does and provides human feedback and fully automated training without the requirement of an onsite coach. Dr. Sahin's team is working directly with ASD youth to demonstrate and iteratively refine the platform. The team has interviewed dozens of employers and schools to determine the precise platform features most desired for successful employment. The resulting version will be offered to colleges and employers for use in the real-world environment.

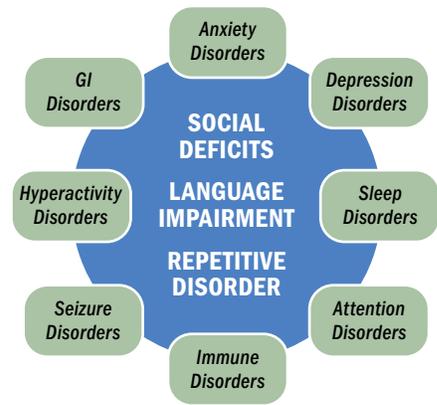
¹ Buescher AV, Cidav Z, Knapp, M, Mandell, DS. 2014. Costs of autism spectrum disorders in the United Kingdom and the United States. *JAMA Pediatrics*. 168(8):721-728.

² National Autism Indicators Report: Transition into Young Adulthood 2015. A.J. Drexel Autism Institute, Drexel University. Available at <http://drexel.edu/autismoutcomes/publications-and-reports/publications/National-Autism-Indicators-Report-Transition-to-Adulthood/>.

³ Ibid.

ASD and Co-Occurring Conditions

Children and adults with ASD face many behavioral and social challenges on a day-to-day basis. In addition to those challenges, individuals with ASD are often faced with other medical issues that occur in conjunction with ASD and produce symptoms that can mask ASD and vice versa. Thus, co-occurring conditions complicate ASD diagnosis and treatment, as well as their overall quality of life. The ARP recognizes the impairments these co-occurring conditions can cause for individuals with ASD. As such, the ARP emphasizes research focused on co-occurring conditions of ASD. The ARP supported studies described below represent some of that research



James Adams, Ph.D., Arizona State University

Many individuals with ASD suffer from severe gastrointestinal (GI) problems due to abnormal gut bacteria. With an FY15 Clinical Trial Award, Dr. James Adams utilizes microbiota transfer therapy (MTT) to establish healthy gut bacteria in ASD patients. This therapy involves administration of a potent antibiotic to reduce pathogenic bacteria, followed by administration of full-spectrum human gut microbiota to restore healthy gut microbiota. A pilot study in which MTT was administered to 18 ASD children with GI problems demonstrated a significant reduction in GI symptoms, as well as significant improvements in ASD symptoms. Dr. Adams is now evaluating the efficacy of MTT in adults with ASD who have GI problems. This research could help eliminate GI problems in individuals with ASD, improve their quality of life, and reduce their ASD symptoms.



Kenneth Gadow, Ph.D., Stony Brook University

Many adults with ASD experience debilitating depression. Compared to the general public, individuals with ASD are approximately four times more likely to develop depression in their lifetime and five times more likely to attempt suicide. The symptoms of depression are harder to identify in an individual with ASD because they may be hidden by the common features of ASD; consequently, depression in individuals with ASD is undertreated. With an FY13 Pilot Award, Dr. Kenneth Gadow is investigating the biological basis of depression in adults with ASD using brain imaging technology. He will also attempt to identify biomarkers of depression in individuals with ASD and understand the role of environmental stressors. A greater understanding of depression and the identification of biomarkers that may predict vulnerability could lead

to improvements in identifying and classifying depression in individuals with ASD and improve the effectiveness of interventions.



Geraldine Dawson, Ph.D., Kimberly Carpenter, Ph.D., Duke University; Grace Baranek, Ph.D., University of Southern California (formerly with the University of North Carolina)

Anxiety is extremely common among individuals with ASD and is one of the greatest sources of stress for them and their families. Yet very little is known about the early risk factors of anxiety. With

an FY13 Idea Development Award, Drs. Geraldine Dawson, Kimberly Carpenter, and Grace Baranek seek to identify early risk factors for anxiety disorders in ASD. They propose that sensory over responsivity (SOR), an exaggerated or prolonged behavioral reactivity to ordinary stimuli, is associated with anxiety symptoms. They are conducting an in-depth study of the relationship between SOR and anxiety symptoms in preschool-aged children with ASD, using parent reports, observation, and brain-based measures. Preliminary results show an association between SOR score and the number of anxiety symptoms in children with ASD, as well as a five-fold increased chance of anxiety in children with ASD when high levels of SOR were determined. This study has the potential to enhance the understanding of early risk factors for anxiety in children with ASD, which could result in better treatment planning to prevent anxiety disorders in these high-risk children

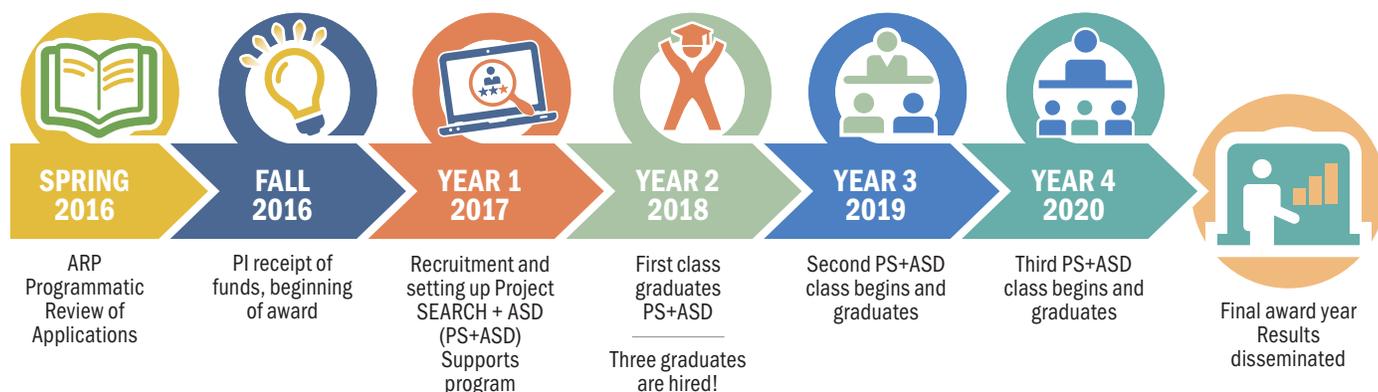
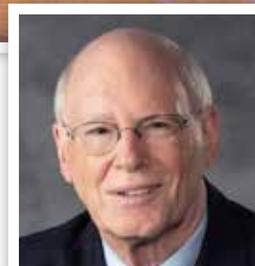
Looking Forward

Individuals with ASD experience difficulties with the transition from school to employment and are often unemployed and underemployed at higher rates as compared to those with other types of disabilities. Military dependents with ASD may be especially impacted by frequent relocation and are at a greater risk for poor outcomes due to the lack of consistent access to programs that assist with transitioning to employment. With an FY15 CDMRP Autism Research Program Clinical Trial Award, Dr. Paul Wehman (as Principal Investigator [PI]) and Dr. Carol Schall (as Co-Investigator) have begun investigating the effectiveness of Project SEARCH in military dependents in a clinical trial examining the effects of a 9-month internship for transition-aged military dependents with ASD. The award will span a total of 4 years, ending in FY20.

Project SEARCH is an intensive, 9-month employer-based program designed to improve social communication, behavior, and employment outcomes of military dependents with ASD. Youth with developmental disabilities in their last year of high school are embedded in a large community business such as a hospital, government complex, or banking center. Students rotate through three 10-12 week internships within the business, during which they log approximately 720 hours of internship time learning marketable skills and 180 hours of classroom time, for a total of approximately 900 hours embedded in the business setting. In addition to these important training components, Project SEARCH requires collaboration between multiple community partners to support youth in attaining employment upon completion of the program.

Participation in the Project SEARCH model has been shown to improve independence, social responsiveness, self-management, work skills, and quality of life. However, studies on the needs of military dependents with ASD in this transition group do not currently exist. Further research is necessary to investigate the clinical impact of this model in this population of youth. In order to meet the unique needs of military youth with ASD, Wehman, et al., (2014) enhanced the Project SEARCH model by adding autism supports to the original model, yielding Project SEARCH plus ASD Supports (PS+ASD). This modification includes intensive Applied Behavioral Analysis, an on-site behavior and autism specialist, and staff training in ASD and the Project SEARCH Model. PS+ASD is an excellent match for military dependents with ASD because it provides the opportunity for youth to learn job skills on base. In the event the family is relocated, youth in the project can generalize the skills learned to new installations.

This model of intervention provides the elements needed to encourage a seamless and successful transition to employment for military dependents with ASD. Dr. Wehman's team has begun implementing the PS+ASD Model at Fort Eustis in Virginia as part of an ARP-funded grant and has completed the first year of implementation. To date, 50% of the initial class has acquired employment at federal facilities. In early September 2018, the second class of PS+ASD interns will begin at Fort Eustis. If shown to be successful, PS+ASD will support professionals and military personnel by identifying viable treatment models for military dependents in the transition to employment.





For more information, visit:

<http://cdmrp.army.mil>

or contact us at:

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