Written Public Testimony of Marsha Mailick Seltzer, Ph.D., Chair of the Intellectual and Developmental Disabilities Research Centers Association (IDDRCA)

House Committee on Appropriations Subcommittee on Labor, Health & Human Services, Education, and Related Agencies
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Mr. Chairman, on behalf of the Intellectual and Developmental Disabilities Research Centers Association (IDDRCA), I thank you for this opportunity to share with you and your Committee some of the exciting recent achievements in the world of intellectual and developmental disabilities research. I am Marsha Mailick Seltzer, Director of the Waisman Center at the University of Wisconsin and Chair of the IDDRCA. Unfortunately, as I share with you exciting research developments occurring within our network of research centers, I also must share the impact of NIH budgets on our research efforts and the challenges that recent budgets put on the work of the Centers.

During the last few fiscal years critical research being conducted at Intellectual and Developmental Disabilities Research Centers (IDDRCs) has slowed due to cuts in the NIH budget. Since the doubling of NIH funding ended in 2003, funding for NIH has failed to keep pace with biomedical inflation and as a result, NIH has lost more than 13% of its purchasing power. Recently funded DDRCs experienced approximately an 11% cut, even though they received outstanding scientific evaluations. To address our concerns, we respectfully ask the Committee to increase NIH funding by approximately 6.6%, $1.9 billion, to $31.1 billion for FY 2009. This would restore funding lost to NIH since 2003. In addition, we ask that you increase funding by approximately 6.6% to $1.34 billion for the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) and restore cuts in IDDRC funding.

NICHD was established in 1963 with Congressional action to establish “centers of excellence” in intellectual and developmental disabilities research. The IDDRC program was the nation’s first sustained and integrated effort to prevent and treat disabilities through biomedical and behavioral research. To commemorate this year’s 45th Anniversary, NICHD and the IDDRC program were officially renamed in honor Eunice Kennedy Shiver who worked tirelessly to establish them. Currently, 14 members of our association are supported by core funds from NICHD. In addition, seven other research centers are affiliate members of our association because of their common interest to share research and participate in the activities of this esteemed network. The disabilities and disorders the members of the IDDRCA study include autism, Down syndrome, fragile X syndrome, cerebral palsy, and literally hundreds of other causes of intellectual disabilities in children and adults. Today, the IDDRCA is the world’s largest concentration of scientific expertise in the fields of intellectual and developmental disabilities. Our Centers, and the network they form, substantially foster communication, innovation, and excellence in research. We work collaboratively on a wide range of research projects, and together with the Society for Developmental Pediatrics, produce the highly regarded quarterly journal, “Intellectual and Developmental Disabilities Research Reviews.” Each edition highlights important new research on a specific developmental disability or a critical prevention or treatment breakthrough.
Our research Centers are located within premier research intensive universities and often are affiliated with major medical centers that provide academic, scientific and clinical expertise as well as institutional support. Collectively, our work represents a multidisciplinary, vigorous, and innovative research program directed at understanding, treating and reducing the incidence of developmental disabilities. Additionally, our investigators are engaged in a very important mission - training the next generation of scientific investigators and clinicians in this area of great importance to America’s children and families.

Although a significant portion of the research portfolios at the Centers consists of fundamental studies that are directed at understanding the biological and behavioral processes in animal models and human subjects, each Center also directs considerable attention toward seeking solutions to practical issues and problems. Our connection to the University Centers for Excellence in Developmental Disabilities (UCEDDs) is critical in translating our research to practice. The scope of the research conducted at the Centers encompasses every known major dimension of intellectual and developmental disabilities.

Over the last four decades there has been a huge payoff in the federal investment in the Intellectual and Developmental Disabilities Research Centers. Numerous disorders that cause intellectual disabilities can now be prevented or treated to improve developmental outcomes. The Centers’ scientific achievements have helped improve quality of life for individuals and families affected by disabilities. Among the most exciting aspects of this work are the fundamental biological and environmental triggers for many of these disabilities that are being revealed and especially breakthrough research on prevention and intervention strategies. I am pleased to share some examples with you.

**Recent Breakthroughs in the Causes of Intellectual and Developmental Disabilities**

As I noted, there are literally hundreds of causes of intellectual and developmental disabilities. Over the past four decades the investment made in the Developmental Disability Research Centers has led to the discovery of a substantial number of these. Here are some recent examples:

- Researchers at the Vanderbilt University IDDRC discovered genetic mutations that disrupt a key protein that is critical for brain development and controlling mood and emotion in children and adults. These mutations are highest among individuals with autism who exhibit symptoms of obsessive-compulsive disorder. This finding should help us finally pin down some of the causes of autism, and eventually aid with early diagnosis and intervention.

- Researchers at the Children’s Hospital of Philadelphia IDDRC discovered the cause of Cornelia de Lange Syndrome. This inherited disorder causes mental retardation, growth retardation, abnormal limb development, cardiac dysfunction and other developmental problems. This discovery may open new paths to prevention and treatment.

- Researchers at the University of Alabama Medical Center IDDRC utilized molecular biological and genetic engineering approaches to determine how cytomegalovirus infection in pregnant women disrupts and damages fetal brain development. This discovery may lead to the development of an effective method to prevent these effects.

- Researchers at the University of North Carolina IDDRC used brain imaging techniques to identify generalized enlargements of brain matter in very young children with autism. These abnormal increases appear to begin in the latter part of the first year of life, suggesting...
that this may be a critical period for the onset of autism. This finding may lead to both earlier diagnosis and earlier intervention for this disorder.

- Researchers at the University of Wisconsin IDDRC demonstrated for the first time a **critical role of early social deprivation in the development of brain systems** underlying the formation of human social bonds. This research grew from numerous observations that children who were reared in foreign orphanages and then adopted between 1 and 5 years of age into families in the United States often suffer from long term problems in forming normal emotional and social relationships with their adoptive families and peers. This discovery has immediate and broad implications for the development of treatments targeted on the disrupted brain region.

- **Rett syndrome** is a genetically caused progressive neurological disorder that leads to severe mental retardation and autism in females. Researchers at the Baylor College of Medicine IDDRC in Houston have discovered that a specific protein known as MeCP2 plays a causal role in the brain pathology of this disorder. Researchers at Children’s Hospital in Boston IDDRC and other centers are building on this discovery in an effort to determine additional effects of this gene mutation that may give rise to defects in human cognition. This landmark discovery may eventually pave the way for effective preventive treatments.

- Researchers at the Baylor College of Medicine recently demonstrated that multiple mechanisms of inherited **childhood epilepsy** appear to originate from a prenatal impairment of a neurotransmitter released at thalamic synapses in the brain. They have developed a new brain imaging technique that is now allowing them to pinpoint the genes that cause temporal lobe epilepsy in children with this disorder. This discovery may lead to methods for preventing these effects.

- Other researchers at Baylor recently discovered that a molecule known as Math1 is essential for the normal development of the entire neural system in terms of our ability to coordinate auditory, vestibular, and proprioceptive systems so as to be able to sense our position in space. This same molecule has already been shown to impact several other specific neural systems. The disruption of this molecule for any reason may lead to serious neural developmental problems. The discovery of its central role opens the door to investigate its potential impact on a wide range of disorders.

- **Fragile X syndrome** is the most common inherited cause of mental retardation and the most common single-gene neuropsychiatric disease known. The biology underlying Fragile X syndrome, is rapidly revealing itself in research being conducted at several IDDRCs. Research with animal models of this disorder has suggested that several potential intervention approaches that may correct for the abnormal protein expression that impacts neural development and appears to result from the disorder. Initial tests of novel intervention approaches in animal models are underway.

- Researchers at the University of Wisconsin IDDRC have been examining a key symptom of **autism** – an inability to respond appropriately in social interaction with others. They have found that when children with autism look at faces that are expressing emotion, they show accentuated activation in brain circuits associated with emotional arousal and threat. When they avert their gaze from these faces, brain activation in these regions is reduced. This information may contribute to the development of effective therapeutic interventions for this core trait of the disorder.
Recent Breakthroughs in Prevention and Therapeutic Intervention – Translational Research

Although the IDDRCs have a long history of research on prevention and intervention approaches, these efforts have been accelerating in recent years with the NIH’s increased emphasis on translational research. Well over one hundred clinical trials are currently underway at all IDDRCs with some centers reporting more than 30 such trials underway or recently completed. The potential impact of new interventions that are presently under investigation for individuals with intellectual and developmental disabilities is truly astounding. For example:

- More and more very low birth weight premature babies are surviving, but many will have significant intellectual and developmental problems. Researchers at the University of Kansas IDDRC have developed a small high tech device that measures the oromotor functioning of very young premature infants to determine their ability to effectively suck and then quickly trains them to suck normally. This intervention can prevent these developmental problems associated with inadequate early nutrition and will likely be standard equipment in NICU’s throughout the world within a few years.

- **Learning disabilities** affect 10-20% of the world’s population. A common genetic cause of these disorders is neurofibromatosis Type 1. Researchers at the UCLA IDDRC have discovered that a commonly prescribed type of drug known as Statins can reverse the neurological effects of this disorder in a mouse model. Efforts are now underway to test the effects of this drug on humans who have this common disorder.

- **X-linked adrenoleukodystrophy (X-ALD)** causes progressive paraparesis and severe disabilities in children, and was the focus of the movie “Lorenzo’s Oil.” Researchers at the Kennedy Krieger IDDRC in Baltimore are presently conducting a large clinical trial to determine if administration of Lorenzo’s Oil affects the rate of progression in pre-symptomatic patients and significantly reduces the risks associated with the disease.

- Research at Kennedy Krieger has also revealed that almost 20% of individuals with autism spectrum disorder have total cholesterol levels well below the 5th percentile suggesting that hypocholesterolemia may be a factor contributing to this disorder. These researchers are now testing whether the drug Semivastatin, which is known to increase cholesterol production, will have a positive effect on children with Smith-Lemli-Opitz syndrome, a disorder associated with decreased cholesterol production that also carries a high risk of autism.

- Children of mothers who drink alcohol during pregnancy are at-risk for **Fetal Alcohol Syndrome** disorder, which is associated with significant life-long cognitive and social impairments. A study being conducted at the University of Washington IDDRC has demonstrated that a brief intervention targeted on pregnant women who report drinking alcohol was highly successful in achieving abstinence in these women with substantial positive effects on their children’s development as compared to women who did not receive this brief intervention.

- **Communication and language development** are severely impacted by mental retardation as well as autism. Researchers at several Centers are investigating innovative early intervention techniques intended to enhance development in these children. Promising results have been recently reported by investigators at the UCLA, Vanderbilt, and University of Kansas IDDRCs.

Many of these clinical intervention trials that are presently underway across the IDDRC network are...
only possible due to the unique concentration of scientific talent and specialized resources associated with these Centers. The potential of these studies to enhance the development and functioning of children and families in their country and around the world faced with the challenges due to hundreds of different causes that lead to intellectual and developmental disorders has never been greater. The range of disorders under investigation include Autism Spectrum Disorders, Down syndrome, Fragile X Syndrome, Fetal Alcohol Syndrome, Specific Language Impairment, Muscular Dystrophy, a wide range of Learning Disabilities, and dozens of rare, complex disorders that we are just now coming to understand.

While we have made extraordinary progress over the past four decades, we still have far to go. With knowledge generated by the IDDRCs, we will be able to:

- Use brain imaging and genetic methods to better understand the causes of specific disabilities and design strategies for treatment.
- Develop new therapies to prevent or reverse some of the symptoms of specific disabilities.
- Better understand the process of brain cell development and enrichment through studying the interplay of the brain’s own chemistry with a child’s experiences.
- Prevent many types of developmental disabilities by treating maternal infections and viruses transmitted to their infants.
- Capitalize on the brain’s natural “plasticity” to optimize brain development in children born with developmental disabilities through early intervention or by extending the period of brain development.
- Design learning environments so all children have improved academic outcomes, including those with learning and intellectual disabilities.
- Determine which child with a disability will respond best to which speech or communication learning approach.
- Develop culturally competent psychological and medical assessment and treatment procedures for children born into minority families.
- Prevent and treat behavior problems among children and adults with disabilities that are especially prone to such difficulties, such as children with autism, fragile X syndrome, or Rett’s syndrome.
- Assist families in preparing their adult sons and daughters with disabilities for successful lives of their own and prepare older people with developmental disabilities for coping with the normal process of aging.

Recommendation to Subcommittee

In order to continue and build upon the capacity of IDDRCs, we again respectfully ask the Committee to increase NIH funding by approximately 6.6% to $31.1 billion for FY 2009. This would restore funding lost to NIH since 2003. In addition, we ask that you increase funding by approximately 6.6% for NICHD to the level of $1.34 billion for NICHD in FY 2009 and restore cuts in IDDRC funding. I thank you Mr. Chairman for taking time to learn about the IDDRC network and the scope of work being conducted at these Centers across the nation. Together we believe that we are making strong headway in finding solutions to the many diseases and disabilities, which affect the children and adults of our society. For a directory of IDDRCs across the country please visit: http://www.aucd.org/ddreportal/directory/directory.cfm