2012 INTERAGENCY AUTISM COORDINATING COMMITTEE STRATEGIC PLAN UPDATE: QUESTION 1 WHEN SHOULD I BE CONCERNED?

WHAT IS NEW IN THIS RESEARCH AREA, AND WHAT HAVE WE LEARNED IN THE PAST TWO YEARS?

Prevalence

Several noteworthy new studies from the U.S., South Korea, and England update the recognized prevalence of autism.

In the U.S., the Autism and Developmental Disabilities Monitoring Network (ADDM), supported by the Centers for Disease Control and Prevention (CDC), released its most recent surveillance data showing a prevalence of 1 in 88 children or 1.1%—an increase of 78% since the first report in 2002—with larger increases among racial/ethnic minority groups (CDC, 2012). The average age when children were initially diagnosed with ASD, however, remains essentially unchanged, at 4–5 years of age. A second U.S. study found a sharp increase in autism in children (based on parent report) over an 11-year period (Boyle et al., 2011). Importantly, such an increase was not found for other neurodevelopmental disorders other than attention deficit hyperactivity disorder.

Looking internationally, a South Korean study found an ASD prevalence of 1 in 38 or 2.6% of children when a large population sample of school-aged children was evaluated (Kim et al., 2011). Notably, two-thirds of those identified had not been previously diagnosed with autism or received any services. A British study found a prevalence of 1 in 100 adults, most of whom were not previously diagnosed with ASD (Brugha et al., 2011). The large majority of adults with ASD identified in this study were living independently but at lower levels of socioeconomic success than non-ASD peers.

Taken together, these studies suggest that some, but not all, of the increased prevalence observed in children is a result of improved identification and that there may still be a sizable population of children and adults with undiagnosed autism.

Diagnosis

The Diagnostic and Statistical Manual of Mental Disorders (DSM) definition of autism will be revised in 2013 when the new version, DSM-5, is released. The goal is to consolidate all current diagnoses under one category (autism spectrum disorder) while making its criteria more appropriate to diagnosis of very young children, adults, and girls. While early studies raised concerns that the new criteria would exclude some people from diagnosis, recent findings suggest this will not happen and that the other goals of the revision will be achieved. Specifically, similar rates of diagnosis were reported in a study based on well-characterized research samples (Huerta et al., 2012) and in preliminary results of the DSM-5 validation studies (Regier et al., 2012). However, there is still a need for prospective studies of the new criteria with larger sample sizes, and no data have yet been collected on adults.

In addition to evaluating the new criteria, recent analyses suggest that the method by which diagnostic information is collected is also critically important. Diagnoses that include information from both clinician observation and parent or caregiver report were found to be more accurate than diagnoses that rely on just one approach or the other (Huerta et al., 2012; McPartland, Reichow & Volkmar, 2012).

Furthermore, because diagnostic criteria are based on behavioral evaluation, clinical diagnoses are inconsistent among practitioners. Variations in diagnostic data from the infant sibling studies (Ozonoff et al., 2011), the CDC ADDM surveillance network sites (CDC, 2012) and the Simons Simplex Collection sites (Lord et al., 2012) suggest that clinical diagnoses still remain more variable than they should. This situation may ultimately be resolved by the development of laboratory tests for autism biomarkers, refined by observation and reporting. Although the criteria for diagnosis are behavioral, the hope is that medical evaluation will identify subtypes and decrease this variability.

Early Screening and Detection

Work on early screening tools has accelerated during the past two years, with two studies using questionnaire-based tools to screen for children at-risk for ASD as early as 12 months old in community settings (Pierce et al., 2011b and Turner-Brown et al., 2012). However, researchers continue to have difficulty attaining sufficient sensitivity (the number of children correctly identified as having autism) without excessive rates of "false positives," in which some children are identified as being at-risk for autism but do not go on to receive an ASD diagnosis. Specificity - correctly identifying the children that do not have ASD by accurately distinguishing ASD from other developmental disabilities or typically developing children - also remains a challenge.

Simplified ASD assessment tools for use across the lifespan are also in development (Allison, Auyeung & Baron-Cohen, 2012), but have not yet met the need to appropriately identify adolescents and adults of all ages with ASDs (Pilling et al., 2012). Additionally, new research continues to highlight disparities by gender, race, and ethnicity in identification of ASDs (Valicenti-McDermott et al., 2012; Kočovská et al., 2012), while gaps remain in understanding the reasons for these disparities and evidence-based ways to close these gaps.

Early Diagnosis

Symptoms of autism may not be visible in the first year of life and currently are not measured reliably until the end of the second year. However, several groups are looking for performance-based measures to bridge that gap. For example, one study in toddlers as young as 14 months showed a strong correlation between a preference for fixating on geometric images and subsequent ASD diagnosis (Pierce et al., 2011a). Similarly, another research group found an association between atypical eye contact at 7 – 13 months and subsequent diagnosis of ASD (Bedford et al., 2012). A relationship was also identified between differences in vocalization at 6, 9, and 12 months and diagnosis of ASD at 24 months (Paul et al., 2011), as well as research indicating that a child's temperament in the first two years of life, such as increased perceptual sensitivity or reduced interest in cuddling, may predict a future ASD diagnosis (Clifford et al., 2012).

Brain recording and imaging techniques are also showing promise in identifying early biomarkers for autism. Using brain imaging (diffusion tensor imaging, DTI), researchers have identified white matter fiber tract development differences in 6-month-old infants who would later be diagnosed with ASD (Wolff et al., 2012). This suggests that aberrant development of brain pathways may precede the manifestation of autistic behaviors in the first year of life.

Other research has explored electroencephalography (EEG) data as a potential biomarker and quantifier of risk in the first year (Bosl et al., 2012; Elsabbagh et al., 2012). It is thought that EEG signals may contain information about the architecture of the neural networks in the brain and that early detection of abnormalities in EEG signals could be used as a biomarker for ASD and other developmental cognitive disorders. Using this type of signal processing approach—specifically multiscale entropy—to determine if a neural "signature" of autism risk could be observed, researchers were able to classify high versus low risk with over 80% accuracy at nine months of age (Bosl et al., 2012). However, it is uncertain whether this is predictive of which infants develop ASD. Another research group found that atypical event related potential (ERP) responses to eye gaze in high risk infants predicts which infants developed ASD (Elsabbagh et al., 2012). It is too early to tell if this work translates to the general infant population, but it may point the way to very early identification of ASD in children from known at-risk groups. Finally, other studies have made progress toward detecting biological markers for autism through blood screening – looking at gene expression (Glatt et al., 2012) or gene pathway analysis (Skafidas et al., 2012).

WHAT GAPS HAVE EMERGED IN THE PAST TWO YEARS?

The age at which autism is diagnosed in most children has not changed, even though diagnosis is now possible significantly earlier. Better diagnostic tools and skills have been developed, but their existence has not yet translated to earlier detection in the general population.

Data systems—using the existing ADDM infrastructure or other data collection sites–to understand how the upcoming DSM-5 changes impact diagnosed prevalence and age at identification are recommended. Autism Speaks has funded a study to prospectively examine the impact of DSM-5 criteria on diagnosis at one ADDM site, but more studies are needed with both younger and older individuals.

CDC's ADDM ASD prevalence estimates are now available every two years based on large U.S. populations; however, these data are based on retrospective cohorts of children at age eight years. Population-based data on younger children are needed, and new data collection is underway for children that are four years of age. However, the goal of obtaining rapidly available population-based estimates on large community samples continues to be a challenge.

The American Psychiatric Association (APA) has proposed a new disorder— Social Communication Disorder (SCD)—to describe people with communication problems whose

severity is not enough to warrant an ASD diagnosis. The community is concerned that there are no therapies or services currently associated with SCD. There is a fear that it will be interpreted as mild ASD without the need for supports.

The British study identifying the prevalence of ASD in the adult population (Brugha et al., 2011) suggests that a significant portion of the adult ASD population remains undiagnosed, despite the existence of screening tools and increasingly widespread public awareness of autism. Unrecognized adults with autism have emerged as an overlooked and underserved population. Some studies show that adults with autism continue to be socially disadvantaged and have significantly lower academic and career attainments as compared to non-ASD adults in similar surroundings (Brugha et al., 2011; Henninger & Taylor, 2012). Autism is a lifelong disability, yet research efforts to date have primarily focused on childhood and adolescent detection and intervention. More emphasis must be placed on individuals of all ages.

As the field shifts to pre-symptomatic diagnosis, a series of new, complex bioethical issues are emerging since diagnosis and treatment could be indicated for an infant without behavioral symptoms. Many in the autism community have expressed concern that research into early detection will lead to prenatal tests for ASD and that the existence of such tests may have family planning implications. On the other hand, very early detection in infants may be one of the keys to provide the best outcomes for people who will grow up with ASD in the future. Prenatal testing could also have significant quality of life implications if it facilitates effective early intervention. Work leading to prenatal tests for ASD potential should be informed by a full discussion of the bioethical issues cited above.

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