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Nosology and diagnosis of Rett Syndrome

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Abstract

Rett Syndrome is one of the least commonly occurring autism spectrum disorders (ASD), but certainly one of the most devastating. A genetic profile has been identified, but checklists still have an important role for prescreening, especially before expensive genetic testing, and to provide precise strengths and weaknesses with respect to the core features of the disorder. Furthermore, research is now demonstrating subprofiles of genetic mutation which may be linked to profiles of behavioral responding and general symptom profiles. We review the literature on the nosology and assessment of Rett Syndrome in light of these developments. Specific symptoms and assessment techniques are discussed and potential future research avenues are reviewed with an eye to strengths and weaknesses of the current knowledge base.

Keywords: Rett Syndrome; Nosology; Assessment; Autism spectrum disorders; Genetics; Checklists; Behavioral symptoms

The autism spectrum disorders (ASD) are a group of conditions with similar core features (Matson, Nebel-Schwalm, & Matson, 2007; Matson & Wilkins, 2007, 2008). All ASD are characterized by a core group of behavioral symptoms which are believed to have multiple biological determinants (Andersson et al., 1989; Gillberg, 1992). Individuals diagnosed as having an ASD share deficits in social skills, communication, emotional reciprocity, and have restrictive, repetitive patterns of interest and/or stereotypic behavior (Balconi & Carrera, 2007; Chung et al., 2007; Gillett & LeBlanc, 2007; Hilton, Graver, & LaVesser, 2007; Lee, David, Rusyniak, Landa, & Newschaffer, 2007; MacDonald et al., 2007). Having said this, the nosology of ASD is in the early stages of development and, therefore, much has yet to be learned about etiology, classification, and assessment as part and parcel of the description of these disorders (Matson & Boisjoli, 2007, 2008; Matson & Wilkins, 2008). Additionally, knowledge of symptom patterns, onset, and course are of critical importance for better understanding and treating these problems (Matson & Smith,

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2008). Government agencies worldwide have made the examination of these issues a top priority.

Other disabilities often co-occur with ASD including intellectual disability (Ben-Itzchak & Zachor, 2007; Matson, Dempsey, LoVullo, & Wilkins, 2008), comorbid psychopathology (Matson & Nebel-Schwalm, 2007b), self-injury and aggression (Dominick, Davis, Lainhart, Tager-Flusberg, & Folstein, 2007; Matson & Minshawi, 2007; Matson & Nebel-Schwalm, 2007a; Matson & Wilkins, 2007; Plant & Sanders, 2007), and a host of general difficulties in learning such as spontaneous imitation of skills (Ingersoll & Gergans, 2007). Therefore, another critical area of further investigation is to establish the underpinnings of these other disabling conditions to determine their influence on ASD symptomatology and behavioral expression of these disorders. The ASD where the greatest success has occurred in identifying genetic causes is Rett Syndrome (RS). This disorder will be the focus of our review.

1. Rett Syndrome

RS is a neurodevelopmental disorder first described by Andreas Rett, a pediatrician at the University of Vienna in 1966 (Wenk, 1997). Despite this, RS has only been recognized as a distinct condition in the professional community since 1983 (Hagberg, Aicardi, Dias, & Ramos, 1983). As such, RS is one of the ''newest'' and least studied of the ASD generally speaking. Having said this, particularly impressive discoveries regarding the genetics of RS have occurred relative to other ASD. Since its first description, RS has been determined to be a neurological disorder caused by an X-linked mutation.

The prevalence of RS is approximately one case for every 10–15 thousand people (Hagberg, 1989), and occurs almost exclusively in females (Laurvick et al., 2006). This life-long pervasive condition is found across racial and ethnic groups internationally (Elefant & Wigram, 2005). Developmentally, a child with RS may be difficult to distinguish from typically developing children for the first 6–18 months of life. At some point during this time period, however, motor regression, decelerated head growth, and severe intellectual disability begin to occur (Hagberg et al., 1983; Moog et al., 2006). Until recently the mechanism that precipitated these developmental irregularities was unknown. Then, in 1999, the gene encoding methyl-CpG-binding protein 2 (MECP2) located at chromosome Xq28 was identified as the cause of the condition (Amir et al., 1999). Despite this important development, researchers have continued, out of necessity, to conduct studies to help further describe the range and core behavioral manifestations of RS and to explore variations on the core genetic disability that characterizes the condition. Since no cure currently exists, these studies are important for screening, treatment planning, and to evaluate the course of the condition. Thus, behavioral manifestations of RS, both in heterogeneity of behavioral expression across individuals and in developmental course over time, are significant.

2. Nosology and assessment

The nosology and assessment research has generally followed two courses. One direction has been the study of neurological patterns of behavior such as sleep, abnormal movements, and EEG (Einspieler, Kerr, & Prechtl, 2005; Laan, Brouwer, Begeer, Zwinderman, & Gert van Dijk, 1998; Nomura, 2005; Segawa, 2005). A second approach has been to study and describe the person's behavioral manifestations. An overview of these two areas of study follows.