Rett Syndrome: A Review of Current Knowledge

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Rett syndrome was first described in 1966 by Andreas Rett. To date, this syndrome has been reported only to afflict females. The disorder is characterized by a progressive loss of cognitive and motor skills as well as the development of stereotypic hand movements, occurring after an apparently normal 6 to 18 months of development. Although Rett syndrome is thought to afflict as many as 10,000 girls in the United States, fewer than 1,200 have been identified thus far. A lack of awareness of this disorder is thought to play a critical role in the failure to differentially diagnose this syndrome. The present article presents a review of our current knowledge concerning this disorder. Information is provided related to the clinical manifestations, etiology, prevalence, pathogenesis, and treatment of the Rett syndrome.

Rett syndrome, at least in its classical form, is a phenotypically distinct progressive neurological disorder with a characteristic pattern of cognitive and functional stagnation and subsequent deterioration. The disorder was first described by Rett (1966, 1969) following his serendipitous discovery of a number of girls displaying strikingly similar behavioral characteristics and developmental histories. Unfortunately, Rett reported substantially increased levels of blood ammonia (hyperammonemia), a finding that was subsequently found only rarely associated with this disorder. This false lead, coupled with very limited exposure (Rett, 1977) of this information in the English language medical literature, resulted in a general failure to recognize Rett syndrome as a nosologic entity. In fact, the syndrome had been virtually overlooked until Hagberg, Aicardi, Dias, and Ramos (1983) published their report of 35 girls from France, Portugal, and Sweden with Rett syndrome in the Annals of Neurology. This landmark account awakened the...
Individuals with Rett syndrome exhibit a characteristic course of development (Naidu, Murphy, Moser, & Rett, 1986). Prenatal and perinatal histories of these persons are generally unremarkable. Parents report normal physical and mental development for the first 7 to 18 months of life as evidenced by physical growth and psychomotor and verbal behavior (Gillberg, 1987). This apparently normal period of development is followed by a slowing or cessation of the acquisition of developmental milestones (e.g., walking in many cases). Rapid deterioration of behavior is evidenced by loss of acquired speech, voluntary grasping, and the purposeful use of the hands. The girls begin to exhibit a lack of sustained interest in persons or objects and demonstrate limited interpersonal contact, however, eye contact is maintained (Holm, 1985; Trevathan & Naidu, 1988; Witt-Engerstrom, 1987). This deterioration is typically accomplished by age 3, occurs within 1 year or less, and results in apparent severe to profound mental retardation and stereotyped behaviors. The developmental deterioration is accompanied by the onset of deceleration of head growth, coarse, jerky movements of the trunk and limbs, a stiff-legged, broad-based gait with rather short steps and swaying movements of the shoulders when ambulating (Coleman & Gillberg, 1985; Hanefield, 1985; Kerr & Stephenson, 1986; Naidu et al., 1986; Percy, Zoghbi, & Riccardi, 1985). A leading symptom of the syndrome involves stereotypic hand clapping, “hand washing,” and hand-to-mouth movements similar to those displayed in Figure 1 (Ishikawa et al., 1978; Leiber, 1985). As individuals with Rett syndrome approach adolescence they are frequently subject to increased spasticity and vasomotor disturbances of the lower limbs, possible loss of existing ambulation, scoliosis, and a diminished rate of growth. Facial grimacing, bruxism (teeth grinding), hyperventilation, apnea (breath holding), aerophagia (air swallowing), constipation, and seizure activity also sometimes accompany the syndrome (Trevathan & Naidu, 1988). Hagberg and Witt-Engerstrom (1986) proposed a staging system to facilitate the characterization of the disorder patterns and profiles from infancy through adolescence. Their system suggests four clinical stages and was derived from a synthesis of clinical observations over the years in 50 Swedish cases of Rett syndrome. The purpose of the staging system is to provide average guidelines for stage patterns thought to be of use when confronted with the diagnostic problems resulting from the complex symptomatology and longitudinal profile of the