A Family History Study of Asperger Syndrome

Mohammad Ghaziuddin

Asperger syndrome (AS) is a childhood-onset disorder often described as a mild variant of autism. Although classified as a distinct disorder in the DSM-IV, its overlap with autism continues to be a matter of ongoing debate. While the family genetic origins of autism are well established, few studies have investigated this topic in AS using current operational criteria. In this report, we examined the family psychiatric history of 58 subjects with AS diagnosed according to DSM-IV criteria (48 males; mean age 13.34; mean full scale IQ 104.87). All subjects had a history of mild autistic social deficits; focused special interests; normal level of intelligence; and an odd and often pedantic manner of speaking. None had a previous diagnosis of autism. Of the 58 subjects with Asperger syndrome, three had first degree relatives with AS; nine (15%) had a family history of schizophrenia; and 35 (60%) had a family history of depression. Of the 64 siblings, four had a diagnosis of AS and none of autism. Compared with a group of 39 subjects with normal intelligence autism (high functioning autism, HFA; 33 males; mean age 15.34; mean full scale IQ 85.89) subjects with AS were more likely to have relatives with depression; schizophrenia; and the broader autistic phenotype. Possible reasons for and implications of these findings are discussed.

KEY WORDS: Asperger syndrome; autism; depression; schizophrenia; family history; genetics.

INTRODUCTION

Asperger syndrome (AS) is a type of pervasive developmental disorder characterized by autistic social dysfunction; focused interests; and subtle communication deficits occurring in the presence of normal intelligence. There is no history of formal speech delay. Introduced only about a decade back in the DSM-IV (APA, 1994), it is being diagnosed with increasing frequency. Its prevalence estimates have ranged from 2.5 per 10,000 (Fombonne & Tidmarsh 2003) to as high as 7 per 1000 (Ehlers & Gillberg 1993). In contrast, the prevalence of autism is usually given as 4 per 10,000 and that of the broader autistic phenotype as 4 per 100 (Folstein & Santangelo, 2000).

Although Asperger syndrome is widely believed to cluster in families, few systematic studies have investigated its family genetic aspects. Evidence for its genetic origin comes from case reports and studies of probands with classic autism, not those of probands with Asperger syndrome. For example, in a family history study of autism, out of 137 siblings of autistic probands, only one was diagnosed with Asperger syndrome (Bolton et al., 1994). Compared to a control group of siblings with Down syndrome, 5.8% in the autism group were diagnosed with autism, atypical autism or Asperger syndrome, compared to 0% in the Down syndrome group (none out of 64 siblings with Down syndrome). In contrast to Asperger syndrome, evidence for the familial loading of autism is well-established. In addition to carrying a high risk for autistic disorder, close relatives of subjects with autism show a preference for solitariness; deficits of social and narrative language; a resistance to change; a desire for sameness; and mild deficits of executive...
functioning (Bailey et al., 1995; Piven et al., 1994). Sometimes referred to as the broader autistic phenotype (BAP) or the lesser variant, these deficits are not severe enough to justify the full diagnosis of autism. In order to investigate the familial aspects of AS and determine its degree of relatedness to autism, it is important to perform studies focusing on large series of probands with AS (Spiker, Lotspeich, Dimiceli, Myers, & Risch, et al., 2002). The purpose of this study is to address this issue.

Two main reasons account for the paucity of findings on the familial aspects of Asperger syndrome. First, studies have not used standardized criteria for the diagnosis of AS. A decade after the inclusion of the disorder in the DSM classificatory system, studies continue to use modified criteria or include subjects with both autism and Asperger syndrome (Ghaziuddin, Tsai, & Ghaziuddin, 1992; Miller and Ozonoff, 1997). The problem is partly confounded by the manner in which the criteria are currently formalized (see Gillberg, 1998). Second, the boundaries of AS are not clearly demarcated. Earlier assertions of a clear distinction between autism and Asperger syndrome have so far proved specious. Indeed, Asperger syndrome needs to be separated not only from autism but also from PDDNOS; the broader autism phenotype (BAP) or the lesser variant of autism; and from schizoid/schizotypal personality disorders. The latter distinction is particularly important because of the known association of these conditions with schizophrenia (Kendler et al., 1993). Thus, research focusing on the familial aspects of AS can shed light on its relationship not only with autism but also with related conditions.

Asperger himself believed that the condition was strongly genetic in nature, and that fathers of patients that he described were often highly intelligent. Among the 200 children he saw over a period of 10 years, almost all had at least one parent with similar personality traits (Asperger, 1944). Subsequent studies on this topic also emphasized its genetic roots. In particular, Van Krevelan (1971), one of the earlier researchers who attempted to carve out Asperger syndrome from autism, proposed that the condition was over-represented in the fathers of children with AS and that, to a large extent, was passed down from fathers to sons. He suggested that Asperger syndrome was more genetical-based than autism (1971). Although more recent research has not specifically investigated Van Krevelan’s hypothesis, it is nonetheless believed that AS, like autism, is a strongly genetic disorder. Wing (1981) found that out of 34 cases, 5 of the 16 fathers and 2 of the 24 mothers, showed behavioral traits resembling those of Asperger syndrome. In Gillberg’s series of 23 patients with Asperger syndrome, several of the parents showed similar personality traits (Gillberg, 1989). In Wolff’s series, out of 32 male patients, 7 fathers and 12 mothers had similar traits, compared to one mother and no father in the 32 males in the control group. Among 33 girls similarly examined, only one mother and four fathers were definitely affected compared to two mothers and two fathers in the control group (Wolff & McGuire, 1995). A few case reports have also been published describing the familial clustering of Asperger syndrome. Ghaziuddin, Metler, Ghaziuddin, Tsai, & Giordani et al. (1993) described a family in which the father had features of schizoid personality disorder and his three sons had a diagnosis of Asperger syndrome. Volkmar et al. (1996) described a 15-year-old youngster with Asperger syndrome. Both the proband and his father showed discrepancies between the verbal IQ and the performance IQ, with the verbal abilities being higher. The proband displayed a split of 50 points on the verbal performance IQ (verbal IQ 140, performance IQ 90), and the father showed a split of 43 points (verbal 129, performance 86). Deficits in the social use of language and on MRI examination were also found. In the discussion of their paper, the authors stated that the major reasons for including Asperger syndrome as a diagnostic entity in the DSM-IV system of classification rested “both on its differentiation from autism and the apparently higher frequency of transmission of this condition within families” (Volkmar et al., 1996). However, what is meant by a higher frequency of transmission has not been spelled out. The present study was, therefore, undertaken to clarify the pattern of familial aggregation of subjects with Asperger syndrome with reference to the presence of autism spectrum disorders and major psychiatric disorders in the first degree relatives.

METHOD

Subjects were referred to the author over a period of 5 years, and were derived from community sources, such as mental health centers and schools, and psychiatric clinics. For inclusion in the study, subjects had to have a diagnosis of a pervasive developmental disorder; a full scale IQ of 70 or above on an individually administered test of intelligence; and the presence of at least one biological parent.