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Neuropsychiatric comorbidities in autism spectrum disorders without intellectual disability

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Abstract

Epilepsy and autism spectrum disorder tend to co-occur in the population with intellectual disability. However, in the autistic population without intellectual disability, the prevalence of epilepsy is also much greater than in the general population. The special health needs in children having autism spectrum disorder without intellectual disability, namely those with high-functioning autism spectrum disorder have become recognized in recent years, yet comorbid neuropsychiatric symptoms such as anxiety, attention-deficit/hyperactivity disorder, and epilepsy still sometimes remain undiagnosed and untreated. Heightened awareness of such comorbidities will help these children to access appropriate treatment. Whether the epilepsy associated with high-functioning autism spectrum disorder is the same or different from that associated with intellectual disability, and whether the autistic profile associated with epilepsy in high-functioning autism spectrum disorder is the same or different from that without epilepsy, should be answered by future studies.

INTRODUCTION

Evidence from a community-based study[1] and numerous clinical reports indicate that a high proportion of individuals with autism spectrum disorder (ASD) suffer from one or more comorbid neuropsychiatric disorders. An association between epilepsy and ASD is well recognized, and comorbidity tends to be accompanied by intellectual disability. According to a meta-analysis of 23 studies[2], the pooled prevalence rates of epilepsy are 21.4% for individuals with ASD (defined as autism and/or pervasive developmental disorder) and intellectual disability, and 8% for those without intellectual disability, both of which are notably higher than the rate of 0.5% for the general population. In addition, sex seems to be another factor influencing the prevalence rate of epilepsy in the autistic population; epilepsy is more prevalent in autistic females than in autistic males, suggesting a close association between epilepsy and a female-predominant subgroup with ASD.[2]

Recently, heightened awareness of milder autistic conditions without intellectual disability has led to a higher overall prevalence rate of ASD of 2.6%[3], and has highlighted the clinical needs of children with ASD who have been undiagnosed until school age. In fact, a recent U.S. study found that most children with ASD were first identified as having ASD after age 5.[4] Further, it is reported that being older at first diagnosis of ASD is one of associated factors to reduce quality of life (QOL) for adults with high-functioning ASD, together with having a comorbid psychiatric disorder and being female by a nationwide survey conducted in Japan.[5] Taken together, it is clear that the early identification and treatment of ameliorable comorbid neuropsychiatric disorders such as depression and epilepsy is important to improving the QOL for autistic individuals with or without accompanying intellectual disability.

PREVALENCE OF EPILEPSY IN AUTISM SPECTRUM DISORDER WITHOUT INTELLECTUAL DISABILITY

Previous studies have reported a relatively lower prevalence of epilepsy in high-functioning ASD compared to that in ASD with intellectual disability, but the prevalence is still greater than that found in the general population. A large cohort study in the U.K. identified epilepsy in 8.7% (2/23) of children with Asperger syndrome compared to 16.7% (5/30) of children with childhood autism.[6] A large population-based survey in Finland found epilepsy, defined according to the International League Against Epilepsy (ILAE), in 18.2% (34/187) of children with autistic disorder and 12.1% (11/91) of those with IQ >70.[7] However, no firm statistical conclusion can be drawn about the type of epilepsy from these data. A clinical

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study of 100 boys with Asperger syndrome made a conservative comorbidy estimate of epilepsy in 4 patients.[8] Another clinical study comparing 26 patients with Asperger syndrome and 16 patients with high-functioning autism found no significant differences between the groups in electroencephalogram abnormalities (8.7% vs 13.3%), epilepsy (7.7% vs 6.3%) or clinical variables.[9]

Recently, we conducted a small-scale study in the west of Tokyo to determine the comorbid neuropsychiatric disorders associated with high-functioning ASD (HFASD).[10] The target population was primary school children aged 6-12 years in mainstream classes (n=1,374), of which 775 participants were screened using teacher-report autism questionnaires. Following semi-structured diagnostic interviews with all screen-positives and randomly selected screen negatives, 7 children were identified as having definite ASD and 3 as having broader ASD. None had intellectual disability. One or more diagnoses according to the Text revision of the Diagnostic and Statistical Manual of Mental Disorders, the fourth edition (DSM-IV-TR) was found in 72% of children with definite HFASD and 100% of children with broader ASD, findings consistent with those of the UK study.[1] The distribution pattern of comorbid disorders is also similar; anxiety or phobic disorders and oppositional or conduct disorders being the most common, with a prevalence of up to 40%. Most of these children were undiagnosed and had received no professional health interventions in terms of these comorbid disorders. Epilepsy was found in one boy in the HFASD sample (1/7, 14.3%). He was diagnosed as having complex partial seizure upon his first seizure at age 4 and has been treated using valproic acid. He is currently seizure free but has attention problems. In addition, two girls in our sample (one with Asperger syndrome, one with broader ASD) had repeated generalized seizures over the last 1-3 years, although they were not diagnosed with epilepsy. Since some individuals with ASD are still at a risk of developing epilepsy after puberty, the rate of 14.3% should not be overestimated. Our sample was small, however, the results emphasize that there does seem to be a high rate of children who develop epilepsy in autistic population without intellectual disability.

Many issues regarding the association between epilepsy and HFASD remain unanswered. Pediatric neurologists may want to know whether the epilepsy associated with HFASD is the same as that associated with ASD plus intellectual disability; or from another viewpoint, child psychiatrists may want to know how the autistic profile associated with epilepsy in HFASD is different from that without epilepsy.

CONCUSIONS

Recently, the special health needs of children with HFASD have been recognized. The prevalence of epilepsy is much higher in children with HFASD than it is in the general population. Children with HFASD are likely to have additional psychiatric symptoms such as anxiety and attention-deficit/hyperactivity disorder, but such health problems are often undiagnosed and untreated. Comprehensive neuropsychiatric evaluations of children with HFASD or children with epilepsy will lead to early identification of treatable health problems and the provision of appropriate treatment. Some behavioral problems in ASD can be improved with antiepileptic drugs.

Given that there are approximately 2-3% of children having ASD, and 10% of children with subthreshold autistic traits[11], an approach using quantitatively measured autistic traits may be also helpful to explore the association between epilepsy and autism.

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